PHYSIOLOGYNEWS
spring 2003 | number 50

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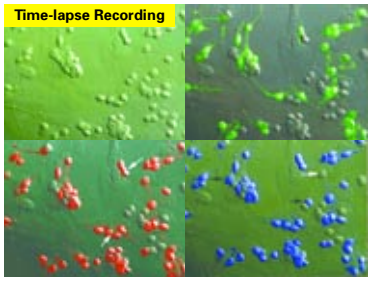

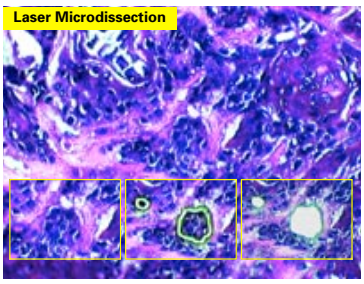

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Cover image

Phantoms in the machine? A visual reconstruction of figure 2 in Christof Schwiening's article *pH phantoms – a physiological phenomenon?* on p17.

PHYSIOLOGYNEWS

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Action Points

Affiliate Travel Grant Scheme:
The deadlines for receipt of applications during 2003 are the last day of March, May, July, September and November.

BSc Intercalated Bursaries:
The main deadline for receipt of applications is 30 June, 2003 (~10 awards), with a second deadline of 30 November, 2003 (~3 awards) for institutions where projects are not decided until the course has begun.

Membership applications:
The deadlines for the receipt of Full Membership application forms during 2003 are the last day of March, June, September and December.

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

Forthcoming Scientific Meetings:

Dublin (8 – 10 July, 2003)
Abstract submission period 7 – 16 April, 2003

Manchester (10 – 12 September, 2003)
Joint meeting with the British Pharmacological Society
Abstract submission period 2 – 11 June, 2003

Cambridge (17 – 19 December, 2003)
Abstract submission period 15 – 24 September, 2003

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

Physiology News:
Letters and articles and all other contributions for inclusion in the Summer issue, No. 51, should reach the Publications Office by 12 March, 2003 at the latest.

Physiology News Online:

Physiology News is now available on our website www.physoc.org

Guidlines for contributors

These guidelines are intended to assist authors in writing their contributions and to reduce the subsequent editing process.

oup of Physiology News
are that all articles are written in
inalistic style so that they 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 author's 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 2,000 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 errors during retyping. It is helpful to give brief details of the computer, operating system and software package(s) used.

Submission deadlines
Please contact the Executive Editor in the Publications Office (see Contents page for details) for submission deadlines. Late submissions will be deferred to a subsequent issue.

Illustrations/author's photographs
Authors are encouraged to submit diagrams, drawings, photographs or other artwork to illustrate their articles or, if they cannot provide these themselves, to suggest appropriate illustrations. A photograph of the author(s) should also accompany submissions. Photographs may be colour or black and white, prints or transparencies or tiff files with a minimum resolution of 300 dpi. Electronic colour figures should be in CMYK mode.

References
Authors are requested to keep the number of references to a minimum – preferably no more than two or three. Please cite all references in the style of *The Journal of Physiology* (see Instructions to Authors 2003, www.jphysiol.org)

Suggestions for articles
Suggestions for future articles are welcome. Please contact the Executive Editor or a member of the Editorial Group of *Physiology News* (see Contents page for details).

As 2003 dawned, universities and their financial problems at last featured prominently on the government's agenda, mainly due to the debate about how to fund increased student numbers. The option of top-up fees has provoked the most heated exchanges, particularly the suggestion that an elite group of universities – roughly speaking, the so-called Russell Group – would use a free market in fees to break away and form a kind of 'Premier League'.

By the time this issue appears we should know the government's plan for UK higher education. But the fact that the statement is awaited with such anticipation – and trepidation – serves to illustrate, yet again, that universities in the UK primarily have one customer, the government. Students are also customers up to a certain point – witness the redundancies in several university departments of engineering now that 6th formers increasingly reject engineering and other 'hard science' degrees – but the primary force shaping the future of the UK universities remains government policy.

As a result of this, the last 20 years have seen UK universities change hugely at the behest of successive government initiatives and the ever-increasing accompanying burden of audit and rankings. Student numbers have expanded hugely, with no real increase in funding. Class sizes have risen, whether in lectures or tutorials, as student-staff ratios have doubled. The way we teach has also been reshaped by the demands of exercises like TQA, which have imposed a huge burden of bureaucracy on the system. As a consequence, the issue of what is academically best in university teaching has to fight with the demands of the balance sheet – how can we teach the most students for the least money with the least number of discipline-specific specialist staff?

A similar picture pertains in research. Turnover – in the shape of grant funding, easily countable in thousands of pounds per year per academic – is king. Bureaucracy has flowered, with universities creating Graduate Programmes and Graduate Schools, often virtual, with a whole paraphernalia of courses in generic skills, personal records of achievement, advisors, in-course assessment and so forth. Research policy overall is driven by the need for RAE rankings, as universities constantly reorganise, amalgamate, and abolish departments in order to maximise RAE scores. This is not to criticise the RAE panels, who do a thankless job with professionalism and integrity. The problem is the use that universities make of the ratings.

Of course, not all the developments have been bad. Graduate students do need generic skills, and practice at presenting data, and there should be some check on their progress. New ways of teaching, such as problem-based learning, have been brought in, particularly in medical courses. And we should periodically re-assess what the best way is to organise a department. But how many of the changes of the last two decades do we really believe were academically driven, or justified?

And there is a more systemic danger than simply dancing to the government's tune. This is the creeping takeover of managerialism in the upper echelons of British universities. If the main point of the system is to maximize financial turnover, and to score well in government league tables, then the people in charge of the system will inevitably become managers whose prime job is to ensure that these 'outcomes' are delivered.

At one level, this is manifested in increased control of universities' academic priorities by non-academic, or at best ex-academic, administrators. This has become far more common, since management by statistics and balance sheet obviates the need for academic judgement. Take, for instance, a department that scores unexpectedly poorly in the RAE. Any manager can see that this demonstrates clear underperformance, with the solution typically being to remove the department from the next RAE by dismantling it or merging it. This reasoning requires precisely no academic judgement in-house, since the academic verdict has already been delivered by the RAE panel.

There is also the more insidious danger that Heads of department and other senior academics are themselves transformed into balance-sheet managers. This danger is arguably greater as departments get larger by successive mergers. Few departments remain where the Head is responsible for 10 people whose work he or she knows well. Faced with managing 40 or more staff, many of whom are little known to them, the easy solution for a Head is to reach for the spreadsheets and the tick-list. Alternatively, many universities have instituted formal appraisal systems – more bureaucracy.

All this bureaucratic oversight and reorganisational drive clearly looks good to someone – the Department of Education? The government? But does it actually improve university teaching and research, or scholarship? After all, it is quality teaching and research that is the true mission of universities, not good scores in league tables. This is true even if the league table is one that explicitly grades research output, like the RAE. In any large organisation it is very tempting to substitute an external verdict for one's own judgement, as the UK's burgeoning consultancy industry demonstrates. But who is best qualified to assess how well a university department is doing? Its members? Its Head? Or an external panel judging a paper submission?

Whatever our view, we can probably all agree that the answer is not 'a university administrator'.

So senior academic staff in universities, including scientists, face a major challenge as 2003 starts. If – hopefully when – the government delivers increased funding to the universities, they have to try and make sure that extra money that reaches the system is spent to improve teaching and research, not targeted *a priori* on measures to improve balance sheets, performance statistics and league table placings. They have to behave like academics, not administrators, and fight their corner for academic priorities.

Good luck to them. They will need it.

Austin Elliott

Welcome to the University of Newcastle

Barry Argent

Physiology is alive and well in Newcastle! Many of you will have heard that a major restructuring of the University of Newcastle upon Tyne has taken place over the past couple of years. On 'big bang' day, 1 August 2002, the number of faculties was reduced from seven to three by a process of amalgamation and more than 70 Departments became 28 Schools. The purpose of these changes is to increase the efficiency of the University's operations and to create some financial headroom so that we can invest for the future. The restructuring is core to our declared aim of making Newcastle one of the top 10 research universities in the UK.

As part of the restructuring, the three Biomedical Science departments, including Physiological Sciences, were amalgamated into a new School of Cell & Molecular Biosciences, totalling close to 50 academics. The Epithelial Research Group (Adrian Allen, Barry Argent, Colin Brown, Dianne Ford, Mike Gray, Judith Hall, Barry Hirst, Jeff Pearson, Nick Simmons, David Thwaites, Andi Werner) and the Cell Signalling Research Group (Tim Cheek, Keith Jones, Alex McDougall, Trevor Jackson, Michael Whitaker), whose laboratories have just undergone a major refurbishment funded by a £750K grant from the Wellcome Trust, are both located within this new School. However, our Sensory Systems Group (Anya Hurlbert, Gary Green, Adrian Rees) have moved on to pastures new in either the School of Neurology, Neurobiology and Psychiatry or the School of Biology. Regrettably, David Sanders decided to leave the University during the restructuring while Jim Reed has been forced to retire through ill health. Their contributions are sorely missed. Of course, there was a tinge of sadness that such a successful unit as the Department of Physiological Sciences, which had scored 5A in both of the last RAEs and 24/24 in the QAA for its Degree Programme, should have been disbanded. However, when the basket gets shaken up it is inevitable that some of the golden eggs will get broken. We take comfort from the fact that the aim of the restructuring process is to make the whole University work as well as the Department of Physiological Sciences did in the past!

Looking to the future the School of Cell & Molecular Biosciences, which is made up of units graded 5 and 5* in the 2001 RAE, is one of the strongest research groupings in the University and has a political voice to match. The School has a post-genomic perspective and much of the research activity is directed to the analysis of the function of gene products, i.e. functional genomics. The practical benefits of being in a larger unit are already becoming apparent in terms of increases in the efficiency of teaching and administration. On the research front we look forward to a bright future with the opportunities for interaction and collaborative research with our new colleagues who have expertise in biochemistry, genetics, molecular biology and microbiology being much enhanced.

This Newcastle meeting is a designated meeting on Epithelia and Membrane Transport. Newcastle has a long history of excellence in epithelial research. As well as the 11 academics listed above there are three research fellows, 13 post-doctoral workers and 21 postgraduate students in the Epithelial Research Group. Our aim is to understand epithelial transport

Below The University Quadrangle

Bottom The University Arches

processes at the cellular and molecular level, and how their function and dysfunction relates to the whole organism *in vivo*. Over the past 10 years we have assembled a group of active researchers who can deploy a variety of methodologies ranging from genomics and proteomics, sophisticated electrophysiological techniques through to whole animal physiology, including transgenic mouse models. Our strategy for future development is to capitalise on our collaborative strengths, our shared expertise, and our unique concentration of techniques (from molecular through cellular and tissue to whole organism) to provide added value to our research. We address important physiological and pathophysiological problems related to epithelia, with particular focus in the following areas:

i) understanding the molecular and cellular mechanisms underlying coordinated responses of the intestinal epithelium to changes in diet, with an emphasis on transporter genes involved in protein-nitrogen assimilation and in zinc homeostasis;

ii) understanding the molecular and cellular regulation of chloride channels in pancreatic and renal function and their dysfunction in cystic fibrosis and renal disease;

iii) how individual gene products are integrated to produce functional mucus secretions;

iv) how an inventory of drug transporters already identified at the molecular level act to optimise drug delivery, disposition and excretion.

We have an active seminar programme (partly funded by the Society) and hold an annual two-day research conference. Our research funding comes from the MRC, BBSRC and the major research charities, and there are longstanding industrial links in areas such as mucus secretions and their interactions (Reckitt Benckhiser), and intestinal and renal drug transport (AstraZeneca, Glaxo-Wellcome/SmithKline Beecham). Current active grants total almost £2m and include several major awards in excess of £300k from the research councils.

The centrepieces of the April meeting will be two symposia, which reflect the interests of the Newcastle Epithelial Research Group. *Transport & Signalling: From Gut to Brain and Back Again* (organised by David Thwaites and Andi Werner) covers signalling in the gut, the transport of nucleosides, drugs and amino acids, and neurotransmitter transport into synaptic vesicles. *Epithelial Electrolyte Transport: Multi-Tasking & Hidden Talents* (organised by David Thwaites and Mike Gray) covers ion channels, bicarbonate transport by SLC26 family transporters and its relationship to cystic fibrosis, and the latest on the regulation of NHE3 by NHERF and the role of NHE3 in congenital diarrhoea. The organisers have assembled an impressive panel of international speakers and these symposia promise to be memorable occasions.

In addition, we are privileged to host a number of the Society's Lectures during the meeting including the A.A. Harper Lecture (Michael Schemann, Freising-Weihenstephan, Germany), the Biller Prize Lecture (Louise Robson, Sheffield, UK), the GI Tract Designated

Entrance to the Medical School

Epithelial Research Group and guest speakers at our 2002 conference. Newcastle symposia organisers are in the back row: Andi Werner (fourth from left), Mike Gray (10th from left) and David Thwaites (11th from left)

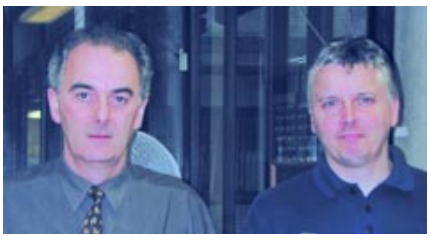
Top Barry Argent, Peter Hegyi (fellow) and Bernard Verdon (post-doc)

Centre Barry Hirst, Georgina Carr (PhD student) and Maxine Geggie (technician)

Above Amy Windass (PhD student) and Colin Brown

Below Andi Werner, Keziah Preston-Fayers (PhD student) and Chris Graham (post-doc)

Bottom Ralph Bridgett and Bill Saint who run the School workshop



Lecture (Gary Shull, Cincinnati, USA), the Epithelia & Membrane Transport Designated Lecture (Shmuel Muallem, Dallas, USA), and the Renal Physiology Designated Lecture (Edward Weinman, Baltimore, USA). A meeting not to be missed if you are interested in Epithelia and Membrane Transport!

Now that the Department of Physiological Sciences has gone, the main focus for the discipline of physiology in Newcastle has become our Physiological Sciences Degree Programme. Despite our dispersal to different Schools we remain committed to the provision of high quality teaching in physiology (QAA 24), medicine (QAA 24) and dentistry (QAA 23). We also contribute to other degree programmes within the School of Cell & Molecular Biosciences (all QAA 24), including our new Biomedical Sciences Degree. Recruitment into the popular Physiological Sciences Degree Programme is being maintained and the growing reputation of Newcastle University means that the quality of our entrants is improving. Currently we have a final year of 45 students, made up of 40 physiologists and five intercalating medical students. Perhaps the major benefit to arise so far from the merger of the old Biomedical Sciences Departments is improved efficiency of our teaching. Indeed, teaching in the first half of all our three-year degree programmes, to the 200 plus students within the School, is now common. While this has inevitably resulted in a reduction in the physiology content for students studying the subject at single honours, this is compensated for by their wider exposure to the molecular biology and immunology that underpins modern physiology. Moreover, this restructured teaching has had the added benefit of increasing the exposure of students on other degree programmes, such as biochemistry, genetics, microbiology and immunology, to more advanced physiology teaching. For the last 18 months of their study, the students divide up into the smaller degree specific groupings. Physiologists in Newcastle also intend to maintain their contribution to the wider promotion of physiology, in particular by active participation in the varied functions of the Physiological Society. Currently, David Thwaites is the convenor of the GI Special Interest Group, while Mike Gray is on the Editorial Board of *Experimental Physiology*.

As well as the organisational restructuring of the University, those of you who have not visited Newcastle recently will notice that a physical restructuring has also been taking place in both the University and the City. The architecturally uninspiring entrance to the Medical School has been converted into a space age structure by construction of a new 400 seat lecture theatre and a new research building, the Henry Wellcome Building, which houses our psychologists. The City itself has also changed following massive investment by both

Top Medical student lecture in the new, 400 seat, David Shaw lecture theatre

Above A medical physiology practical

Above The Sage Gateshead Music Centre (currently under construction) with the Tyne Bridge in the background

Below Angel of the North

Newcastle and Gateshead Councils. The most spectacular results of this investment are the Gateshead Millennium Bridge, the Sage Gateshead (a magnificent music centre) and the Baltic (a modern art gallery) where we shall have the meeting dinner. And, of course, Antony Gormley's masterpiece, Angel of the North, stands sentinel on our southern approaches. Newcastle has always been famous for its nightlife (as some of you will know from previous Society Meetings!), but we are now becoming a major cultural centre as well. These recent developments and much more underpin the Newcastle-Gateshead bid to become the European Capital of Culture in 2008. But fear not, in the midst of this cultural onslaught we have not forgotten our roots and we still boast about our excellent beer and our above average football team! Geordies the world over have a reputation for hospitality and we extend a warm welcome to the Physiological Society.

Barry Argent
School of Cell and Molecular Biosciences
University of Newcastle upon Tyne

Memories of Leeds…

Right The Worsley Building

Far right Stewart Sage, Chair of the Editorial Board of *The Journal of Physiology*

Below Melanie Rees, Meetings Secretary's Assistant and Chris Fry, Chairman of the Executive Committee and, *below right*, Mark Dunne, Meetings Secretary, acknowledge the Society's appreciation as they come to the end of their terms of office

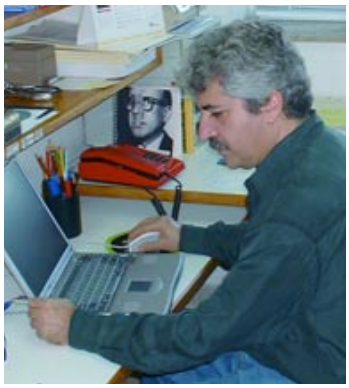
Right Ann Silver (left) and Melanie Rees

Below Staff from the Department of Physiology in Leeds whose efforts helped to ensure a successful meeting

Bottom left John Sulston (left) and Colin Blakemore

Bottom right Melanie Rees, Bill Winlow and new Meetings Secretary Bridget Lumb

Recollections from Tenerife 2003: a truly first joint meeting



Rafael Alonso, Congress Chairman

In 1996 a representative group of British physiologists travelled to Salamanca to actively participate in the XXVII Annual Congress of the Spanish Society of Physiological Sciences (SECF). Two years later, a substantial delegation of Spanish physiologists held their XXIX Congress in Liverpool coinciding with a British meeting. The agreeable and stimulating experience on both these occasions gave rise to the idea of organising a truly joint meeting. To meet the British requirement of a 'sunny place', Tenerife was chosen and the University of La Laguna designated the role of the host institution. Finally, the first joint meeting between the British and the Spanish societies took place in Puerto de la Cruz from February 13 to 17. On behalf of the Local Organising Committee, I would like to thank the active participation of all attendants and to express my gratitude to those British friends who contributed with us in the organisation of the scientific programme. As it has been a successful and enjoyable experience for everybody, I believe that it is time to start organising the next one.

A view of the north coast of Tenerife and the Teide volcano

About 400 participants, including 67 invited speakers, with roughly the same number from each society attended the meeting. It included seven mini-symposia on a balanced selection of subjects, five plenary lectures, three meet-the-expert sessions, and three discussion forums. In addition, two satellite courses for pregraduate and graduate students, and a satellite debate also took place. A total of 305 abstracts were accepted. Some of them were presented in previously designated symposia, and the rest were presented either as oral communications or posters. Their distribution into different subjects is shown in the Table. Further information can be obtained at http://www.seccff.org/congresoXXXII/index.php.

Fifty years of Spanish physiology: Negrin's legacy

When our British colleagues read Juan Negrín's name in the preliminary programme, they asked me about who he was. As not even many young Spanish physiologists know Negrín's contribution to the development of Spanish science, a brief introduction would be worthwhile. Juan Negrín (1892-1956) is best known as the Prime Minister of the Spanish Government during the Civil War (1936-1939). However, he must be recognised as one of the founders of modern Spanish science (Tuñón de Lara *et al*, 1996). When he was 14 years old, Negrín moved to Germany and started his medical education in the University of Leipzig, in the *Physiologisches Institut* founded by Carl Ludwig in 1865. During this period Negrín worked under the instruction of Theodor von Brücke on the interactions between the endocrine and the nervous system, and the regulation of the vascular tone. In 1916, after gaining his doctoral degree, Negrín planned to join Walter Cannon's laboratory at Harvard University. However, he was forced to return to Spain to lead the Laboratory of General Physiology that had been created in Madrid as the brainchild of Santiago Ramón y Cajal. Only a few years later he became Professor of Physiology at the University of Madrid. He

then led an important project aimed to the development of experimental physiology and the creation of a number of active research groups in Spain.

Negrín's involvement in the organisational and financial problems of science in Spain at that time stimulated him to become involved in social issues. In 1934 he gave up his academic activities and totally dedicated his time to politics. The outbreak of the Spanish Civil War in 1936 and his exile in 1939 marked the tragic endpoint of this story.

To commemorate the 50th anniversary of its first meeting, in conjunction with the Juan Negrín Foundation, the SECF has created the Juan Negrín Prize to honour an outstanding career in physiology. On this first occasion it has been a pleasure to award it to Erwin Neher.

Physiology in Spain

The SECF was created in 1952 and had its first annual meeting a year later in Madrid. Since then, it has not only been the source of all home-grown generations of Spanish physiologists, but also the origin of several scientific societies on a broad scope of fields, such as biochemistry, cellular and molecular biology, endocrinology, neuroscience, and pharmacology. This scientific divergence has probably had an undesirable atomising effect. Thus, while some of these disciplines have developed with the impulse of new and fashionable experimental technology, physiology has somehow remained within the academic boundaries of teaching. In the last few years, however, the idea of reinforcing the core role of physiology to understand the underlying principles of the functioning of living beings – *the logic of life* (Boyd & Noble, 1993) – is clearly emerging.

Nevertheless, Spanish physiologists –either engaged with the SECF or with any of its derived societies— have extended into a wide number of departments. Most of them work in universities and in research institutes, and very few really do work in industry. A large number of Spanish physiologists mainly belong to the fields of endocrinology and neuroscience, with an important focus on the cellular and molecular approaches. These trends are particularly important in several Spanish regions, where interdisciplinary research institutes have recently been, or are in the process of being, developed.

Physiology at La Laguna

Host Departments and teaching tasks

The host group that organised this meeting belongs to the Departments of Animal Biology and Physiology, together being comprised of about 25 permanent academic staff. Both are situated in the Faculty of Biological Sciences and the Medical School, respectively. Even though the buildings are not so old and there is enough space for laboratories, the structure has deteriorated considerably and the need for modern facilities is now extremely urgent. Because of this, several members of these Departments, together with others from the Departments of Anatomy, Biochemistry and Molecular Biology, Cell Biology, and Medicine are working in the creation of a new research institute targeted to basic and applied biomedical sciences.

The two host Departments teach physiology to medical (current intake 125), nursery (75), physiotherapy (70), pharmacy (200), and biology (150) students. Most members of the staff are also engaged in two doctoral programmes, one on Life Sciences and the other on Basic Biomedical Research, and another part also participate in a Neuroscience programme.

Top Lago Martianez at Puerto de la Cruz

Above A typical old corner of Puerto de la Cruz

Research activities

Physiology in Tenerife could be considered as a relatively young research field, since it started in both the Faculty of Biological Sciences and the Medical School in the mid 70s. However, after three decades of active research several physiology teams are currently rated as being in the highest positions in the University of La Laguna. The main research lines in the host Departments are related to neuroscience, marine

The local organising committee.
From left to right: Mario Díaz, Raquel Marín, Guadalberto Hernández, and Rafael Alonso

science, and reproductive neuroendocrinology. In addition, members engaged in active research are integrated into more interdisciplinary groups with people from other Departments and clinicians working on different aspects of developmental, metabolic or neurological diseases. Presently, the different research teams can be grouped into the following areas:

Neuroendocrinology and oestrogen-mediated neuroprotection
Reproductive physiology has been a permanent research area in La Laguna. While whole animal studies were the current model to investigate the reproductive system in the past, more cellular and molecular approaches are now being used to characterise the interactions between peripheral hormones and central neurons. Thus, Rafael Alonso, Guadalberto Hernández, and Pedro Abreu, in collaboration with the industry, are characterising the mechanisms and signalling pathways by which oestrogens and selective oestrogen receptor modulators interact with the female rat gonadal axis at both hypothalamic and pituitary levels. Manuel Mas is extending classical studies of erectile responses in rats with spinal lesions with the dynamics of nitric oxide release at central and peripheral levels. In addition, together with andrologists, he is evaluating the evolution of sexual function in human subjects with spinal lesions and the response to erectogenic agents. Carmen González is working on neuroimmunoendocrine interactions and the role of local agents in the regulation of pituitary secretions. A particular area of recent interest is the characterisation of novel mechanisms involved in oestrogen signalling both in endocrine and neuronal cells. An integrated team composed of Rafael Alonso, Mario Díaz, Raquel Marín, Borja Guerra, and Araceli Morales is using neuronal cell lines to analyse the interactions between oestrogen hormones and their potential neuronal targets. One of the main aims of this research line is the identification of neuroprotective effects of oestrogens and the characterisation of the specific receptors and the underlying action mechanisms.

Ion channels, membrane lipids and cellular responses to apoptotic agents
Mario Díaz runs a group currently working on the mechanisms by which oestrogen and antioestrogen compounds modulate several types of ion channels in excitable cells. By using electrophysiological, biochemical and imaging techniques they are studying how oestrogens modulate contractile activity of mouse intestinal smooth muscle. These effects are apparently due to direct interactions of steroid molecules with L-type calcium and $BK_{(Ca)}$ channels. In addition, Mario Díaz together with Covadonga Rodríguez, Tomás Gómez and Eduardo Almansa are studying the role of membrane lipid composition on the function of several intrinsic membrane proteins, including ion channels and membrane transporters. They are also working together with a group led by Antonio Lorenzo on the identification of the physiological basis for the essentiality of certain fatty acids on fish growth and development.

Temporal dynamics encoding information in the nervous system
Julián González, Luis de Vera, and Ernesto Pereda are using linear and non-linear technical approaches to analyse temporal series from brain and heart electrical activity, both in humans and experimental animals. A particular area of interest is the analysis of the non-linear relationships between cardiorespiratory and brain activities during awake and sleep stages, as well as during some noxious situations such as sudden death in the newborn. Furthermore, by using these mathematical approaches, they are also characterising the interdependencies and intrinsic variability on brain-derived electrical signals while performing specific perceptive tasks. By using similar methodological and conceptual approaches, Juan V. Sánchez-Andrés is analysing the temporal signals which encode relevant information in excitable cells, such as the pancreatic

beta cell and the pyramidal neurons of the hippocampus. The general hypothesis underlying this research line is that the characterisation of the signalling mechanisms participating in synchronous cellular activity may help to understand the pathophysiology of some diseases involving alterations in the pattern of excitability.

Neuronal vulnerability and neuroprotection

Manuel Rodríguez and Tomás González (from the Anatomy Department) are trying to characterise the mechanisms underlying neuronal degeneration of the dopaminergic system in Parkinson's disease. During the last few years they have developed some useful animal models of Parkinson's disease which allow them to carry out direct testing of the working hypothesis. Thus, the role of intrinsic and extrinsic factors affecting dopaminergic synapses are being analysed by a combination of electrophysiological, behavioural, and morphological methods. In addition, in collaboration with a team of neurologists they are working on the design of different pharmacological and surgical strategies in the prevention and treatment of Parkinson's disease.

Neurochemical monitoring and neuroimaging

José L. González-Mora works in an interdisciplinary group mainly involved in the development of new techniques aimed at real-time monitoring of neuroactive molecules in experimental animals. In addition, in collaboration with other Departments of the University of La Laguna and members of the Institute of Astrophysics, they are developing some devices to ameliorate sensorial deficiencies in people suffering from neurological diseases. In this respect, a virtual acoustic space has recently been designed to allow perception in blind people.

Top Mario Díaz at the confocal imaging system

Centre Guadalberto Hernández trying to get blood from the hypophyseal portal vessels of the rat

Bottom Raquel Marín in the culture room

CATEGORIES	ORAL	POSTER	TOTAL
Autonomic function		3	3
Blood-brain barrier		3	3
Cardiovascular & respiratory control	10	12	22
Cell signalling	10	17	27
Cellular neurophysiology	18	16	34
Comparative physiology		17	17
Development & plasticity		4	4
Epithelial & membrane transport	10	23	33
Gastrointestinal tract		13	13
Heart & cardiac muscle		6	6
Integrative neurophysiology		9	9
Ion channels	7	14	21
Microvascular & endothelial physiology	8	2	10
Muscle contraction	8	6	14
Neuroendocrinology	8	14	22
Renal & respiratory physiology		9	9
Reproductive physiology		7	7
Sensorimotor physiology	10	7	17
Smooth muscle	10	13	23
Teaching		7	7
TOTAL	99	202	301

Table Subject distribution of oral communications and posters

As mentioned above, the need for interdisciplinary approaches has induced us to work towards a highly integrated research project. About 30 staff members and an equivalent number of fellows are now in the process of establishing the Institute of Biomedical Technologies of Tenerife (ITB). By incorporating people from a broad scope of disciplines, we are developing a strategic plan aimed at the search for technological solutions to those biomedical problems derived from the interaction between ageing and environmental injuries. Thus, the general framework of the ITB will be that of biodegeneration, with a particular emphasis on their neural aspects. We are confident that next time we organise a meeting it will be hosted in the new facilities of the ITB.

Rafael Alonso

Chairman of the Joint Meeting at Tenerife
Chairman Elect of The Spanish Society of Physiological Sciences

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Limbs in limbo: the problem of targeting

Keri Lee Page focuses on the problems inherent in an action as apparently simple as scratching an itch

Keri Lee Page

If you had some food on your cheek, you'd probably wipe it away and if you had an itch you'd most likely scratch it. We do these things instinctively, without a second thought. But directing the trajectory of a moving limb so that it meets up with a target in space is a complex computational task. For targeting to be successful, a human or animal must translate a set of spatial co-ordinates – the target position, encoded by exteroceptive sensory inputs – into a co-ordinated temporal activation of motor neurones, which is ultimately responsible for the final movement. There is also the problem of kinematic redundancy. This is when the same target can be reached by an infinite number of different motor patterns, requiring that targeting networks must have some criteria for 'selecting' the most appropriate motor action. Nevertheless most animals, from cockroaches to cats and cephalopod molluscs, can do it all as well as we can (Figure 1)

Much of what we currently know about vertebrate limb targeting comes from studies of episodic reaching in primates and rhythmic scratching in cats. In the early 1900s Sherrington demonstrated that chemical or tactile stimulation of the body surface in cats and dogs can elicit rhythmic directed scratching movements of a hindleg. Many animals have scratch reflexes that have several forms, depending on the location of the stimulus site. This is well known in the frog and turtle but is not the case with cats. In turtles three distinct reflexes exist (rostral, caudal and pocket scratches) with blends of each occurring at stimulus transition sites.

Invertebrates do remarkably well at the same tasks. Locusts clean their antennae with an antennal cleaning groove on the tarsus. This groove is brought into contact with an antenna by a stereotyped three-step motor sequence involving both the head and the forelegs (O'Shea, 1970). Targeting can also play a role in other contexts: in stick insects, for example walking and climbing use targeting. The middle and hind legs are targeted to step down directly behind the tarsus of the anterior leg, no matter how the position of this limb is perturbed (Cruse, 1979).

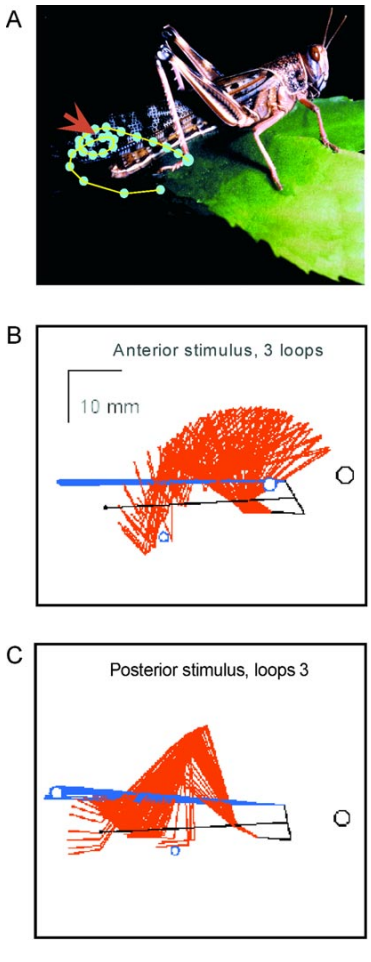


Figure 1 A Photograph of *Schistocerca gregaria* with trajectory for a posterior scratch superimposed. **B** Stick diagram of leg movements during a scratch directed towards an anterior stimulus site. **C** Stick diagram for a posterior stimulus site

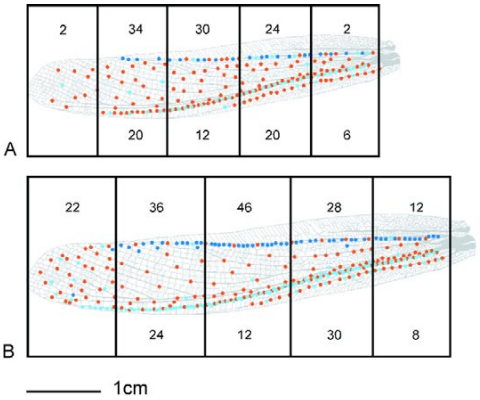


Figure 2 Wing hair distributions for male (A) and female (B) wings. Coloured dots correspond to three hair length categories. Wings were divided into 9 bins that split the surface area into 5 anterior to posterior segments and into dorsal and ventral halves. The wing tip was treated as a single bin. Numbers are the mean probability of a scratch being elicited by stimuli in the corresponding bin

Targeted scratching in locusts

My research in Dr T Matheson's lab in the University of Cambridge Zoology Department focuses on targeted scratching in locusts as a model system, and addresses the problems inherent in an action as apparently simple as scratching an itch on a wing (Matheson, 1997).

Tactile stimulation along the length of the wings elicits different targeting movements of the hindleg that scratch the stimulus site (Figure 1). For this targeting to be successful, the stimulus position first has to be encoded. This is usually done by way of a somatotopic map of afferent neurones from the mechanosensory hairs on the body surface. These arborisations synapse

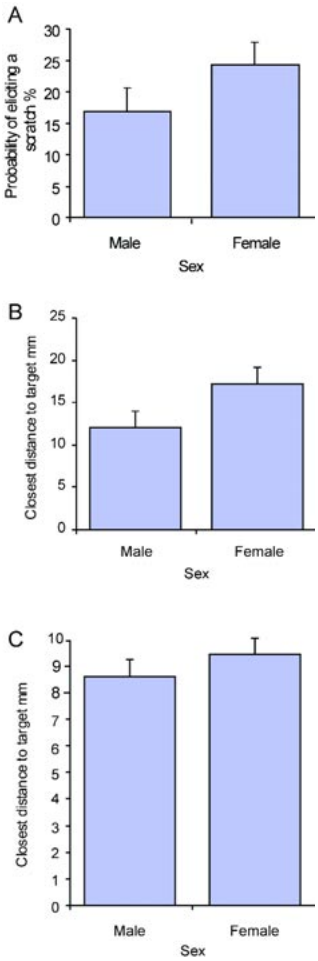


Figure 3 A Scratch probability in males versus females. **B,C** Accuracy in terms of closest distance to target in both males and females for an anterior stimulus site (B) and a posterior stimulus site (C)

onto interneurones at the second level of the map in such a way that each interneurone represents a distinct area of the body surface called a receptive field.

Maps have been described for the mechanoreceptors on locust legs, but have not yet been described for the wing surface. As a first step, a count and distribution analysis of the wing hairs has been conducted. This reveals a characteristic spread of hairs along the main veins of the forewing. Where hairs are more densely distributed, the likelihood of eliciting a scratch with tactile stimulation is increased, resulting in probability differentials across the wing surface (Figure 2).

Surprisingly, there is a significant difference in the number of hairs between males and females – over and above that which would be expected due to the females' larger body size. The larger number of hairs in females correlates with an overall increased probability of scratching for a given stimulus. Despite the larger number of mechanoreceptors on female wings, the females do not target with greater accuracy than males (Figure 3). This may indicate that increased sensory input causes greater levels of excitation in the central networks of females but that receptive fields are no more finely tuned by the presence of additional hairs. In other words, the hairs may synapse onto the same number of interneurones in both sexes.

The position of a limb is known by a 'position sense' arising mainly from proprioceptors within the joints. In locust scratching, hind leg position is primarily described by feedback from the femoral chordotonal organ. This receptor spans the femur-tibia joint and monitors the static position of the limb as well as direction, velocity and acceleration of any tibial movement (Figure 4).

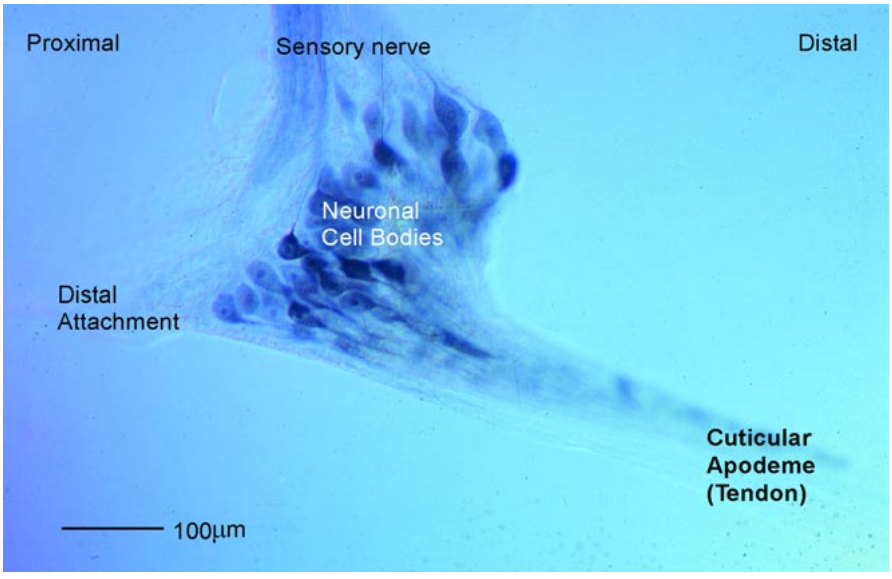
As the tibia is moved, the cuticular apodeme (tendon) stretches the body of the chordotonal organ accordingly, resulting in stimulation of the receptors. The receptors project into the central nervous system where their patterns of branching correlate with each response type. Identified local and ascending, intersegmental interneurones have been proposed as candidate neurones for the convergence of spatial information from the wing and positional information from the chordotonal organ of the hind leg. Interneurones with bilateral arborisations may be responsible for the distribution of spatial information that enables simultaneous targeting of the contralateral leg. Limbs in other body segments may also receive information from ascending interneurones, enabling interganglionic co-ordination (Matheson, 2002). This produces reflexes in the middle and forelegs which contribute to increased body stability while the hind leg is busy scratching.

Interneurones involved in collation must be integral to the network responsible for computing the final motor pattern. Non-spiking interneurones in the metathoraic ganglion which are known to control sets of leg motor neurones, are likely to be responsible for much of the interjoint coordination that is characteristic of a scratch.

Are central pattern generators involved in targeted scratching?

In locusts, scratches are incredibly variable. This suggests two possible scenarios: firstly there may be many

Figure 4 Light micrograph of the locust hindleg femoral chordotonal organ showing the somata of the approximately 55 largest neurones that respond to movements of the femur-tibia joint



distinct receptive fields that elicit discrete motor patterns which differ along the anterior to posterior axis. Alternatively, there may be a single motor pattern that is modulated in a continuously variable way by somatosensory feedback from the wing hairs. Recent work in the lab suggests that the latter explanation is correct. Descriptions of the circuitry that might underlie these alternatives, and the evidence that supports them is convoluted.

The existence of central pattern generators (CPGs) is supported heavily by studies of vertebrate targeting. The scratch reflex can be elicited in the decerebrate cat and spinal turtle (Robertson *et al* 1985). Some studies on locust scratching indicate discrete motor patterns for different stimulus sites. This too suggests the existence of a set of distinct CPGs, being activated by specific inputs. These distinct patterns remain in a de-efferented and decerebrate animal (Berkowitz *et al* 1996). My work, however, indicates that interfering with proprioceptive feedback has a significant effect on the motor pattern's efficacy (Figure 5). Such findings would imply that feedback is used to fine-tune the outputs from CPGs. Moreover, other work in the lab suggests that for sites on a wing, a single CPG output exists, that is strongly modulated by somatotopic input encoding the stimulus site. An alternative view of motor pattern generation is therefore being considered at present: is a rhythmic CPG in the traditional sense actually present at all? An alternative is that a population-coding scheme amongst interneuones may produce both linear targeting and under some conditions, cyclical repeated movements. Such a notion might describe the generation of cyclic targeting movements without relying on the standard concept of an autonomous oscillating unit.

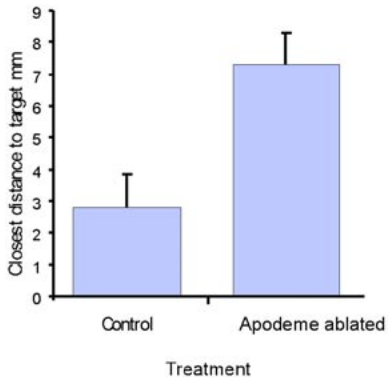


Figure 5 Ablating the chordotonal organ apodeme removes proprioceptive feedback and reduces targeting accuracy

In order for targeting to remain accurate, the networks must behave plastically with regard to external perturbations. For example, if a load is added to the hindleg of a scratching locust, feedback from the campaniform sensilla and femoral chordotonal organ allows compensation for the extra weight, so that accuracy is not reduced. In frogs too, loading does not affect the animal's ability to remove the stimulus. It will be interesting to see from our future experiments with locusts, how manipulating the proprioceptive signals from the chordotonal organ will affect targeting accuracy and whether the system is plastic enough to recalibrate the proprioceptive feedback over time, bringing the accuracy back into line.

Future implications of targeting studies

Targeting studies have wide ranging implications for technology and future research. The principal focus of vertebrate studies is to consider mapping in the spinal cord and also the role the motor cortex plays in the processes linking sensation and action. Mathematical models of these processes may eventually give rise to developments in robotic prosthetic-limb design. Invertebrate studies too, have important implications for robotics, since the invertebrate targeting paradigm should prove easier to model. Modelling of neural networks involved in the targeted stepping movements of stick insects has led to the development of WalkNet – an artificial neural network that controls six-legged walking (Cruse *et al*1998). WalkNet has since been proven successful by its implementation in Tarry, a six-legged robotic insect (Figure 6) Biomimetic robots like these not only have consequences for the future of autonomous robots but also for the study of targeting, as the robots themselves throw up new lines of enquiry in the real animals studied by neuroscientists.

Figure 6 Tarry 1 and 2. Developed and built by the Department of Engineering Mechanics at the University of Duisburg and tested with WalkNet at the Department of Cybernetics at the University of Bielefeld. Each model is approximately 40cm in length

… if you had an itch you'd most likely scratch it

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pH phantoms – a physiological phenomenon?

Recently Christof Schwiening's lab has shown that fast local pH shifts can occur in nerve cells. But now he is perplexed. The shifts seem to be large, even during modest amounts of electrical activity. Why has no one seen them before? Are they just phantoms? If they are real, are they important or not?

Christof Schwiening

pH and neuronal excitability

Only small changes in pH are required to produce marked alterations in neuronal excitability. It has been known for over 150 years that excessive carbon dioxide acts as a CNS depressant, whilst a lack of carbon dioxide induces hyperexcitability (see references in Somjen & Tombaugh, 1998). Indeed, you can test the effect yourself by first hyperventilating (which lowers carbon dioxide levels in the blood) and then by rebreathing air expired into a paper bag (which raises carbon dioxide levels). Over the past 50 years this link between CO_2, pH (see Box 1) and neuronal excitability has been the subject of much experimental work (Tombaugh & Somjen, 1998). Nevertheless, I think it is fair to say that most neuroscientists regard pH as irrelevant when considering synaptic mechanisms. Of course all experimental electrophysiologists take extreme care with the pH of their patch and bathing solutions – heaven forbid that they are more than 0.1 pH unit out. Experimentally pH is clearly important, but physiologically relevant? Never! For example take an up-to-date review on neuronal synaptic plasticity (Zucker & Regehr, 2002) and look for a mention of pH – there is none. How is it that pH has come to be so ignored?

Intracellular pH regulation

The downfall of pH lies partly in its very importance. Since the rates of all enzyme reactions are sensitive to pH, but to different degrees, it has long been supposed that pH must be under extremely tight control. Were this not to be the case then a metabolic mess would occur, with some reactions proceeding too fast and others too slowly. The result of this mess would be a decline in normal physiological function. This view of *pH homeostasis* is supported by the exquisite control our bodies place on blood pH through the modulation of breathing. Furthermore, the fact that almost all cells maintain intracellular pH (pH_i) about 1 pH unit more alkaline than would be expected from passive diffusion of H^+ (or indeed H_3O^+ or OH^-)[1] across the plasma membrane supports this idea of active *pH regulation*. Thus, the view now commonly held is that pH, at least of nerve cells, is stabilized at an optimum level by pH regulating mechanisms (Figure 1).

It was with the study of pH regulation that my interest in neuroscience began. As a PhD student I impaled locust neurones, generally unsuccessfully, with ion-sensitive microelectrodes in an attempt to discover the mechanisms that regulated pH. At the time the idea generally held was that the gradual leak of H^+ into cells, down its electrochemical gradient, and metabolic H^+ production represented the H^+ load that the regulating mechanisms tirelessly fought. To investigate pH regulation it was deemed necessary to perturb pH by the addition of exogenous acid and study the ionic dependence of the subsequent pH recovery (Thomas, 1984). It was already known that snail neurones and squid giant axons regulate pH with a plasma-membrane Na^+-dependent Cl^-/HCO_3^- exchanger (Figure 1). To many in the

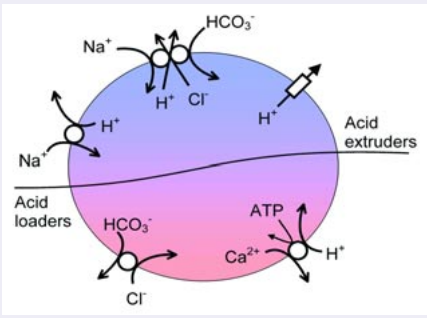

Figure 1 In most neurones pH_i depends upon the activity of several plasma membrane transport mechanisms. Not all acid fluxes are shown here e.g. HCO_3^- flux through GABA-activated channels, and H^+ flux on the glutamate uptake transporter.

Carbonic basics

BOX 1

$CO_2 + H_2O \leftrightarrow H^+ + HCO_3^-$

The reversible hydration of CO_2 gives rise to acid equivalents (H^+) in a reaction catalysed by the zinc-containing enzyme carbonic anhydrase (CA). There are at least 14 different isoforms of CA in mammals. It is found in the cytoplasm, mitochondria, attached to membranes and in fluid secretions. CAII is amongst the fastest enzyme known – its operation is nearly as fast as diffusion of H^+ will allow. CA inhibitors slow the reaction between H^+ and HCO_3^-, and thereby magnify pH shifts. CA inhibitors are used to treat a diverse set of disorders including; glaucoma, mountain-sickness, migraine, epilepsy and even cancer.

BOX 2

Red blood cell calcium pump

Much of what we know about the plasma membrane calcium pump (PMCA) comes from work on the red blood cell (RBC). For instance in 1982, some 10 years before our work on snails, Niggli *et al* showed that the RBC PMCA counter-transports H^+ (although there was some dispute on this point; see Rossi & Schatzmann, 1982). But this counter-transport of H^+ was of little physiological importance since the transmembrane calcium flux is small and HCO_3^- movements on the Cl^-/HCO_3^- exchanger dominate pH. Interestingly, those working on neuronal pH were unaware of this RBC work showing a link between calcium and pH.

In 1993 Gatto and Milanick reported that the fluorescein-based pH-sensitive dyes are potent inhibitors of the PMCA. Worryingly some scientists are still using such fluorescein-based dyes, such as BCECF, to measure pH in cells that rely on the PMCA to extrude calcium.

department in Bristol my study on locusts was esoteric and rather dull. Maybe they had a point.

During my first post-doc, in the USA, I saw others trying to make the study of pH both exciting and trendy. I was introduced to a phenomenon we called the 'ugly monster', a pH change resulting from the activation of an extracellular solute receptor. I was also set to work on the intense activation of acid extrusion in hippocampal neurones, which I was told might underlie memory! Both, unfortunately for me, turned out to be artefacts. Finally, I got involved in an expression cloning project, but it came to nothing. I left after a year, wary of both artefacts and molecular biology. As I travelled back across the Atlantic no doubt there was a collective sigh of relief from the lab!

Activity dependent pH changes

In 1992 I was being funded by the MRC to look at calcium buffering in snail neurones (a model nerve cell). I was failing to measure calcium levels with calcium-sensitive microelectrodes whilst Helen Kennedy was having problems persuading colleagues that snail neurones showed no sign of a plasma-membrane Na^+/Ca^{2+} exchanger. At the time it was widely believed that neurones extruded the bulk of their calcium on the Na^+/Ca^{2+} exchanger. Roger Thomas, on the other hand, was having plenty of luck measuring extracellular surface pH shifts. I wondered if I could measure surface calcium changes. By lowering extracellular calcium to about 1/50th of its normal level I was able to see calcium disappearing from the external surface during depolarisation (presumably entering the cell through voltage-gated calcium channels) and then gradually re-emerging following repolarization. Removing external Na^+ did not prevent the reappearance of calcium, but the intracellular injection of vanadate (an inhibitor of ATP-dependent pumps) did. This seemed to implicate the calcium pump in snail neurone calcium extrusion. Furthermore, after a month of frenetic experiments, I managed to show that the calcium extrusion was coupled to the inward transport of H^+ and that it was the calcium pump that gave rise to the extracellular alkaline shifts that Roger had been recording. We were very excited by this discovery of the counter-transport of H^+ on the plasma membrane calcium pump (PMCA; also known as the Ca^{2+}-ATPase or calcium-hydrogen pump) since it seemed to us that it might explain a whole host of pH changes in the CNS. *Nature* was, however, not impressed – and who can blame them, after all this was work from snails – and the work was published in an austere but august journal (Schwiening, *et al* 1993). Now I believe it is reasonably well accepted that some of the pH shifts seen in the vertebrate CNS do indeed arise from the counter-transport of H^+ on the PMCA (Trapp *et al* 1996).

Of course those working on red blood cells had known for some time that their PMCA could transport protons – but this was considered by them an irrelevance in a system with little calcium permeability and oodles of other H^+ flux (see Box 2). It is a shame that for 10 years those working on neuronal pH regulation were seemingly unaware of the RBC literature.

Armed with a Wellcome Trust Career Development Fellowship I then set about looking at activity-dependent pH shifts in neurones.

BCECF v HPTS

My initial experiments using a pH-sensitive dye called BCECF failed all too frequently. This fluorescein-based dye was hard to load into snail neurones through the patch pipette. The pipettes frequently blocked and my signals were buried in the noise. At that point I began to try out other pH-sensitive dyes. I found a cheap dye (£15 per gram, of which I still have some left) called HPTS which seemed to perform excellently, although few others used it. Presumably its lack of popularity was because it was not available in a membrane-permeant form. To my horror I also discovered, from the red blood cell literature, that BCECF was a potent inhibitor of the PMCA! (see Box 2) Most workers measuring pH in neurones, at the time, seemed unaware of both the blocking effect of BCECF on the PMCA and the link between the PMCA and pH. This was to some extent reasonable since, at the time, it was assumed that most neurones had little PMCA activity. My experiments with the non-blocking pyranine-based pH-sensitive dye HPTS and a potent blocker of the PMCA, eosin, seemed to show that the PMCA was the main endogenous acid loader in snails. When the PMCA was blocked the calcium-dependent pH shifts temporarily disappeared before reappearing possibly due to mitochondrial dumping of acid. In 1996, with another two years of my Fellowship to go, I

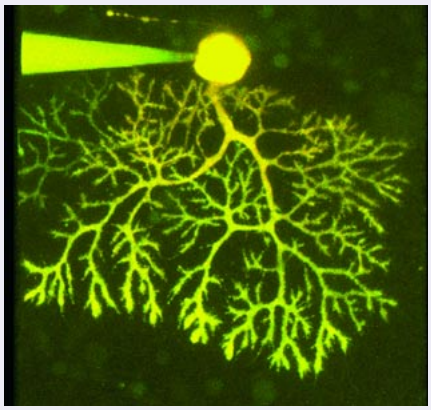

Figure 2 A confocal reconstruction of a patch-clamped Purkinje neurone (cell body diameter ~25µm), in a cerebellar slice, taken at the end of an experiment.

took up a lectureship in Cambridge.

My first attempts to measure regional pH in neurones were made using a fluorescence imaging system and freshly isolated rat hippocampal neurones. It was, frankly, a disaster from start to finish. Then after those three frustrating years with few results but many ideas, the MRC awarded us with a *de novo* Co-Operative Group Grant. This included the funds to buy a confocal microscope and investigate, amongst other things, pH shifts in snail neurones and rat cerebellar Purkinje neurones (Figure 2).

Confocal microscopy in Cambridge

To make spatial recordings of pH we (Debbie Willoughby and I) planned to image the pH-sensitive fluorescence of HPTS (Willoughby *et al* 1998) on the confocal microscope. Because the confocal scans a beam of light across the preparation, rather than illuminating it all in one go, the very bright cell body fluorescence does not (necessarily) obscure the weak dendritic and axonal signals. At the time, neither of us had had any experience of confocal microscopy and we were given the impression that there were many obstacles ahead. Indeed, the signals we obtained from the processes were small, less than a hundredth of those that could be got from the soma. Furthermore, since the diffusion of the dye, from the patch-pipette to the processes, was relatively slow we had to be careful not to 'bleach' too much of the dye. But, since we could use quite a high concentration of the dye, these turned out to be relatively minor problems. One of the great advantages of HPTS, over most of the fluorescein-based dyes, is that when excited with either the 488 nm or 458 nm line of the Argon ion laser the entire fluorescence is pH sensitive – there is no pH-insensitive 'pedestal' fluorescence. This allows the single wavelength fluorescence shifts to be calculated without the need for any laborious calibrations.[2] To our knowledge this was the first time that HPTS had been used on a confocal to follow regional pH, and it took quite a time before we felt confident with the measurements we were making. Figure 3 shows such a calibrated ΔpH image of a snail neurone during a depolarisation to +40mV. The lamellipodia are clearly subjected to much larger alkaline pH shifts than the cell body. Although some had predicted that such pH gradients must exist in neurones (eg Tombaugh, 1998), seeing them directly was very exciting.

Rat Purkinje neurones

The choice of cerebellar Purkinje cells for our mammalian neuronal preparation was fortuitous. They turned out to be ideal for confocal imagery and easy to patch. The data analysis was, however, more of a challenge and led me to write a little bit of software (see my home page if you want a copy!) to perform regional pixel-by-pixel F/F_0 plots (see Box 3). Characterizing the pH_i shifts was also not simple. The Purkinje cells are architecturally complex and attempting to control membrane potential throughout the dendritic ramifications with the patch pipette is almost certainly a lost cause.

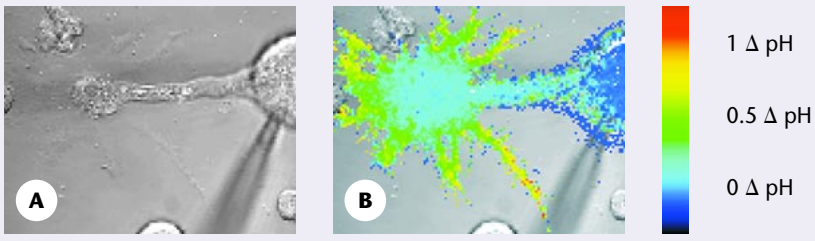

Figure 3 A Transmitted light image of a whole-cell patch clamped snail neurone. **B** The transmitted light image superimposed on the pseudocolour HPTS confocal ΔpH image taken during a 1s depolarisation to +40mV. Warmer colours indicate a rise in pH. The lamellipodial alkalinization is due to H^+ efflux through voltage-gated proton channels.

BOX 3

Fluorescence measurement of pH

Determination of *absolute pH* with fluorescent dyes requires 'ratiometric' measurements. Typically this involves the pixel-by-pixel division of dye fluorescence excited by two different wavelengths. The two wavelengths are chosen such that one produces a pH-sensitive fluorescence and the other a pH-insensitive fluorescence. In this way one can correct for dye concentration, illumination and fluorescence collection variables as well as path length. However, the lasers in conventional confocal microscopes cannot emit the wavelengths necessary (~400 nm) to produce a pH-insensitive signal from our favoured pH-sensitive dye, HPTS. Hence we are forced to make single-wavelength fluorescence measurements. Such single-wavelength measurements of pH-sensitive fluorescence cannot be calibrated with accuracy. However, HPTS has an unusual property that does allow relative fluorescence shifts (F/F_0) to be turned into calibrated *pH shifts*, even if the absolute pH can only be guessed[2]. This calibration of the F/F_0 signal works best when the dye is in a stable system – i.e. for measuring relatively rapid pH transients.

A new generation of blue diode lasers, as used in DVD technology, should allow future confocal users to make absolute pH measurements without needing to resort to expensive UV-lasers or two-photon microscopes.

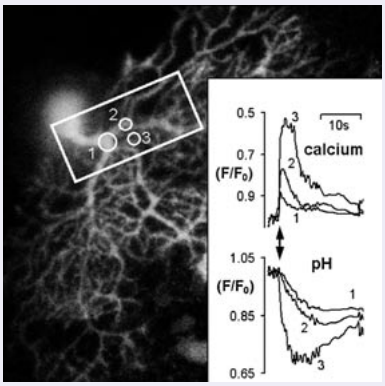

Figure 4 Simultaneous regional calcium rise and acidifications, following a single short (10 ms) depolarisation to 0 mV, in the regions indicated on the partial 3D reconstruction (1 primary dendrite, 2 secondary dendrite, 3 tertiary dendrite). Superfusate buffered with HEPES, patch solution containing CsCl, x40 objective (Schwiening & Willoughby, unpublished).

In the end blocking inhibitory input with bicuculline and dialyzing with Cs^+ (to block K^+ channels) turned out to be about the best we could do for voltage clamp recordings. But, as you can see from the prolonged dendritic calcium trace in Figure 4, this tended to result in the dendritic regions 'hanging up' at positive potentials for rather longer than the cell body. Thus we also used trains of back propagating action potentials (again with bicuculline present, but no Cs^+). The results were very similar in both cases. Electrical activity, even in the presence of physiological amounts of CO_2/HCO_3^- and carbonic anhydrase activity, caused dendritic pH shifts (~0.1 pH unit for either 1 s depolarisation or a 10 s burst of action potentials) that were about three times larger than that seen in the cell body. By combining a calcium-sensitive dye (Fura-red) with our pH-sensitive dye we began to look at whether these heterogeneous pH transients occur as a result of differences in the calcium transients, or whether there might be other factors at work, such as local pH regulation.

Of course, there are many questions remaining. Although we know that these pH shifts are dependent upon calcium influx, we do not know what is causing them. We assume that it is the PMCA, but it could equally result from the uptake of calcium into internal stores (mitochondria or endoplasmic reticulum). We do not know whether pH_i is uniform across the Purkinje cell at 'rest'. If the dendritic spines are the sites of H^+ influx into the cytosol, it is possible that the pH shifts there might be much larger (and indeed faster). Then we come to the question: do these pH shifts really occur physiologically? After all these are brain slices where the blood supply has been removed, they are at room temperature, the cells are being dialyzed with a patch pipette solution and artificially stimulated. This is far from physiology. But imaging pH in nerve cells in a functioning brain during physiological stimulation (eg tickling a paw) takes more money than the MRC can currently pay and more time than the University, driven by research assessment objectives, will allow. But, we can dream!

If we cannot perform the experiment, can we at least muse on the possible roles of these pH shifts? There are a couple of pieces of evidence that might suggest that they are important in normal physiology. Both sets of experiments involve modifying pH buffering. Firstly, in experiments on isolated hippocampal neurones, it has been shown that increasing the concentration of intracellular pH buffer can modify neuronal calcium signals. (Tombaugh, 1998). The introduction of excess pH buffer into cells should not directly alter pH_i. It has been suggested that the pH_i shifts that normally occur during electrical activity (Trapp *et al* 1996) might be blunted by the additional buffer. However, in his study, Tombaugh was unable to make recordings of these dendritic pH shifts. The second set of experiments, or rather observations, are from human clinical studies.

Cerebellar ataxia

Certain types of CNS disorders can be treated with inhibitors of carbonic anhydrase (such as acetazolamide). Such inhibition is well known to magnify the size of activity-dependent pH shifts. Amongst these disorders are two that are known to involve mutations of the P/Q-type calcium channels (hemiplegic migraine and episodic ataxia type II; see review by Kullmann, 2002). The clinical effectiveness of acetazolamide has been assumed to be due to an effect on resting pH_i. However, given that the disorders are associated with impaired calcium influx during depolarization – and therefore presumably smaller calcium-dependent pH_i shifts – it is more likely that acetazolamide is simply restoring the otherwise blunted pH_i shifts (Figure 5). Such a hypothesis, of course, relies on the assumption that pH_i shifts play an important role in normal neurophysiology and that their absence results in a profound dysfunction. This is not what most neuroscientists currently appear to think.

Whither?

At this point it is not clear that we know the full extent of these local pH signals since they have not yet been measured in locations where they are likely to be largest; pre-synaptic terminals and dendritic spines. Nevertheless, the investigation of the physiological (and indeed clinical) importance of these pH shifts seems worth some effort.

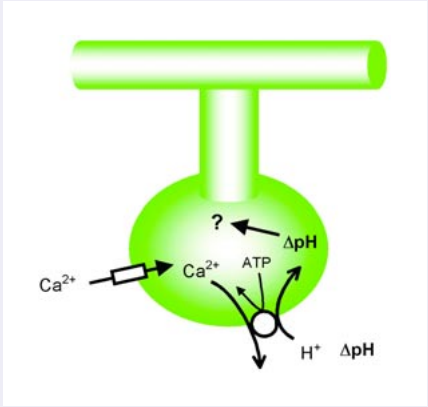

Figure 5 Calcium fluxes at dendritic spines could result in physiologically important pH shifts (ΔpH). Carbonic anhydrase inhibition would be expected to magnify these shifts (by reducing pH buffering, see Box 1). In cases where impared calcium fluxes (eg episodic type II ataxia) result in smaller than normal pH shifts, carbonic anhydrase inhibition might be able to magnify the pH signals and restore normal function.

However, we have few tools (eg blockers) with which to study these functions. In order to remove the pH signals it is currently necessary to abolish the transmembrane calcium fluxes – hardly a specific blocker! Manoeuvres designed to enhance the pH shifts have little to add to our knowledge since they might only reveal what the physiological buffer systems may normally attempt to prevent.

To restrict our interest to neurones would also be a mistake. There must be researchers working on non-neuronal cells for whom local pH shifts could also be important. Preparations in which either large calcium fluxes and concomitant high levels of PMCA activity are known to occur (eg cochlear hair cells) or where moderate calcium fluxes occur in regions with little cytoplasmic volume (eg ciliated portions of olfactory receptors) are both likely to show local pH shifts. Finally, there is also mounting evidence that local pH shifts might regulate calcium fluxes during calcium release from stores. This is something that is currently making our MRC Co-op twitch.

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[1] I use H^+ here to represent an acid equivalent, of course it could equally be H_3O^+, $H_5O_2^+$ and so on. Furthermore a movement of H^+ in one direction could equally be a movement of OH^- in the other direction. For the sake of this article such differences should cause us little worry.

[2] It does, however, require knowledge of the pK of HPTS and the approximate starting pH_i. Of these two variable the starting pH is least certain, however the calibration is relatively insensitive to pH at neutral and acidic values. The formula is:

$$\Delta pH = \log (F/F_0) - \log (1-(F/F_0-1).10^{(pH-pK)})$$

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Nitric oxide microsensors

Roger Wadsworth reports on a symposium to discuss the physiological measurement of nitric oxide using electrochemical microsensors held at the European Society for Microcirculation 2002 meeting in Exeter

Roger Wadsworth

There is impressive evidence that derangements in nitric oxide (NO) occur in all of the main cardiovascular diseases. This has fuelled continuing interest and speculation in the possibility that alteration in NO may be causative in certain cardiovascular diseases, or that delivery of additional NO may be beneficial in therapy. This evidence, though extensive, is almost all indirect, being based principally on interpretation of end-organ responses to inhibitors of NO synthase, and the detection of by-products of NO metabolism. The development of the NO microsensor provides a method for real-time measurement of NO concentration, and a symposium was held at the European Society for Microcirculation 2002 meeting in Exeter (August 2002), to discuss the *Physiological measurement of NO using electrochemical microsensors*.

At the symposium, Malinski described the initial concept of the NO microsensor and its subsequent development into a variety of configurations suitable for particular applications (Malinski & Taha, 1992). Devynck described the advantages and limitations of coated microelectrodes to monitor NO from cultured vascular

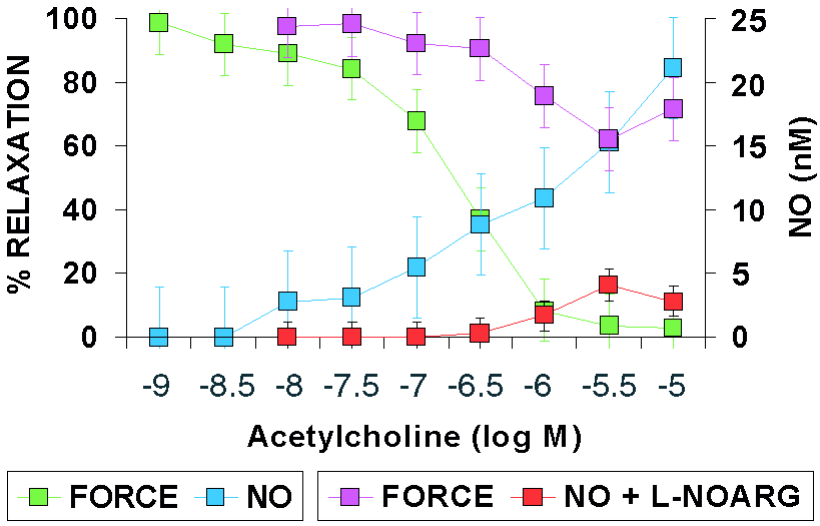

Figure 1 Simultaneous recording of NO concentration and relaxation in rat mesenteric artery. The artery ring was precontracted with noradrenaline and then acetylcholine was added cumulatively. Note that a small remnant of NO formation and relaxation remain in the presence of L-nitroarginine 100 µM (see Simonsen *et al* 1999 for further details)

cells (Pontié *et al* 2000). Mas described the application of a NO microsensor to measurement of NO in vivo, using the corpus cavernosum penis as a model vascular bed (Escrig *et al* 1999). Kutzsche *et al* (1999) described the effects of hypoxia and reoxygenation on cerebral NO concentrations in pigs. Delli Gatti described the effect of plasma lipoproteins on NO production in cultured endothelial cells (Vergnani *et al* 2000). Stankevicius *et al* (2002) used NO microsensors to show that nitric oxide release in arteries from renal hypertensive rats is impaired.

There was also a workshop oriented to practical applications and technical questions, which generated a lively and spontaneous discussion. Boer outlined many pitfalls but ultimate success with the measurement of NO measurements in isolated arteries (Piepot *et al* 2000). Gonzalez-Mora described equipment for differential pulse voltammmetry (Escrig *et al* 1999). Zhang *et al* (2000) described that characteristics of a commercially available series of NO microsensors.

One example of the application of NO microsensors in blood vessels is shown in Figure 1.
A ring of rat mesenteric artery was held in a small vessel myograph in Krebs solution. A NO microsensor (30 micrometres diameter) was inserted into the lumen using a micromanipulator. Relaxation of the artery with acetylcholine was accompanied by NO formation, detected at the microsensor. The concentration of NO detected was approximately 10 nM at maximal relaxation; however, the endothelium has a considerable reserve capacity and higher concentrations of acetylcholine generated more NO, over 20 nM. The NO synthase inhibitor L-nitro-L-arginine 100 µM caused a very pronounced, though not complete, block of NO formation and relaxation.

Anyone interested in the technique or applications is welcome to contact R M Wadsworth for further information (r.m.wadsworth@strath.ac.uk).

Our present state of knowledge of the role of NO in cardiovascular disease can be likened to someone who has heard of, but never seen, an elephant – they know approximately what it looks like and where it can be found, but they have little knowledge of its behaviour, its function, or how to make more of it (Figure 2).

Figure 2 13th century carving of an elephant in Exeter Cathedral

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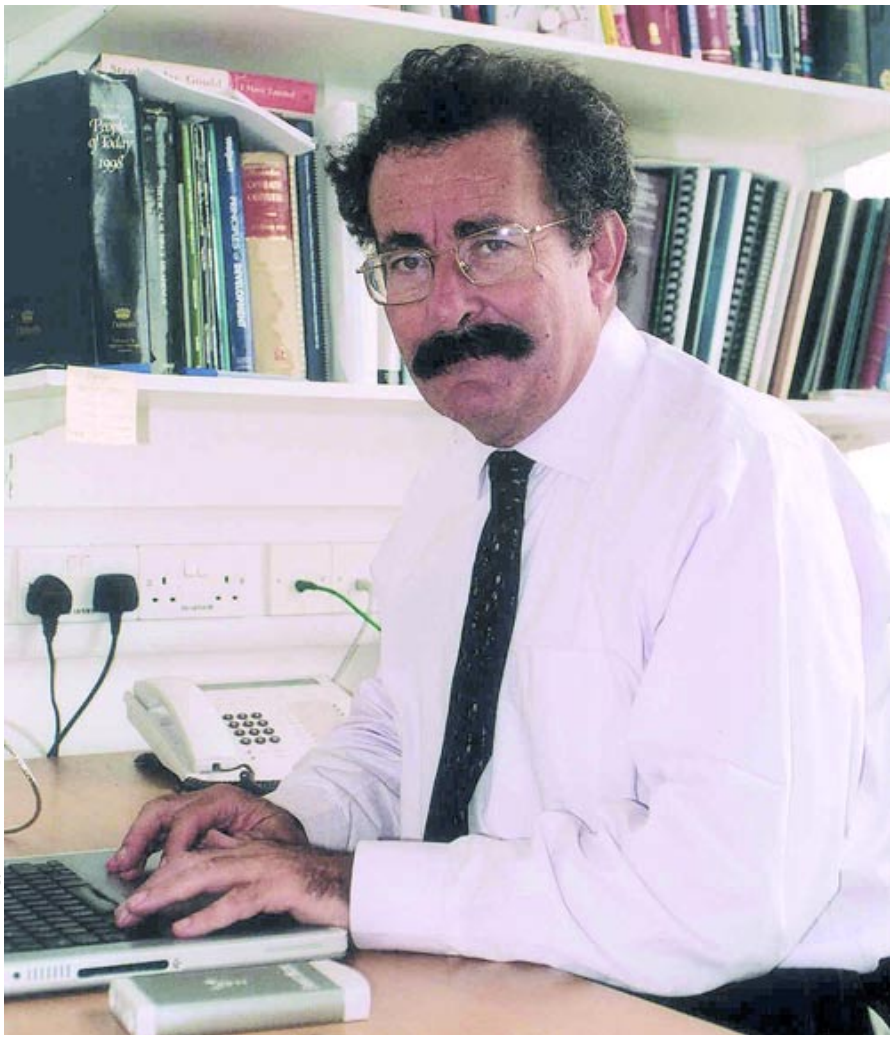
Adapted from an article published in the *British Society for Cardiovascular Research Bulletin*

Labouring Lord

An interview with Professor Robert Winston



Professor Robert Winston

I was just nine years old in 1978, the year Professor Robert Winston and his team created the world's first 'test-tube baby'. Twenty-four years later, over a million test-tube babies have been born and I am sitting in Winston's office, surrounded by a collage of hundreds of photographs of children, children, *children*: mostly newborns, some minuscule in incubators, several smiling toddlers, and some now as spotty teenagers – all of whom would not be here if Robert Winston had not had a hand in their conceptions.

Moments later, I am led to his other office, this one in a slick, modern and much brighter building. Professor Winston soon appears, well-tanned but looking a tad vexed behind his trademark glasses and moustache. He shakes my hand then hurriedly runs through his gruelling schedule with his PA.

When it's my turn, he apologises if he seems distracted and irked, which he clearly is: he has to fly to the States the next day to give a talk and his laptop has crashed. On it is the only copy of his talk, he explains, and he still has a hideously crammed schedule to get through today.

I thus drop the question about his views on the new company set up to provide sperm for lesbian couples, *Man Not Included*. Instead, I ask what advice he has for undergraduates thinking about embarking on an academic career in research, given problems with relatively poor stipends and salaries, funding, short-term contracts and a poor career structure.

'I think the prospect for young scientists isn't that bad. If you went round this laboratory, where there are 24 young scientists on this floor, most of them female, I think most of them are engaged and excited by what they're doing and not depressed at all. I think they feel very vibrant, actually. There are major problems within the universities because they're not properly funded, but there are some indications that the government is taking that on board.

'It's not the PhDs and the young scientists who are depressed,' he adds. 'I'd say it's the senior ones. The environment that they're having to administer is a difficult one,' Winston says, adding optimistically: 'But that will change, I suspect.'

On his bookshelf is a card, a detail of Michelangelo's *The creation of Adam*. It seems particularly apt in Winston's office. Many ask whether he feels like God, bringing life into the world, a comparison he dislikes.

'No. I don't believe that I'm a creator of life. I'm merely an agent that helps life into the world a bit. I think reproductive physicians who start thinking of themselves in grandiose terms – and I think some of my colleagues do – are likely to do a disservice to themselves and to their patients.

'What this subject ought to show very clearly clinically to its practitioners is how fallible we are. Therefore, above all, there should be a sense of humility about it, because most of the time we find we aren't actually helping. It's a difficult technology which doesn't work an awful lot of the time, and that ought to keep us more humble than we sometimes are.'

It certainly is a difficult technology.

According to the Human Fertilisation and Embryology Authority (HFEA), IVF success rates for 2000/2001 averaged 25.1% for women aged under 38 and 21.8% for those aged 38 and older. Still when you compare that to Nature's own surprisingly low success rate, which averages about 15%, it is no wonder that some regard his work as god-like.

Obviously, successful cases bring much 'personal satisfaction' to Winston, but he stresses that unsuccessful cases have their own particular and important value as well.

'One can get a tremendous amount of satisfaction from helping people through failure. A lot of my work is actually doing that – knowing one's limitations, trying to persuade people not to go through treatment, trying to help them to take that decision. Trying to make that a positive experience can be the most challenging aspect of reproductive technology therapy. It can be very, very rewarding and can be immensely beneficial to the couples themselves. One shouldn't overlook that, I think it's very significant.'

Science and communication

As is apparent through his television programmes and his work in the House of Lords, Winston is strongly committed to improving communication between scientists, politicians and the public. While he feels that scientists are taking positive steps in engaging more with the public, he believes that more effective methods should be embraced more often.

'I think that scientists are still a bit dismissive of the more popular approaches to science. They still think in a very cerebral fashion about science, they still express themselves very cerebrally and they still are rather dismissive of, for example, trying to do things on BBC 1 or writing columns in *The Sun*. In my mind, that's almost the most important end because that's going to get to the biggest public, it's going to get to the people who actually are important. A BBC 1 television programme that's watched by five million people should be as just as valuable as writing an esoteric book that sells 3000 or 4000 copies but is extremely well written and wins a non-fiction prize.'

The public's distrust of scientists has remained fairly constant for years. Issues such as the BSE scandal, the foot-and-mouth epidemic, concerns over the use of animals in medical research, GMOs, and the ongoing debate about the MMR vaccine have recently fed this distrust. Winston feels that this distrust is largely the scientific community's own doing.

'More scientists are engaging a bit better than they did, but we still tend to present ourselves as being very certain, whereas science is about uncertainty. We still are not prepared to really understand why members of the public have difficulty with issues such as the perception of risk. I think there's more to be done with the *science* environment than with the *public* environment. We still talk about the "public understanding of science" when it should be the scientists' understanding of the public that's the real issue.'

Winston said in a recent interview that 'transgenic humans' was 'the real debate' that needed to be debated. When I ask him to elaborate, he dismisses that specific comment, but points out that the entire GM issue is one that needs to be discussed and communicated more effectively.

'We're not handling the issues of GM in general very well. I don't just mean in humans, but in general. I think there's a huge misunderstanding about how it can be controlled, the relative good it can do, and so on. I think transgenic technology has already offered a great deal to human and animal biology, and could offer a great deal more. But if it's not really understood, then I think that's another example of an area where there needs to be better communication.'

Science and the media

When I ask how well the British media is reporting science issues responsibly, a long, thoughtful pause indicates his ambivalent feelings. While he extols several broadsheet science journalists, and science writers such as Steve Jones, he excoriates much of the rest.

'It's extraordinarily variable,' he says, chin in hand, gazing out of his window towards Wormwood Scrubs prison. 'Sometimes it's appalling. Frankly, the way BSE was reported was abysmal. The way much of cloning was reported was also quite dreadful, prurient.

'There's good and bad. But there's certainly clear evidence that we need improvement. The difficulty is not so much the science writers as the newsprint journalists and the news conveyers on television. It troubles me deeply that, for example, it's impossible to have a serious scientific discussion on *Newsnight* although science regularly comes up on *Newsnight*. It's got to the stage now where they ring me and invite me to come onto the programme and I generally don't because, frankly, I'm not at all convinced that they seem capable of really understanding why scientists feel that they're not presenting scientific work in a way that is at all reasonable. To present science as entertainment may increase your viewer figures, but it doesn't actually help the issues that you are discussing.'

Science, ethics and embryonic stem cells

Despite being distracted by his laptop at times, glancing to see if it's rectified itself, Winston is an engaging interviewee. He is articulate, intimidatingly erudite, and witty – but also occasionally prickly.

Sticky questions of religion and ethics in scientific matters, such as embryonic stem cell (ESC) use, clearly ruffle Winston on this occasion. When I ask him whether he has an opinion as to when human life becomes a human person, he grows frustrated and impa-

tient. While expressing deep respect for many central values in Catholicism, Winston finds this debate particularly Catholic, and particularly perplexing.

'I am puzzled by the concentration on the definition of the beginning of life. I find it difficult to understand how a fertilised egg, which may be fertilised abnormally and have no possibility of being viable, can be equated with a born child. And I have no understanding of how a fertilised egg, which has only a 15% chance of becoming a viable child on average, can be regarded as being inherently so valuable that you would not be prepared to pursue improvements in human health, save the mother's health, save the mother's life, if necessary, in preference to that embryo.'

Those who condemn the use of ESC lines on ethical grounds often cite scientific advances in adult stem cells as an additional reason for halting their use. While adult stem cell research may show their surprising multipotency and therapeutic potential, it's early days yet and Winston cautions against scrapping ESC research.

'The truth is that there isn't enough information to choose and it would be foolish to abandon one branch of research in favour of another before either is much more than fledgling form, given the fact that ESCs are being wasted at the present time. The push should be to try to use them maximally, to try to see whether or not there are certain advantages in using them.'

When we touch upon human cloning, a contemptuous laugh encapsulates his dismissive attitude towards those who claim to be on the brink of successfully cloning humans. Does he feel we need internationally binding regulations in place to control it?

'I can't get worked up about cloning. I think it's an issue that is irrelevant. I just think we've wasted so much time getting outraged and engaged by a technique which is of no real value to anybody and, actually, is not likely to work. I think there are much more important things. Why have international regulations on cloning but not on stem cells or transgenic animals or animals in research, or human medical research? I think cloning should be seen for what it probably is: a dead end that is of no great value, and a couple of pompous and rather bombastic individuals, one American, one Italian, who make periodic announcements about how many children they've cloned.'

New Year wish list

When I ask Winston to comment on what issues the UK biosciences need to address in 2003, he dwells silently for several moments.

'My main concern is the Medical Research Council. I'm rather concerned that the institution of collaborative grants and the abandonment of a policy of having project grants has, in many ways, not always been helpful; I think it's resulted in the MRC actually narrowing and reducing its constituency, and therefore reducing its influence over medical research in Britain. I think that one of the issues for the new Chief Executive will be to try and review whether or not it might not be better to spread the money slightly wider, given that there was a slightly increased budget.

'Another issue remains with the MRC: it would also be quite good to see a bit more transparency about the way grants are applied to review. I think that might be possibly true across UK science generally. Whilst peer-review is a very good thing, I think that sometimes the mechanisms aren't as transparent as they might be.

'I think there are so many issues really. I think we're not doing enough to explain to the public and politicians *why* this investment in science is needed. To most people, for example, the letters BBSRC and MRC are meaningless; people don't know what they stand for or what these bodies are doing. We should be doing much more about communicating, in a rather simpler way than we generally do, what we expect to achieve from our research. I think science is often seen as a rather esoteric pursuit for the benefit of a few people rather than for the benefit of society as a whole.'

Reluctant celebrity

The scope of Winston's work as a researcher, clinician, a medical media celebrity and a Labour Peer who recently chaired the House of Lords Select Committee on Science and Technology is enviably exciting. While he admits somewhat ruefully that 'sitting in a laboratory would be the most satisfying thing to do,' I ask him whether he enjoys the celebrity status that his work has brought him.

His reply – and not the first time in my interviewing him – seems brusque and catches me off-guard. However, I realise that such replies reveal a fundamentally humble and humane streak to Robert Winston. While he obviously derives immense pleasure from his media work and fulfils the role aptly, it is secondary to why he does it, and his surprisingly serious reply reaffirms that streak:

'I don't think I understand the word "celebrity". I don't approve of "celebritisation" at all. That's not what I try to achieve. The reasons for the profile are because I think that there's a great need to present the value of science – and unless we do that we're doomed. If there's a spin off of being slightly better known as a result, that's a penalty I have to accept.'

Bill Parry

This interview contains extracts from *Humane Instinct*, published in *Biobits* (November 2002), the newsletter of the Institute of Biology.

A physiologist digresses about piping

As a physiologist in Scotland, Geoffrey Walsh cannot miss the potentialities for the study of pipers and piping

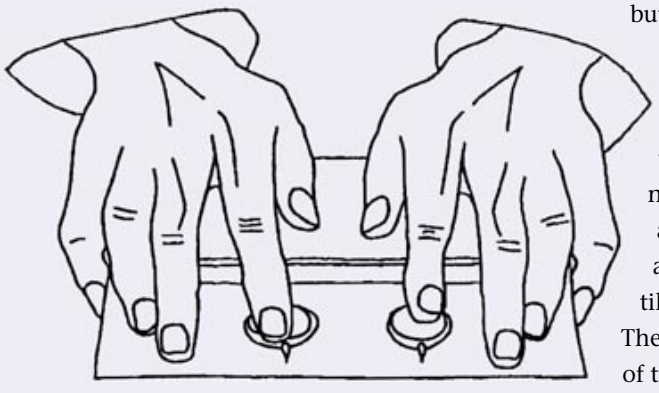
Geoffrey Walsh

There are a number of different types of bagpipes (cf Figure 1); when the word is used without qualification it invariably refers to the Great Highland Bagpipe of Scotland. The sound is continuous, there are no gaps; by contrast the Northumbrian pipes are usually played 'staccato'. The fingers of a piper can move with extreme rapidity, the commonest grace note, 'High G', is made by flicking the left index finger, its hole is vented for merely about 20 ms.

For many years I worked in the Edinburgh Medical School and was especially interested in muscles, the way they work and the way they control movements (Walsh, 1992). A physiologist in Scotland cannot miss the potentialities for possible studies of pipers and piping. In my youth I had played no instrument but belatedly, at the age of 47, took up the flute; the basic fingering was not difficult to learn. I found that moving two or more fingers in the same direction at the same time normally was not difficult but moving two fingers in opposite directions, as in a 'fork', could be harder. I could find nothing written about this in the scientific or medical literature so built an instrument to make measurements; I have been a radio ham since my youth and like dabbling in electronics.[1] The person was asked to touch one metal button with one finger and at the same instant lift another finger from a second button (Figure 2). With two thumbs and eight fingers there are many permutations and combinations of movement are possible, this allows for great versatility in hand control. The human dominance of the world, for good or ill, has been made possible to a large extent by the extraordinary control by the brain of the hands.

Figure 1 Irish war pipes.
A 16th century woodcut by John Derrick (Flood, 1911).

Figure 2 A study of the movements of the two index fingers. Touch sensitive circuitry was used.



Five years ago, whilst working with Dr Julian Toms at the Health Centre in Portree, Isle of Skye, I met Dr Angus MacDonald, a general practitioner and a piper of distinction, I was amazed that the errors he made on my instrument were much smaller than those I had obtained on medical students in Edinburgh. Intrigued I went to the Piping Centre in Glasgow where the director, Roderick MacLeod, introduced me to six skilled pipers. Similar results were obtained – the errors of the pipers were clearly less than those of the students. Bit by bit I added more data and made measurements on a total of 12 pipers, 127 medical students and 28 young adult classical musicians studying at the Birmingham Conservatoire with the help of Dr Peter Johnson. The errors of the pipers were easily the lowest (Figure 3).

The instruments played by the students at Birmingham were a mixed group; I did not succeed in getting an adequate sample to evaluate the skills of different types of classical musicians. Two years ago I found that in Hanover there is an Institute for Music Physiology attached to a Hochschule where young adults train to reach a high standard as performers (Walsh 2001). It is the – Institut für Musikphysiologie und Musiker-Medizin, Hochschule für Musik und Theater, Hannover. URL-http://sun1.rrzn-user.uni-hannover.de/~n3x3mphy/pages/english1.htm

I got in touch with the director, Dr Eckart Altenmüller, and having by then computerized my arrangements, flew out with a laptop and other apparatus and spent two weeks measuring a variety of different types of finger movement in over 60 musicians. On returning to Edinburgh I ran the same tests on

medical students who had never played an instrument, on pipers at the Army School of Bagpipe Music and of the Highland Regiment and on two members of the Glencorse pipe band. The numbers of instrumentalists and non-musicians is given in the Table.

On all of these persons 14 tests were run, the fingers moving in contrary directions to the beat of a metronome at 120/min. The easiest were contrary movements of the two index fingers, the most difficult contrary movements of the ring and little fingers. It is intended to publish the full details elsewhere. The data files on the computer were subjected to statistical analysis. The results are summarised in Figure 4.

INSTRUMENTALISTS	number
Bagpipers	15
Woodwind players	13
Violinists	11
Pianists	23
Accordionists	10
Non-Musicians	36

Table Numbers of instrumentalists and non-musicians studied

The errors were nearly always of one sort in both the Birmingham and the Hanover studies. When a person attempts to touch one disc and simultaneously to lift another finger it is usual for the finger coming down to reach its target before the other starts to rise, there is 'overlap' (cf. Walsh, 1997). For a while both fingers are in contact with the discs. Occasionally the finger coming down has not reached its target before the other has lifted off, both fingers are for a while in the air, there is a 'gap'. Of the data for Figure 3 only that for the pipers in the lower right panel is negative, indicating a gap. With a woodwind instrument such imperfections lead to the length of the 'resonant air column' being for a while incorrect and unless the error is small the music, if being played legato, will be impaired.

The pipe is an extremely responsive instrument. Frictional losses between the moving air and the wall of an instrument are related inversely to the cube of the bore. Thus a practice chanter with a bore of 5 mm will have about 55 times the 'damping' of a flute with a bore of 19 mm. These losses increase with frequency. Furthermore, of the instrumentalists I studied, only the pipers normally play out of doors; reverberation as in a room or a hall will be absent and will not mask imperfections in the transition from one note to another.

The sounds of the pipes are rich in overtones, a noteworthy study is that of MacKenzie (1995). The harmonics of the drones extend to 10,000 Hz, the limit of my instrument, and may have components too high for the human ear to hear. This rich spectrum will give the listener a multitude of information about changes of pitch. Piping being in Scotland highly competitive, a good judge may be expected easily to recognize unusually fine skills.

The pipes have two tenor drones both tuned to 'A', a base drone tuned to 'A' an octave below, 'Low A' on the chanter is an octave higher than that of the tenor drones and 'High A' is two octaves above the notes on those drones. The acoustics are complex; how is it that after careful tuning the chanters lock together? Even with the best ear a piper will not be able to reach the accuracy of a caesium clock. A Dutch mathematician, Christiaan Hygens (1626-1693), noted that when two clocks were mounted on the same wooden board the pendulae swung at identical rates. Sometimes oscillators (this term can include organ pipes, drones, etc) may fall into step by the transfer of tiny amounts of energy; there is 'entrainment'. Lord Rayleigh (1842-1919) found that when two organ pipes were fed from the same wind chest the notes became identical. When the reed on one of the drones of a pipe closes, the pressure in the bag will rise and if another reed is nearly opening it is likely to do so at once; So far I have not come across measurements of the pressures in the bag of a bagpipe; the situation with the pipes is more complex than in Rayleigh's observations because there are four rather than two oscillators, three drones at running sensibly stable frequencies, and the chanter of the notes which are constantly changing.

What happens to the breathing of pipers? To supply the three drones and chanter considerable air flow is needed.

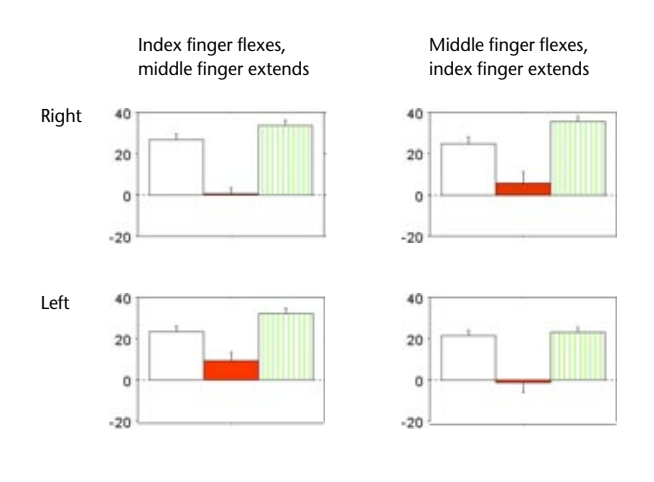
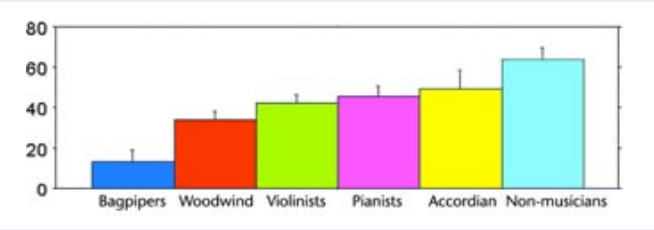


Figure 3 Means errors (ms) of conservatoire students (unfilled), pipers (filled) and medical students (vertical lines). Bars = 1 S.E.M.

Figure 4 Overall means for overlap times. The pipers have lower errors than any of the other groups. There were 15 pipers, 13 woodwind players, 11 violinists, 23 pianists, 10 accordionists and 36 non-musicians. All were right handed young adults. (Bars = 1 S.E.M.)



When inexperienced persons breathe to the same extent as pipers they become dizzy; some neophytes may faint – experienced performers are free of these effects.

There is a great deal of interest in the science of sport; athletes believe the information helps them improve their performances. By contrast there is an almost complete dearth of information about the ergonomics of playing any musical instrument, a curious anomaly. The equipment used by athletes is for the most part simple, and special study is unnecessary. By contrast the physics of musical instruments is complex; many fine papers may be found in *The Journal of the Acoustical Society of America* and *Acustica*.

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Thanks are due to the numerous people who acted as subjects and to Mr Robert Gibbon for drawing Figure 2.

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Cannon's Peak – a challenge to Society members

A mountain named after a physiologist – do you know of other geographical features named in this way?

A year or two ago I was contacted by Professor Owen Wade regarding the adventures of Walter Cannon, best known for his gastroenterological work, but who, with his wife Cornelia and a French-Canadian squatter named Comeau, was first to climb a local mass previously called Goat Mountain on 17 July, 1901. This may have been during Walter and Cornelia's honeymoon and could have ended in disaster, since on their way back they were almost killed by a landslide: '*we saw a huge rock come rolling off the top of the mountain… followed by a continuous stream of small stones which poured on the very spot where we had been eating our lunch*'.

It seems that Walter and Cornelia were in what is now Waterton-Glacier International Peace Park by Lake McDonald in Montana when they spotted Goat Mountain. They were told it had never been climbed, so off they went with hobnail boots, backpacks and minimal other gear. After a fairly hard climb, with Walter getting stuck in a crevice at one point, they worked their way up a narrow shelf on the bare mountainside, up a difficult scree and thence to the top. The views were magnificent with snow-capped peaks, glaciers and lakes. That night they made it back to their camp and next morning were awakened by a horseman with a string of pack animals. He was working for the US Geological Survey and had tried to reach the top of Goat Mountain a few weeks earlier. They told him of their adventure and he took their names.

Seven years passed and they were invited to dine with a colleague in the Harvard Department of Geology, where they were introduced to a topographer from the Geological Survey and recounted their tale to him. '*A few days later the mail brought a beautiful contour map of the area of Glacier National Park, and there, at the head of the Lake, was Mt. Cannon. Because there were two Goat Mountains in the region another name for one of them had to be found, and the government had given our name to the one we had been first to climb.*'

The area is phenomenally beautiful and unspoilt and it must have been a great thrill for the Cannons to have the mountain, albeit a relatively small one, named after them. As Professor Wade says at the end of his letter "I do not know of any other geographical feature named after a physiologist [or even a physiologist's spouse, Ed.] – I expect there are some and perhaps publication will reveal others known to members of the Society!"

So there's the challenge, are any other geographical features named after physiologists? Please tell us if you know of one. Whatever it is you don't have to climb or swim it or whatever, unless of course you actually want too!

Bill Winlow
Editor

Quotations in italics are from : Walter Cannon (1945). The Way of an Investigator. Norton and Co. Inc., New York. The book is difficult to find, but Professor Wade found a copy in Birmingham University library.

Suffering for science

Keri Lee Page comments on the Cambridge neuroscience research centre inquiry

As 2002 drew to a close, passions were running high in the neurophysiology community, as an inquiry into Cambridge University's plans to build a £24m neuroscience research centre on the outskirts of Cambridge turned into a public debate over the scientific validity of the animal model paradigm.

The planning inquiry, which began on 26 November, 2002 was called after South Cambridgeshire District Council turned down the University's original application on the grounds of public safety matters.

The University had hoped to confine the hearings to discussion of planning issues after the government-appointed planning inspector, Stuart Nixon, ruled that it was not within his gift to 'hear evidence on public health, animal welfare or moral arguments' in a pre-inquiry meeting on 16 September. Nevertheless, Mr Wald, who spoke on behalf of animal welfare groups – Animal Aid and the National Anti-Vivisection Society, which represents NatureWatch, PeTA, Uncaged and X-Cape – insisted that 'the proposal is controversial' and that 'public anxiety is a material planning consideration'.

Cambridge University proposed a 10,000 square metre facility to house all its existing primate research that is currently conducted over several geographically dispersed locations. Up to 60 world-class scientists are hoped to be employed in the centre, which has already secured about £8m in programme grants from the Medical Research Council (MRC) and Wellcome Trust. The Prime Minister, Tony Blair, who believes that the work is 'in the national interest', backs the plans. Basic and clinical research into new treatments for stroke, Parkinson's disease, Alzheimer's, schizophrenia and substance abuse will be performed.

In his proof of evidence, the academic witness for Cambridge University, Sir Keith Peters, said that the research facility 'would rank with some of the finest centres internationally'. Animal rights groups, however, felt that the appellants could not rely simply on 'an assertion of national need' and accused the university of 'intellectual arrogance'. Sir Keith replied that the national need for neuroscientific research is 'self-evident' and that its relevance is fully assessed by a 'particularly stringent' peer review process.

In a joint statement, National Anti-Vivisection Society director, Jan Creamer, and Animal Aid director, Andrew Tyler, said that the university made 'anonymous claims about the usefulness of the experiments which they didn't even bother to support with scientific evidence'. This concern was compounded at the inquiry when it was revealed that Cambridge University, acting in fear for staff safety, disallowed any practising primate research neuroscientist from testifying at the trial. This left Sir Keith – Physician and Head of the Cambridge University Clinical School – wide open to claims from Mr Wald that he was 'unable to say scientifically whether the underlying science can be applied to humans'. Suddenly, the planning inquiry had become a trial of all medical research: experimentation that 'may or may not lead to a cure…basically amounts to scientific dabbling'. Mr Wald challenged. Sir Keith countered: 'If you knew what the answer was, there would be no point in doing the research'.

Keri Lee Page

Nancy Rothwell, President of the British Neuroscience Association, supports the University, saying that non-human primates 'are the only other species with well developed frontal and temporal lobes…and complex behaviours cannot be studied in lower species'. In opposition, Ray Greek, Medical Director for Europeans for Medical Advancement and witness for Animal Aid, explained that while humans and primates have many similarities on a gross scale, we should now be 'looking at the molecular and the genetic level; the level that defines a species'. He added; 'Similarity in structures does not imply similarity in function.' The species differences that Greek alluded to, however, 'tell us a great deal about the relationships between structure and function as they relate to our species' responded Dr Matfield, witness for Cambridge University.

In his proof of evidence, Greek called on drugs like Flosint and Opren which during tests on primates yielded good results but which killed up to 61 people in human clinical trials. Gill Langley, member of the Government's Animal Procedures Committee and scientific consultant to The British Union of the Abolition of Vivisection (BUAV), agrees that 'people are being maimed and killed' because results from primate experiments 'prove misleading when extrapolated to humans'. In the inquiry Greek pointed out that in 1998-2001 'eight drugs were recalled [in the UK] because of side-effects that were restricted to women and not men', a

result that primate testing could not have revealed. He also referred to the major human diseases which he believes have so far been unaided by primate research, such as atherosclerosis, cancer and stroke. 'The abandonment of animal models is absolutely vital for medicine to advance', concludes Greek. In an attempt to prove this point, Mr Wald drew attention to the Alzheimer's vaccine (AN1792) from Elan Pharmaceuticals and Wyeth-Ayerst, which moved directly from successful mouse-based trials to phase II human clinical trials in 2001, without any intervening primate testing. Embarrassingly, Mr Wald was not aware that in February this year the trials were halted after 15 patients developed severe brain inflammation; a fact that Sir Keith was quick to point out: 'I think you will find you have shot yourself in the foot Mr Wald.'

In cross-examination, Sir Keith combated Wald by calling Greek's 'scientific standing' into question: 'the vast majority would disagree with him', he noted. 'Dr Greek alludes to many instances where deleterious side-effects of drugs have not been tested by animal screens. However,' argued Sir Keith, 'it is very probable that a much larger number of drugs with adverse side-effects have been detected by such methods'.

The BUAV received permission from Nixon to show an underground video during the inquiry that contains footage captured by an undercover BUAV investigator who worked as a technician at a Cambridge University primate research unit. Although a Home Office investigation has already cleared the lab of cruelty charges, the highly emotive images of marmosets showed seizures and mental suffering. BUAV made the point that for experimental results to be meaningful the primates must be stress free: 'The stress to the monkeys is self-evident from the video', said Natalie Lieven on behalf of the BUAV.

BUAV and Animal Aid urged Cambridge University to build an animal-friendly neuroscience centre that makes full use of new and alternative technologies such as fMRI, MR, CT and PET imaging methodologies, as well as neuropathology and epidemiology. 'There is considerable ignorance about the uses of other methods as replacements', says Langley. 'This seems to have its roots in a defensive attitude, conservatism and resistance to change.' According to the University, neuroimaging will be a major focus of the planned facility. Sir Keith emphasised, however, that these techniques 'complement animal research rather than substituting for it.' Sir Keith stressed that imaging is still too crude to answer many key questions: 'It's like trying to understand a computer by looking down a microscope at a silicon chip.'

In addition to the strong resistance from animal rights campaigners at the trial, Cambridge University faced further opposition from the district council who called upon various police officers to testify over the risks of increased 'crime and disorder' from violent protesters, should permission for the facility be granted. Matfield testified, however, that since the animal welfare groups campaigning against the proposal make up the less radical end of the animal rights movement, the demonstrations are likely to be 'less frequent, smaller and less aggressive'. The council expressed support for the proposal in principle but made it clear that another site must be chosen. Despite the council's offer, the University insisted that the proposed site was preferred because of its close proximity to the Wolfson Imaging Centre and University complex, which would allow collaboration, and enable scientists to move between multiple sites on a daily basis. 'The whole will be greater than the sum of the parts if this proximity is achieved', said Sir Keith. 'Complete facilities would also mean that the amount of information gained from each experiment will be greater…we could need fewer animals', he added.

The University emphasised the disadvantage that the UK will suffer if the centre is denied: 'This could have a big negative impact on neuroscience in the UK and Europe', says John Capitanio of the California National Primate Research Centre. The research would 'eventually be conducted elsewhere, and possibly in countries with less rigorous legislation and lower standards of animal welfare', confirms Rothwell.

It is easy for most to assume that scientists are testing on animals in a real attempt to reduce human suffering, and that we are indeed researching alternative methods. But is it worth double-checking occasionally? Do we really challenge the animal model to ensure that it is still valid today, and not a relic of earlier times? Could imaging techniques be used to replace some areas of invasive neuroscience? Is the likelihood of scientific fruition high enough to outweigh the primate suffering? What is the destiny of primate research? Maybe the issue is not as cut and dry as we once thought.

The inquiry, which ended on 8 January 2003, was concluded as Nixon compiled a report for the deputy Prime Minister, John Prescott, who will be taking the final decision any time now.

From the balance of opinion apparent at the Cambridge Neuroscience Centre inquiry, it would seem that in the UK, at least, the future of the animal model is skating on thin ice.

Keri Lee Page
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Cellular abnormalities in models of septic shock and in clinical disease

Dear Editor

In spite of the fact that the article by Reade (2002) is entitled *Cellular abnormalities in models of septic shock and clinical disease: one example of how rats and humans differ*, careful reading reveals an acknowledgement of the need for animal experimentation in the final paragraph. We believe the fact that this is not flagged in the title, or in the subsequent four paragraphs, is unfortunate.

Reade's article raises several important physiological, philosophical and political issues which we consider here. While we agree with much of what Reade says, we believe his comments need to be put into an appropriate context.

Physiological issues

Before dismissing them, the strengths and weaknesses of the various animal models of clinical sepsis need to be considered.

As a generalization, the majority of research into experimental shock has employed *in vitro* methodologies, or *in vivo* studies in anaesthetized animals given large bolus doses of bacterial lipopolysaccharide (LPS) which cause substantial hypotension, and death within a relatively short time (for comment see Gardiner *et al* 1995b); Reade's article focuses on these approaches. Although such models have provided useful information about putative mechanisms contributing to the development of the shock state, they have failed to address, properly, the role of these mechanisms in the functional outcome. Nowhere is this more striking than in the assumption that the marked fall in systemic arterial blood pressure following bolus injection of LPS is due to widespread vasodilatation when, if you take the trouble to measure haemodynamics, it is clear the hypotension in those conditions must be due to an acute drop in cardiac output because there is little vasodilatation (Gardiner *et al* 1998).

Some time ago we were concerned about the ability of bolus injections of LPS to simulate the effects of clinical septicaemia, so began to investigate the possibility of replicating some of the cardiovascular sequelae of the clinical condition by giving continuous i.v. infusions of a low dose of LPS for periods of up to 32 hours in conscious rats. This approach has allowed us to delineate the profiles of change in cardiac and regional haemodynamics (Gardiner *et al* 1995b), and to demonstrate significant, but transient, increases in tissue iNOS activity and plasma TNF-α levels. It is notable that, in our model, iNOS activity reaches a peak at six hours and is back to normal by 24 hours, while plasma TNF-α peaks at one hour and is normal by three hours (Gardiner *et al* 1995b; Waller *et al* 1995). This puts into perspective the rodent data alluded to by Reade, and taken by him to indicate fundamental rat/human differences. We have drawn attention to the dissociation between cardiovascular status and iNOS activation in the context of the possibility that NOS inhibition could have detrimental effects in patients with signs of a hyperdynamic circulation (Gardiner *et al* 1995b). Subsequently, we demonstrated functional involvement of opposing vasoconstrictor (Gardiner *et al* 1995a, c, 1996a, b, c, 2001) and vasodilator mechanisms (Gardiner *et al* 1995b, 1999a, b) with different degrees of contribution at different times during infusion of LPS (Gardiner *et al* 1996c), together with temporal variations in vascular sensitivity (Tarpey *et al* 1998). These features are, where they have been investigated, also seen in clinical septicaemia.

On balance, then, we suggest that an appropriate rodent model of endotoxaemia is able to mimic many of the events seen in the clinical situation, in spite of the latter being so variable in aetiology.

Reade also mentions the failure of clinical trials to demonstrate benefit from interfering with actions of individual mediators in septic shock. But this is exactly what would be predicted by our rodent model. Thus, TNF-α antibodies have no effect on the cardiovascular sequelae of LPS infusion in conscious rats, in spite of marked changes in plasma TNF-α levels (Waller *et al* 1995). Moreover, treatment with antibodies to TNF-α and IL-1β, at doses that abolish the haemodynamic effects of administered cytokines, has no influence on responses to LPS (Gardiner *et al* 1998). We have pointed out that it is feasible the antibodies do not reach the sites of production and local action of endogenous cytokines during LPS infusion, and some support for this proposal comes from the finding that inhibition of production of TNF-α and IL-1β production with FR 167653 does have a significant effect on some of the haemodynamic changes during LPS infusion (Gardiner *et al* 1999c).

Finally, Reade refers to observations on arterial smooth muscle from patients with septic shock, showing increased heme oygenase-1 when iNOS activity was decreased. Interestingly, this is a very similar picture to that seen in conscious rats infused with LPS for 24 hours (Tomlinson *et al* 1998).

So, we encourage Reade to continue his important clinical studies, but to place them in the context of findings in an appropriate animal model of septic shock.

Philosophical issues

Reade's feature considers the extremely difficult question of the ethics of obtaining tissues from comatose patients in septic shock, but does not answer it directly, and suggests that tissues obtained as a result of a necessary clinical procedure may be worth studying. However, it is clear that the 'history' of such tissues is going to be extremely variable, even when obtained from the same 'type' of patient (e.g., those undergoing bowel resection following large bowel perforation). In addition, many septic patients will not undergo such procedures, and it seems that there may be almost as many different clinical profiles as there are patients in the ICU. This raises the knotty question of what it is that any model should be simulating. It is possible the answer is that we should have a range of models, representing the range of clinical cases.

Political issues

If we were members of the scientific arm of the BUAV, we would take the title of Reade's article as evidence that animal experimentation is not worthwhile. However, as indicated above, this is not a fair interpretation.

Reade's article is also relevant to the politics of anonymous peer review and, presumably by coincidence, an article on this topic appears in the same issue of *Physiology News* (Cain, 2002). We are all aware that, in these days of fierce competition for funding and RAE grades, decent scientific behaviour has suffered, and anonymous referees are on the look-out for any material to support their offhand criticisms. If Reade's article passed without comment we are concerned that it might provide more ammunition for those dark forces!

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Michael Reade responds:

Drs Bennett and Gardiner write at length about my recent article (Reade, 2002), which highlighted major discrepancies between the function of nitric oxide synthase in cells from patients with clinical sepsis, and those from many studies of rodent models purporting to mimic the human condition. Drs Bennett and Gardiner have published many studies of one rodent model of sepsis, which it turns out has many of the features of clinical human disease. In the light of this, they write in defence of the validity of animal experimentation. They appear to have missed the point of my article. I specifically state that I do not 'suggest that animal experiments have no role to play. Indeed, quite the opposite …'.

My fundamental point was that animal and cellular models are just that – models – of human disease. Any model must be validated against the disease it claims to mimic. It is only by doing this that more accurate representations of disease processes can be developed. I congratulate Drs Bennett and Gardiner, who appear to have developed a better model of human sepsis using rodents than that in the bulk of the published literature. But surely they can only claim their model is 'better' than those preceding it in the light of studies – like mine – of clinical human disease?

Drs Bennett and Gardiner write of 'Political issues', but there is also a political dimension to our own research. As I briefly outlined in my article, it is usually not possible to obtain informed consent from patients with sepsis. Even gathering clinical information, let alone biological samples, without consent, is highly controversial. UK Medical Research Council and European Union guidelines recommend proxy consent, combined with the need for retrospective consent from the patient. Unfortunately, UK law does not allow proxy consent for research. If current European Union recommendations are introduced into UK law as it now stands, essentially all critical care research in the UK will cease, as we have recently reviewed (Reade, 2003). While this would obviously impact clinician scientists, basic scientists such as Drs Bennett and Gardiner would then have no yardstick by which to judge their improved animal models of human disease.

Drs Bennett and Gardiner appear concerned that some might interpret my article as 'concrete proof that animal experimentation is worthless'. Clearly this is not the case. In truth, through different experimental methods we have both done exactly the same thing: demonstrate that the 'conventional' animal models of sepsis are inappropriate. I hope the next steps in this research will bring clinical and basic scientists closer together, in ever more successful attempts to model and then modify the response to sepsis. Only through this co-operation will our research be of benefit to the patients in our hospitals.

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Should we press for open peer review?

A selection of letters in response to the *Editorial* and *Unbelievable* (*Physiology News* **49**, 3 & 25)

Dear Editor

I think this idea of irate colleagues pursuing one at meetings etc is and always has been a red herring. If criticisms are properly justified there's not really a problem (and editors shouldn't make a final decision until they've properly heard the debate). The current system actually allows and encourages poor quality refereeing because no-one has to justify themselves to the degree required in a open system.

I say scrap it and have the entire system open. Papers should only be rejected when they are demonstrably technically flawed or demonstrably wrong in approach or interpretation. With grey areas, we should probably err on the side of publication. The final arbiter for science is reproducibility and internal consistency and that judgement is not down to individuals, but in fact emerges from the corporate enterprise.

John Lee
Rotherham General Hospital

Dear Editor

Poor reviewing by anonymous referees is a scourge of publishing! Here is one suggestion that may improve the system without completely getting rid of anonymity.

I would suggest that papers be reviewed anonymously until acceptance. Upon acceptance, the reviewers that recommended acceptance should be named under the authors: 'Recommended by xxx'. Reviewers who specifically suggested that the paper not be accepted, or who were non-committal, would (at their choice) be left off the list, or specifically listed as 'Objections raised by xxx' or similar to indicate their lack of support for publication.

What are the merits of this system?

- The otherwise thankless task that reviewers do can be acknowledged publicly. As a journal editor, I know that this issue is a problem. With

nothing in it for the reviewers, only the most conscientious citizens will accept review assignments.

- Reviewers who accept a paper can be credited with recognizing good work when they read it. In time, the abilities of a good reviewer -critical to the efficient publication of worthwhile science (and hence to the rate of progress of science) – will become recognized and acknowledged.
- Reviewers who may be falsely accused of letting dross get through can be acknowledged for their reticence!
- Reviewers who accept poor or flawed papers could (and should) be recognized for this, hence obliging reviewers to be more cautious about increasing the 'piles of second or third rate papers' that you note we all have to plough through!

Colin G Nichols
Department of Cell Biology and Physiology
Washington University School of Medicine

Dear Editor

I was very happy to read your editorial in the last issue of *Physiology News*.

I fully agree with your point that refereeing must be open; I do believe that the current system of anonymity, which allows quite a degree of manipulation, is simply

dishonest and indecent. The journal I am currently running (Cell Calcium) has had an open refereeing procedure for the last 22 years, and I am extremely happy with it.

The purpose of peer review is, at least in theory, positive, i.e. referee's comments should improve the quality of a paper, rather than turn it down. I have examples of papers going through several rounds of refereeing, which finally substantially improves the quality of the material. Moreover, whenever referees decide to reject the paper it is always very well documented and based solely on the paper's scientific merit. So you have my supportive voice! And the impact factor (IF) system, when used for judging scientific achievements of individuals, is a disgrace. The IF merely reflects the smartness of editor(s), e.g. publishing one or two special issues per year (which are essentially a collection of reviews) immediately increases the impact factor as do invited reviews.

Alex Verkhratsky
School of Biological Sciences
University of Manchester

Dear Editor

Thank you for your Editorial, the gist of which I fully support. To the argument that anonymous peer review should go, I would add that:

1 We are supposed to live in a culture of transparency and accountability but British science does not currently subscribe to this ethos.

2 You mention the problem of prejudice and bias, but careless review is probably an even greater/more common problem, especially for funding applications. Competitors are easily identified, but damning remarks from referees who have not bothered to check the literature can easily pass unnoticed by those who make the final decision. Often, reviewers are clearly not experts in the field (you can tell that from their comments) but that does not seem to stop them expressing (critical) opinions.

3 Identifying reviewers would also help to identify 'scientific networks/ syndicates'

4 It is often claimed that it would be hard to find anyone willing to offer a critical review. Under those circumstances, failure to find a referee (even from a list nominated by the authors/applicants) could be an alternative justification for a rejection. Nevertheless, I doubt whether this would be exercised much. In my experience, authors/applicants are extremely grateful for VALID criticism of their work: it saves a more public humiliation at a later date.

I await with interest the next installment of your editorial.

Clare Stanford
Department of Pharmacology
University College London

Dear Editor

Your editorial strikes a chord. I agree that referees should put their names to reviews: after all, this is done for book reviews.

The issue of irate colleagues would probably be met by, instead of one line rejections, referees indicating how the work might be brought, in their opinion, up to a publishable standard. That being so, the journal should be prepared to consider a resubmission. I find it disheartening that having gone down this route, *The Journal of Physiology* just does not want to know.

Personally, I value the refereeing process because out of every clutch of referees, at least one knows what he is talking about and makes useful comments. Often, that person is the most moderate of the bunch.

There might be a case for starting a low cost e-journal for papers savaged by referees- perhaps *J Physiol Rejects*. After say five years, the impact factors could be assessed to see where the good papers found a home.

James Morrison
Institute of Biomedical & Life Sciences
University of Glasgow

Dear Editor

I read with great interest your article, and that of the irrepressible Mr Cain, on the subject of peer review. Having myself been only too frequently a 'victim' of what might be called over-subjective refereeing, I am broadly sympathetic with the idea of an open (i.e. non-anonymous) system of refereeing. Producing a signed review of peers' work certainly focusses the mind on the science involved and suppresses the temptation to let loose any prejudice one might feel.

I would also suggest that an open system might carry other benefits. For example, how many times have we been obliged to contact the editor of a journal to chase up tardy referees? I've lost count too. I suspect that, in many cases, the tendency of some referees to sit on a manuscript for a few weeks (months?) might be reduced if the identity of the referee is known to all concerned.

Another point, related to the above, is that of deliberate delaying tactics or even – to put it bluntly – pinching other peoples' ideas. One cannot help but be a bit suspicious when, after a review process lasting six months or more – and ending in rejection – an uncannily similar study is published by a 'rival' laboratory. Again, I suspect that a more open system of reviewing would lessen this kind of thing, or at least make us feel a little less bitter when such 'coincidences' do occur.

Having said all this, the acid test would be: Will referees be happy to put their name to their reviews? In a lot of cases, probably not. Human nature being what it is, etc. If this is the case, I suggest the responsibility – and it's a serious one – to ignore non-objectivity and prejudice lies with the editor/grant committee chairman. As does a more proactive approach to chasing up referees and, in general, making sure that the whole process of peer review is as 'clean' as possible. It's lot to ask, but it's essential to ensure that good science is recognized as such and gets due credit whether it originates in ***ford, ******bridge or ***field.

Len Best
*University of ***chester*

Dear Editor

I give my total support to the concept of grant reviewers being named. There is a lot of rot talked about the need to 'protect' referees but if referees provided their considered, argued, rational comments on an application, there would be no need for 'protection'.

On the other hand referees, scientists though we are, are only human. We all have people we like and to whom we wish to give a helping hand, and those whom we despise for one reason or another. More importantly, perhaps, there is always the knowledge that the more grants one approves, the less money there remains for one's own application. This is a greater problem in the UK than in the US where far more funding is available. If anything, removing anonymity may be viewed as a means to 'protect' referees against themselves from letting any such bias creep into their assessments. An alternative would be to use ONLY referees who are not able to apply to that granting body, such as referees from abroad (though personal likes and dislikes may still occur).

I also feel that granting bodies should be fairer in their appraisals. It is easy to criticize anything, or to suggest additional work (even though no project can answer all the questions), or alternative approaches, or to indicate non-quoted references (ignoring space constraints) etc. in order to make an assessment seem more negative than it really is on hard scientific grounds. Striking a balance is likely to be worse for younger reviewers who are often keen to show off how critical and incisive they can be, whilst not seeing that despite all their detailed reservations, 80 per cent of the work will be done well and the project as a whole will yield valuable data to the field. Granting bodies should be much more objective in seeing through this and making judgements by separating true criticism of the scientific hypothesis or methods to be used from these peripheral comments, and taking an overall view of the value of the project irrespective of the amount of wordage used to criticize. This is especially the case when experienced researchers with a major track and publication record are the applicants. All that may be needed are some constructive, helpful comments from the external referee rather than a critical assessment of the project and applicant as if he/she were a first-year postdoc. (There also needs to be far more caution though in assessing criticism of hypotheses, since this may stifle novel, innovative ideas and challenges to accepted dogma.)

As to papers, it is true that one can resubmit to other journals if rejected, but many of the same comments apply to journal refereeing: the removal of anonymity would increase the objectivity of reviews, increase author satisfaction and reduce the need for repeated revisions, reformatting, delay to publication, etc.etc. The only non-scientific reason for rejection should be lack of space in a journal, and that will presumably disappear as a reason as more publication is effected electronically.

I could go on since, like so many of us, I have suffered at the hands of this antiquated system for too long, but I trust these comments are helpful. I should be more than happy to comment further or in another forum if that would help. I do think that the major societies should lobby hard and collectively to get these reforms passed.

Trevor W Stone
Institute of Biomedical & Life Sciences
University of Glasgow

Dear Editor

Some comments from a lapsed and retired physiologist.

1 Is there a problem? How many complaints about referees? What are the editors' experiences and views?

2 Refereeing is essential for the reputation of the journal and of future authors

3 Anonymity – yes. This allows frank views without giving personal offence or conflicts with funding or status. Any disputes should be resolved by the editor and his advisory panel. He is there to protect the author and see fair play (not always easy as I know).

4 Would it help if the author was anonymous to the referee?

5 Book reviews are different; reviewers should be named. There is no obligation to an editor or a journal; the author is not bound by scientific conventions but is free to discuss and speculate as he wishes. Purchasers gain from knowing the reviewer (his standing and foibles etc.)

Alan Sykes
Walthwaite How, Chapel Stile
Ambleside, Cumbria

Dear Editor

I have read with interest your Editorial comments in *Physiology News* on the question of peer review and would like to offer my views even though, since I am now retired, they may seem a bit dated.

It is my unequivocal opinion, having served both as an editor and as a member and chairman of granting committees, that anonymous peer review of papers and applications is absolutely essential. The proviso, of course, is that there must be at least two independent reviews of any submission, and that if the opinions received are seriously divergent (or if one betrays any evidence of bias) that one or more further opinions be sought. This can, of course, occasionally cause delays in processing, but does I believe provide the optimal method for ensuring that 'the cream will float' and that inferior or trivial work will not.

Congratulations on doing a fine job with the *News*.

Hugh McLennan
Vancouver, BC, Canada

Dear Editor

Responding to your recent Editorial in *Physiology News* and Mark Cain's comment, I offer some thoughts on the referee process. My first paper was published, in *Nature* as it happened, in 1957 and my most recent has just been accepted by a different journal, so readers will see that I have been in the game for some considerable time. Now it happens that I work in two fields of physiology, related in concepts, but with colleagues who do not overlap. In one of these fields I flatter myself that I am a bit of a sage, in the other I am a very definite maverick.

The point that I want to make is simple, and is very clear to me from experimental evidence that I shall not detail. Under the present system of anonymous referees the weight of the report is usually not on the science of the work under review, it is on the reviewers' perception of the team that carried it out. Maybe this is inevitable, now that science has become much more competitive than it was when I started out. The RAE has not helped, nor has the awareness of the accolades that are available from the Nobel and other similar systems. (Lest I be suspected of sour grapes I mention that in the most recent RAE I was returned in a 5* department, though not a physiology department *per se*.)

People asked to review, often rather ignorant of the precise science involved, are none the less very adept at sniping from behind covers, a practice that I was taught to regard as unsporting, except in trench warfare. Often I think they are motivated by much the same thoughts as a dog defending its patch. Charitably, one might suppose that this is because they see the total science cake as limited, and that they therefore act unconsciously to limit the share of it that goes in directions that they do not personally approve.

Maybe it is only a minor irritation to need to select with care journals where one can be confident that one will receive fair referees. It is a talent that one acquires with experience, though it means that one's best ideas may be published where they are less visible than one might wish. The major sadness of the situation is in the grant-awarding system, where new ideas and new techniques can be largely discounted in an established field, unless they can be made to accord with the pre-existing weight of received wisdom. This is bad for science itself, which advances through the revision or overthrow of paradigms that are founded on sand though they may be widely accepted.

Can anything be done to reverse this trend? I believe firmly that the answer is to insist that all referees should be identified to all parties. The journal *Cell Calcium*, where this is done, is respected and publishes high-quality papers. The Editor, Maynard Case, wrote to *Nature* (1996, **379**, 292) in response to John Maddox's defence of confidentiality '*the requirement to sign the report, while reducing the invective, in no way lowers the scientific rigour of the referees who, unable to hide behind unsubstantiated generalisations, are forced to focus on the facts. Is that not what science is all about?*'.

I understand that this would make it more difficult to find people prepared to referee, a point made by Maddox and others. Unless editors (and chairman of grant-awarding panels) have the courage to disregard referees who are clearly prejudiced (however distinguished they may be) this is the only safe way forward, in my opinion. In my quite long experience, very few editors are that bold, with the honourable exception of Sir George Radda.

Gerald Elliott
Department of Optometry and Vision Sciences
Cardiff University

Dear Editor

I strongly agree that authors should normally be told the names of referees. When I act as a referee for a paper submitted to a journal, I almost invariably ask for my name to be divulged to the author(s).

Andrew Huxley
Grantchester, Cambridge

Dear Editor

With very few exceptions I have signed all referees' reports for the last 20+ years. I have had no problems with enraged authors. Very often any criticisms I have make have led to a constructive dialogue. I think anonymity is morally wrong in what should be an open scientific community – but I have never had any success in propagating this view! Perhaps, if you agree, you could help.

John C Waterlow
15 Hillgate Street, London

Staff changes

Members of the Society may have heard that our Chief Executive, Esther Williams, left us at the end of September 2002. This she did for personal reasons and with the amicable agreement of the Executive Committee after having been in post for five months. This had been an eventful time for the Society during which detailed negotiations took place with Blackwell's (the new publisher for our journals) and considerable reconfiguring of the Society's staff occurred.

The best way forward was debated at length by the Officers and by Council. It was considered that continuity and a period of stability were a priority considering that there had been three Chief Executives over the previous year, including a temporary one for over six months, and that three other experienced members of staff had resigned over the Summer. Furthermore, a speedy resolution was thought to be necessary. Consequently, two important decisions were made: firstly that the position of Executive Secretary would more aptly describe what the Society required of its most senior employee; and secondly that internal appointments should be made to the senior executive positions of the Society. The positions of Executive Secretary and Deputy Executive Secretary (with particular responsibility for External Affairs) were advertised internally and interviews were held at the beginning of December. The interview panel consisted of two Officers and three members of Council, one of the latter being on the Editorial Board of *The Journal of Physiology*.

I am delighted to inform you that David Sewell was appointed as Executive Secretary and Maggie Leggett as Deputy Executive Secretary. David has been the Society's accountant since August 2001 and has been effectively the deputy Chief Executive since then except when he was acting Chief Executive in the hiatus early in 2002. He studied Chemistry at UCL then trained to be an accountant. He has worked in both public and private sectors but most recently for a charity, the Red Cross. He has extensive financial experience and has been a company secretary on two previous occasions.

Maggie will be well known to many members for she has worked for the Society for many years; even so some may not be aware that her PhD was in genetics. Her experience in dealing with all things educational for the Society, her links with the British Association and many of our sister societies and her networking of contacts make her well suited to take on particular responsibility for the external affairs of the Society. The establishment of the Biosciences Federation (of which the Society is a founder member) makes it essential for us to give a high priority to this aspect of the Society's work.

Lest more sceptical members start thinking that we have more bureaucracy than ever, let me assure you that because of the increasing centralisation of the Society's work and some internal reallocation of responsibility there will be one less post in the London office in future.

Dafydd Walters

International collaboration – ICSU statement

At the Annual General Meeting of the Society in Leeds in September 2002 there was some discussion about the universality of science.

Specifically, the topic was the stance of the Society in the support of and collaboration with scientists working in countries with which there may be some political disagreement or the action of whose governments were questionable. Comments from members indicated a very strong view that there was no place in the practice of science for discrimination based on nationality, religion, ethnicity, gender, politics, etc. The Society is affiliated through our membership of IUPS (International Union of Physiological Sciences) to ICSU (International Council of Scientific Unions) whose statutes contain statements with which our Society has agreed. It was proposed at the AGM that the relevant ICSU statute, number 5, be placed on the Society's website and our adherence to it be reiterated. This has been done. There was also a request that attention be drawn to it in *Physiology News*. The statute is reproduced here.

ICSU statute 5

'*In pursuing its objectives in respect of the rights and responsibilities of scientists, ICSU, as an international non-governmental body, shall observe and actively uphold the principle of the universality of science. This principle entails freedom of association and expression, access to data and information, and freedom of communication and movement in connection with international scientific activities without any discrimination on the basis of such factors as citizenship, religion, creed, political stance, ethnic origin, race, colour, language, age or sex. ICSU shall recognize and respect the independence of the internal science policies of its National Scientific Members. ICSU shall not permit any of its activities to be disturbed by statements or actions of a political nature*'.

The Guardian newspaper has published several letters and articles on this topic over the past few months. Discussion and interpretation of this statute is unlikely to end soon given the current political unrest in the world and the fact that these statutes affect all scientific disciplines, not just physiology. Perhaps the Editor would be willing to publish articles expressing some of our members' views in the next edition of *Physiology News*.

Dafydd Walters

Speakers in schools database

Earlier in the year many people responded to my email regarding a UK Life Science Committee (UKLSC) initiative to compile a database of academics willing to give talks in schools. The database, stored on www.biology4all.com is freely available and searchable. It has been developed by Dr Peter Robinson, a member of the UKLSC Education Group.

Colin Blakemore (left) with Peter Robinson

The initiative was launched formally at the British Association Festival of Science at the University of Leicester on 12 September, 2002. The Physiological Society president, Professor Colin Blakemore, opened the proceedings, followed by a short talk by Peter. The event was publicised by the media the week before, and has gained significant coverage since.

The launch went well, and there was considerable interest from academics, journalists and members of the public. However, we are all aware that this is only the beginning of the project. More speakers are needed to get complete coverage of the UK. If you are interested, you can register yourself on the database, or email me for further details. Eventually we hope that every school will be aware of the scheme, and they all have access to an academic.

The launch was supported by the Physiological Society. The Biochemical Society, Society for Experimental Biology and the British Society for Immunology support the website.

Maggie Leggett

Research Defence Society

2002 has been a busy year for the Research Defence Society (RDS). They launched a new booklet (*The Hope, the Challenge, the People*), as well as maintaining their usual highly visible media and parliamentary contact, and educational programme. It was therefore fitting that the programme for the RDS Annual General Meeting on 25 November, 2002 included some of the finest speakers. Among them, Dr Simon Festing, the Director of AMRC, gave an interesting insight into campaigning. He gave a very positive view of the current state of in vivo research in this country, and felt that the anti-vivisection movement was at an all time low. However, he recommended building on the current position, and stressed the importance of responding to media enquiries and inaccurate reporting. Tony Gilland, from the Institute of Ideas, painted a somewhat gloomier picture. He pointed out that the ever strengthening ethical and legislative process in this country was suggestive that scientists were guilty until proven innocent. He further argued that a society which elevated the rights of animals over humans was inhuman.

After tea, our President, Professor Colin Blakemore, spoke about mapping the future of neuroscience. As ever Colin was entertaining and easy to understand, describing the mapping of various activities to parts of the brain, and stressing the past and continuous need for animal experimentation.

Last, Professor Lord Winston gave the Stephen Paget Lecture. Lord Winston addressed the question of why as a species we are so infertile, and also outlined the current hazards of IVF. He

A simple question

Why are most research symposia so dull?

A couple of postdocs I know – let's call them Ian and Matt – asked me this the other day. Well, evening actually, after a pint or three. But the next morning, as I stirred my breakfast soluble Aspirin, I got to thinking.

Just why ARE most symposia – and plenary lectures, for that matter – so dull? Duller than the average departmental seminar, if you ask me.

Let's try and think of some reasons.

Reason one: because of the subject matter – science.

Not that science is dull.

But it can SOUND very dull, if you describe it in a very dull way.

Now there are people in the trade who think that no piece of scientific data can ever be dull. To them I have only two words – Asperger's Syndrome. However, for the rest of us, I think we could agree that, talk-wise, the nitty-gritty of the science – the experimental data – is never going to be as interesting to the listeners as it is to the speaker. This is because the speaker was generally (although not necessarily) one of the people who actually planned or did the experiments, and thus has a big personal investment in the data.

But this brings us on to something important, namely:

It is the job of symposium speakers to explain their data. And yes, you could even say, to 'sell' it to the audience. No matter how famous the speaker, and how big a plenary lecture it is, they still have to make us want to listen.

Or at least, they should.

Let's summarize this as 'Scientific Talk Rule One':

- It is not enough to just stand up and describe a load of your experiments

You have to tell people what they are about, why you did them, what they show, and so on, all without talking in impenetrable jargon – be it electrophysiological, neuroanatomical, molecular biological or whatever – or even worse, in abbreviations.

In other words (Rule Two):

- Tell them a story

And (Rule Three):

- Keep it simple and EXPLAIN

Nothing very complicated there, we can all agree.

Unfortunately, in practice it doesn't work out like that.

Experience suggests that many eminent scientists giving invited talks in national and international symposia have never heard Rule One.

Instead, they adhere to 'Professorial Rule 1A'. This is a re-write of Rule One as follows:

It is not enough to stand up and describe a load of your experiments. Instead, you should stand up and describe at least three separate loads of experiments, each enough for a talk on its own, all delivered at breakneck speed in your allotted time plus 15 minutes.

Furthermore, rules two and three should also be modified:

Professorial Rule 2A: Don't bother telling a story. Anyone worth your time and consideration will already know all the background, and all your previous work, so you should jump straight in with the incredibly fascinating minutiae.

And Professorial Rule 3A: In order to make it clear that you still have full command of the techniques your army of assistants use in the lab, you must keep it as complicated as possible and avoid unnecessary explaining.

Result: The audience will be awe-struck by how large your research group is (in order to churn out the huge volume of work you have described) and how cutting-edge your research is (because they didn't understand anything you said). Thus you will have shown them that you are a BIG PLAYER. QED.

Quod erat disillusionem?

Now I don't want to leave you with a completely negative message, so I should say that there IS a simple way to avoid talks like this at symposia, or in plenary lectures.

Don't invite the people that give them to be speakers.

But that depends on the people who organise the symposia. Which brings me on to what I hope will be the next column:

Symposium organisers: the truth.

Watch this space.

Mark Cain

stressed the need for this kind of treatment to be available on the NHS, as otherwise the commercial drive misplaces emphasis and in this case can lead to overuse of the potentially dangerous super ovulation drugs, and reimplantation of more embryos than sense and science dictate.

The Society continues to maintain strong links with the RDS, and to support its activities.

Maggie Leggett

British Association Festival of Science

In 2002 at the BA Festival the Physiological Society organised a session entitled *Health in old age*. The overall theme was *Science and the quality of life*, and as the festival always attracts many retired people we were hopeful of a good audience and lively discussion.

Despite one of the speakers, who will remain nameless, forgetting all her clothes, we were otherwise ready to go at 9.30 on the morning of 14 September at the University of Leicester. The first speaker was Professor Tom Kirkwood, from Newcastle University, talking about *Aging and immobility*. Tom's presentation was excellent, clearly explaining difficult concepts and the progressive disintegration of telomeres and the potential use of stem cells. Needless to say, the audience responded well, questions were intelligent and discussion lively.

Next, Professor James Malone-Lee, from UCL, spoke about incontinence. James was hilarious, dealing with a potentially delicate subject with humour and affection. He communicated an unbelievable passion for the disposable nappy, and was also really interesting, as he explained his personal crusade to stop the use of old crisp packets and dead mice as absorbent materials, and explained the reasons for toxic shock syndrome.

It was a hard act to follow but Olga Rutherford, from King's College London, rose to the occasion admirably. Olga's talk entitled *Bone fit for life* started with some pretty shocking statistics, such as that one in three women would be affected by osteoporosis, and one in 12 men would suffer that same fate and end up with a fractured hip, unable to walk properly again. The audience concentrated as she explained ways of exercising to keep bones healthy and the implications of preventing bone decay. The ensuing debate was lively and Olga did well to deal effectively with some fairly sticky questions, for instance in relation to HRT.

Dawn Skelton, also from UCL, completed the programme. Dawn talked about falling over and the necessity of preventing this in the older population. Again there were alarming statistics such as that one in three people over 65 fall over every year and the even more sobering thought than even during her talk, three elderly people in the UK would have died as a result of a fall. The results of the research presented certainly got the audience going, and many people stayed around afterwards to continue the conversation.

Once again, in comparison with other areas, we attracted one of the largest audiences. One speaker was subsequently hauled off for a radio interview, another to a press conference and I received requests for two of them for the 5.30 round up of the 'best of the festival'. We have featured good contracts with the BA and are now respected as providing a valuable contribution to the festival. I can only look forward to 2003 and the University of Salford. The theme there will be *Sustainable science*, and the Society session will be entitled *Sustainable people*, with talks on making new organs, etc. If you would like to become involved, either as a speaker or to attend, please contact me as soon as possible.

Maggie Leggett

Careers conferences

This year, The Physiological Society took the lead in organising these annual events. They were held at Sheffield University on 2 November, Glasgow University on 16 November and King's College, London on 30 November, 2002. They were attended by over 600 students, of whom one third were postgraduates. There were more exhibitors than usual, with most of the major pharmaceutical companies sending representatives. The normal programme of talks about careers in research, science communication, clinical science and teaching were supplemented by talks on patent law and science sales and marketing. Feedback from the students was positive, with comments such as 'Wicked!' and 'Highly recommended'. If you are an Affiliate and unsure of your next step, be sure to come along to one of the conferences in November 2003. The venues are still being decided, so look out for an email alert in September.

Maggie Leggett

Physiological and Pharmacological *in vivo* techniques workshops

These workshops are a joint venture from the British Pharmacological Society and the Physiological Society, and were run for the first time during August 2002. They developed from a common worry about the ever-decreasing number of undergraduates with practical experience of this kind of work, and the difficulty of attracting PhD students with interest or ability in the area.

The workshops were generously supported by Pfizer, who share the same concerns. For the first year, courses were run at Glasgow University and King's College London. The courses were heavily over subscribed, and the maximum number of students

(27) accommodated. Feedback from both the organisers and attendees was excellent, and many students expressed a wish to continue in the field.

These courses are extremely expensive to run, and we are grateful to Pfizer in the first instance and to other pharmaceutical companies who are promising support in the future. It is hoped that the number of courses may be increased to three in 2004, and possibly extended to allow places for PhD students and post docs. The courses are advertised annually in October, and so if you are interested, keep an eye on the website or email alerts at that time, or contact me directly.

Maggie Leggett

Women in science – what are the issues?

When I took my PhD, I was one of only two women – both 1st year PhD students, in a department of about 25. The attitude and behaviour of my male colleagues varied, from mild flirtation to surprise that a woman should even want to start out on an academic career. I don't think I suffered anything that could be described as harassment or discrimination, but the overwhelming feeling that I was a fraud and not expected by anyone to succeed, and a strong dislike of the competitive banter of the coffee room certainly did nothing to convince me to stay in science. And in my position now, the sex ratios of young physiologist symposia compared with that of the Council or Heads of Department meetings give cause for disquiet.

The Women and Science Day at London Metropolitan University on 23 October, 2002 was the first time I had been in an academic environment that was all female. The atmosphere felt very different – there was one male delegate but he ran off quite early, and the Vice Chancellor (male) departed after giving the opening address. Perhaps women all together are as intimidating as men.

Frances Ashcroft gave an excellent opening address, and described some quite hideous barriers she had come up against on her way up the ladder, from not being offered one job, to being offered less money for another, purely because she was female. Joanne Millington, a forensic scientist from London Metropolitan, and Alison Adam (IT, University of Salford), both gave similar examples of discrimination.

In the discussion session after lunch several points were raised. Women are attracted by science degrees – in fact many Members report their undergraduate classes are heavily female dominated. Women are also well represented among applicants for PhDs. However, somewhere on the post doc junior lecturer ladder they are leaving science in their droves. Lack of family friendly career paths, lack of security in the career and lack of ability to stay in one place were all agreed as reasons why women leave. None of these is easy to solve overnight, although the Greenfield report has been welcomed by Government and certainly raises the issue in the public eye. The organising committee at London Metropolitan (lead by Dr Louise Archer) are in the process of drawing up a Charter based on the ideas generated during the day. There is definitely no longer a need for women to feel isolated. The day culminated in the launch of a new *SWAN* (Scientific Women's Academic Network). Contacting this or your local network is an excellent way to keep abreast of new developments, and form contacts that can help you in difficult times.

Louise Archer, post-doctoral research fellow, London Metropolitan University

Those interested in the London Met SWAN should contact Louise Archer at l.archer@unl.ac.uk.

Maggie Leggett

Claire Martin

Claire Martin, a medical student at Gonville and Caius College, who read Part II Physiology at the University of Cambridge, was awarded the Science Engineering and Technology Prize for the Best Biology Student of the Year (2002) by the World Leadership Forum on the basis of an undergraduate research project she pursued with me in the Department of Physiology.

She examined structure-function correlations in the triad structures, made up of closely adjacent transverse (T)-tubular and sarcoplasmic reticular (SR) membranes of skeletal muscle. These are believed to be the sites at which T-tubular depolarisation triggers release of intracellularly stored Ca2+ into the cytosol of skeletal muscle during excitation-contraction coupling. This involved a systematic study of the effects of extracellular solution tonicity on amphibian muscle anatomy, in particular quantitative measurements of the details of triad junction ultrastructure following cellular volume changes. Three-dimensional reconstructions from successive electron microscopic thin-sections permitted such quantitative examinations of triad anatomy. These results were compared with the propensity of the fully polarized intact muscle fibre to show spontaneous Ca^{2+} release events as reflected in fluo-3 fluorescence measurements using confocal microscopy.

This combination of techniques made it possible to test a hypothesis in

which the intramembrane dihydropyridine receptor (DHPR)-voltage sensors normally suppresses the gating of SR ryanodine receptor-(RyR) Ca^{2+} release channels through the allosteric couplings between these molecules in fully polarised quiescent muscle with DHPR activation by membrane depolarisation relieving this inhibition thereby permitting release of intracellularly stored Ca^{2+}.

Claire secured First Class Honours in her Part II Tripos examinations and is proceeding with her clinical studies in Cambridge University Clinical School.

Chris Huang

Proceedings in 2003

At the Society's Annual General Meeting in Leeds on 11 September, 2002 a decision was made to produce the final Proceedings issues of *The Journal of Physiology* in electronic format only. Therefore from 2003, there will be no printed issues of Proceedings. The abstracts from the UCL scientific meeting held from 17 – 20 December, 2002 will form the first issue to appear online only – http://www.physoc.org/Proceedings/

The decision to have online publication only will not affect the citability of these abstracts. These will be citable as usual with the volume number, but will be cited by abstract number rather than page number. The abstracts will be available, as usual, on the Society web page with additional links from *The Journal of Physiology* website. They will continue to appear on the ISI Web of Science.

Features available with Proceedings online include:

- Email alerts when a new issue goes online
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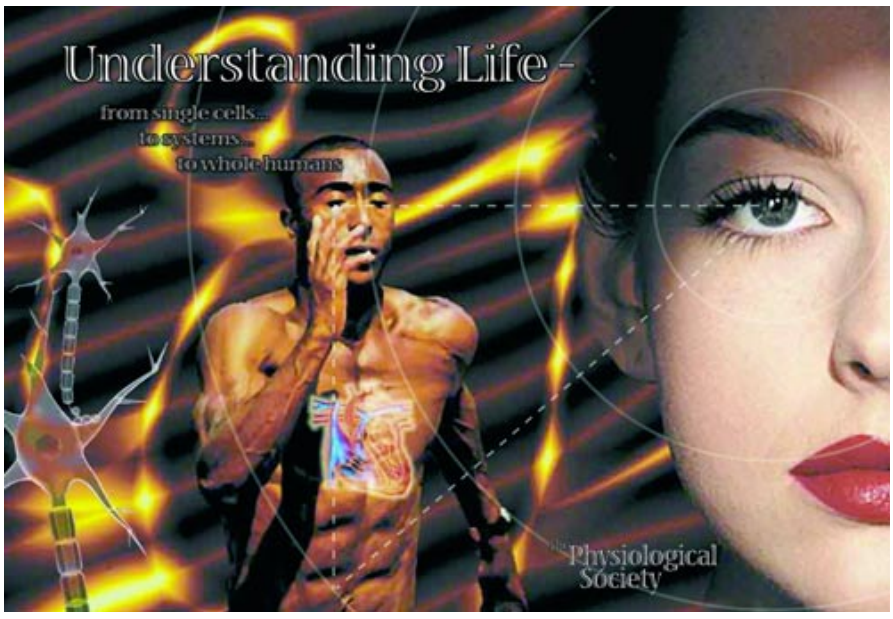
New *Cell to Man*

Many Members will be familiar with the careers booklet *Cell to Man*. It has served us well for many years, and persuaded lots of young people that physiology is the discipline for them. However, it was starting to look a little dated and so throughout last year a small group have been working on a new design. The most influential members of the group were Dr David Pepper, a biology teacher and former Member, and three of his sixth formers who could tell us what the consumer wanted in terms of subjects and images. Many Members also helped with the text, including Rob Clarke, Malcolm Hunter and Ron Maughan. We are also very grateful to Pfizer for their support and particularly to Mike Collis. The result (see below) is a booklet that looks at alcohol and liver physiology, neurophysiology and class A drug abuse, sports physiology and the use of cannabinoids in pain relief. There is also a section with case studies of physiologists pursuing a variety of different careers. Early anecdotal feedback has been excellent, comments including "riveting", "eye catching" and "wicked". If you would like to receive a copy, or several for an open day, please contact me at the office.

Maggie Leggett



Other Society News

Changes in Aberdeen

The telephone numbers for the Department of Biomedical Sciences in Aberdeen, beginning **2730** now begin **5557**, e.g. 273015 is now 555715.

Old volumes of *The Journal of Physiology*

Peter H Hartline (rkucera@attbi.com) has mint condition, bound volumes of *The Journal of Physiology* from the late 1970s to 1984. If anyone needs these journals or knows of libraries that would appreciate copies please contact him. The recipient would be expected to pay for the boxes and shipping, but not the labour to ship.

Young Musician of the Year

Pianist Danny Driver, Physiological Society Undergraduate Prize winner (Cambridge), recently won the Radio 2 Young Musician of the Year.

Any offers?

I am currently a second year undergraduate student studying biomedical sciences at King's College London. My subject covers a variety of fields, but I am mainly interested in genetics, cell molecular biology and physiology.

I am looking for a summer placement in a science orientated workplace. I do not mind what type of job it is, even if it is a voluntary position, as I would like the experience to help me decide whether I am interested in the experimental or theoretical aspects of my degree. The experience would also help me gain a deeper understanding of my subject area.

Shen Lin
shen.lin@kcl.ac.uk

Michael de Burgh Daly

1922 – 2002

Michel de Burgh Daly, MA, MD, ScD Cambridge, FRCP, Emeritus Professor of Physiology in the University of London and Distinguished Visitor Joint Department of Physiology Royal Free Hospital School of Medicine and University College, London from 1984 until his death, formerly Professor of Physiology and Head of Department of Physiology St Bartholomew's Hospital Medical College, London from 1958 to 1984, died suddenly on 1 March, 2002 at home aged 79, two months before his 80th birthday.

Michael was the eldest son of the late Dr Ivan de Burgh Daly, CBE, FRS, and was born in York on 7 May, 1922. He was educated at Loretto School, Edinburgh and Gonville and Caius College, Cambridge. He did his clinical studies at St Bartholomew's Hospital, London and graduated Natural Tripos Part I in 1943, Part II 1944, Physiology with Pharmacology. He then became a House Physician at St Bartholomew's Hospital in 1947 before commencing his career as a physiologist, following in his father's footsteps.

His first post in physiology was at University College, London where he was appointed as assistant lecturer (1948-50) and lecturer (1950-54). In early days as a physiologist he was influenced by Lawrence Mount, Alfred Schweitzer, Eric Neil and Chris Lambertsen in addition to working with his father. During this period he was awarded a Rockefeller Foundation Travelling Fellowship in Medicine (1953-53) which he spent in Philadelphia. He was then made a Locke Research Fellow of the Royal Society (1955-58) in the Department of Physiology University College. At the young age of 36 he was appointed to the chair of Physiology at St Bartholomew's Hospital Medical College and Head of Department – a position he held from 1958 to 1984 until he retired at the age of 62. At this time Professor Spyer invited him to move to the Royal Free Hospital School of Medicine in the Department of Physiology where he was to stay for the next 18 years. This move allowed him to continue with his research without the burden of committees and university politics. He was able to contribute to the department by teaching both the undergraduates and the research personnel who were able to take advantage of his knowledge and experience.

He was a good and dedicated teacher who willingly gave many hours of his precious time to teach others. He knew his own subject well and was meticulous over the details and content of his lectures. He made sure he was up to date and would even contact experts in their fields to get their advice about any advances in the subject of his lectures. However, he was a perfectionist and would not suffer fools gladly. He could not understand why other people could not do the things he did so easily, and some of his research students found him a hard taskmaster. He was still teaching and lecturing up to the time of his death, many years past the normal retirement age. Over the years he must have taught and influenced thousands of medical, science and research students all over the world. Many of his former students are now themselves professors and leaders in their fields, thus his influence on his subject has travelled far and wide.

He served on many committees and was very conscientious in attending them. He sat on the Ethical Committee at Bart's but was also a member of the Personnel Research Ethical Committee MOD (Navy) from 1975, becoming chairman in 1990. He also helped to supervise research in the Navy. He felt that by giving the Navy his expertise on the subject of diving and its implications in man that he would contribute to the safety and welfare of this country.

Research

His interest in the carotid body chemoreceptors and baroreceptors began early in his career. He was well tutored by his father, Ivan de Burgh Daly, who was an expert on the pulmonary circulation and they published papers together on this subject in *The Journal of Physiology* in 1957, 1958 and 1959. After his father retired from Babraham, they collaborated again in the 1970s, resulting in further publications. During the many years of active research which was still continuing at the time of his death, he developed the theme of the peripheral arterial chemoreceptors and respiratory-cardiovascular integration which culminated in his opus magnus, the Monograph of the Physiological Society 46, with this title published by Oxford University Press in 1997. His research covered almost half a century and his thirst for the knowledge of his chosen field led him to study many species of animals including seals in Alaska and monkeys in Australia. He had many

collaborators, some who came to him as research students and others as experts who contributed by having different skills. As a result of this constant stream of theories and experiments published in several hundred research papers, he produced many bricks building up a wall of knowledge, helping us to understand the underlying mechanisms involved in cardiovascular and respiratory reflexes. The studies involved anatomical and physiological experiments in which he always played a very active part. In many of the experiments it took him and an assistant, his technician Derek Bacon, who was with him for 35 years, 12 hours to prepare before any new information could be obtained from the experiment. He was a magnificent surgeon and would silently work for many hours painstaking dissections with magnifying glasses, often with instruments he had designed himself to make the surgery possible. There would be racks of Dale-Schuster pumps modified by him to produce a more natural pressure profile, mimicking that of the normal circulation, and tubes connecting different circulations, allowing all the parameters of pressure, flow, temperature, pH and chemical constituents to be independently controlled. He had a lathe in his office with which he was able to make and modify his research equipment. Subsequently he would spend many hours accurately measuring all his results – a task he found it difficult to delegate. The accuracy of his measurements was made possible by his careful calibration and zeroing of all measuring equipment before and after each experiment. In truth he was a master following from the traditions of other great cardiovascular physiologists such as William Harvey, in whose footsteps he followed.

He re-enacted William Harvey's experiments when he made a film entitled *William Harvey and the circulation of the blood* which received the Gold Medal from the BMA in 1972.

Travel was an important part of his physiological life. He enjoyed being invited to different parts of the world. One of his most momentous journeys was in 1975 when he travelled to Alaska with his colleague, Jennifer Angell-James at the invitation of Professor R Elsner to experiment on seals and to study the cardiovascular and respiratory reflexes. Single nerve fibres from the receptors were also going to be studied. This necessitated both physiologists taking apart their respective laboratories and packing the equipment up and rebuilding it in a laboratory of the University of Alaska. The arrival of all the packets of equipment caused not a little worry and confusion at the customs at the airport but was finally released and was able to continue its journey to the University. The Esquimox caught the seals which were transported from the Bearing Straights and there looked after by the animal technicians who were experts at feeding them by hand with fish. The same technicians were required to obtain giant frogs from the lakes to enable the nerve fibre recording equipment to be tested. Once the experiments were finally started they lasted from 8 o'clock in the morning to 5 am on the following day. However, although they were a huge test of stamina, they were entirely successful and resulted in several publications concerning the diving response and the cardiovascular and respiratory sectors and their reflex responses in the seal. These papers have recently been quoted in a book entitled *Biology of Marine Animals* edited by Jon Reynolds and Sentiel A Rommel 1999 in the chapter *Living in Water: Solutions of Physiological Problems* which was written by R Elsner, at whose invitation the seal studies had been performed. He had many assistants and collaborators over the years, including Dr Mary Scott (now Taylor), Dr Jennifer Angell-James, Professor Robert Elsner, Professor Janice Marshall, Professor Michael Spyer, Dr Jane Ward, Dr John Clarke and many more.

Research Grants

During his scientific life he was supported by numerous grants from such organisations as the Medical Research Council, the Royal Society, the British Heart Foundation, the Wellcome Trust, the Special Trustees of St Bartholomew's and St Mark's Hospital London, the Central Research Fund of the University of London and the National Institute of Health. During his career he received prizes: the Schafer Prize in Physiology, University College London 1953, the Thurston Medal Gonville & Caius College 1957 and the Sir Lionel Whitby Medal Cambridge University 1963.

In addition to all his research he contributed chapters in textbooks: Lippold and Winton *Human Physiology*, Starling *Principles of Human Physiology* and Emslie-Smith Paterson Scratcherd and Read *Textbook of Physiology*.

He was an active member of the Physiological Society, frequently attending meetings and presenting communications, posters or demonstrations and he served on its committee and was made an honorary member in 1986. He was co-editor of *The Journal of Physiology* from 1956-1963 and 1984-1989. He was a member of the Society of Experimental Biology and Chairman of the Monograph of the Physiological Society 1981-1987. He was also a member of the European Underwater Biomedical Society from 1971.

Family life

In 1948 he married Beryl Esmé, younger daughter of late Wing Commander A J Nightingale, whom he met when she was a nurse at Bart's. Family life was important to him and he had two sons and grandchildren to carry on his genes. However, he worked so hard and such long hours that his family must have seen less of him than they would have wished. His complicated experiments would sometimes continue well into the small hours of the night. He had a younger brother who sadly died at the age of 33 in a

helicopter crash in Malaysia. This had a profound effect on him and people who worked with him at the time said that his personality changed as a result, leaving him a quieter and sadder man. He tried to act as a surrogate father to his brother's children. He was a kind, gentle and very polite man with a shy and retiring personality who would help anybody who asked for it. He was in looks tall, slim with blue eyes, commonly found in people of Irish descent. He was very careful about what he ate, he never smoked and drank little alcohol. He always took exercise in his younger days, playing tennis and enjoying walking. He loved to relax with his family at Salcombe where he could walk and watch the boats. He described himself as a model engineer and his main hobby was designing, building and running hydroplanes. He was a superb model engineer and mechanic who made his engines with a lathe from the solid blocks of metal. His class B hydroplane, Nipper 2, held the European record of its class for many years. At the time of his death he was hoping to reclaim the record with another new model which he had designed and was building. He also sailed model boats which he had built.

He remained physically and mentally well until the last, despite having a heart attack in his 60s and more recently some angina which was treated with a coronary artery stent. Michael de Burgh Daly contributed a huge amount to his subject of physiology, both by his own research but also by the influence he had on all those who studied with him and under him. He was one of the last of the classical experimental physiologists, a man who will be missed by family, colleagues and friends.

Jennifer Angell-James
Great Missenden, Bucks

Michael de Burgh Daly Prize Lecture

Many of you will know that Michael de Burgh Daly sadly died last year. Michael was not only a distinguished and respected scientist, he was a valued colleague, enthusiastic teacher (to staff and students alike) and, most importantly, a valued friend to many of us.

Michael had a long association with the Physiological Society. He became a member in 1951 and was elected an Honorary Member in 1986. He served on several of the Society's Committees and Editorial Boards and in 1997 the Society published his seminal monograph on *Peripheral Arterial Chemoreceptors*.

In memory of Michael's association with the Society monies have been donated to the Society to fund an annual or biennial lecture in his name under the auspices of the Cardiovascular/Respiratory Control and Autonomic Function Special Interest Groups, the areas of research to which Michael attributed enormously throughout his career.

The first Michael de Burgh Daly Prize Lecture, entitled *Towards an understanding of cardiovascular and respiratory integration* was given by Professor Janice Marshall (Birmingham University) at the UCL meeting of the Society in December 2002. This was particularly apt since Michael's first lecturing post in 1948 was in the Physiology Department at UCL. Janice was an appropriate choice to give the first Lecture not only because her own research has paralleled and built upon some of the important concepts that have arisen from Michael's findings, but also because she knew Michael personally over a long period. Her Prize Lecture, to a packed Lecture Theatre, summarised some of Michael's elegant experimental approaches and the important conclusions he reached regarding the importance of integration between cardiovascular and respiratory control. She then described how her own studies, firstly on peripheral chemoreceptor reflex responses and the alerting/defence response followed later by studies on the response to acute and chronic whole body hypoxia were explained by and extended the concept of integrative responses.

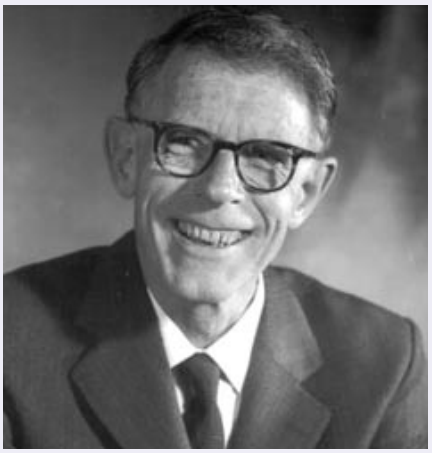
In future years it is hoped that the Prize Lecture, in addition to allowing established investigators to be invited to present to the Society, will provide an opportunity for younger researchers in this field to present their findings.

If any of you would wish to contribute to the fund set up to endow the Prize Lecture and ensure its existence for many years to come, then please send cheques payable to the Physiological Society directly to the Treasurer, Professor JPT Ward at The Physiological Society, PO Box 11319, London WC1V 6YB. Please mark any cheques and covering letters `**Michael de Burgh Daly Prize Lecture**'

David Jordan
Department of Physiology
Royal Free & University College Medical School

David Keynes Hill

1915 – 2002



David Hill, physiologist and biophysicist, died on 18 August, 2002. His father was AV Hill (known simply as AV), a pioneer of biophysics who received a Nobel prize for his measurements of the heat produced by muscles. His mother was Margaret, sister of the economist Maynard Keynes, and of the surgeon and bibliophile Geoffrey Keynes who married a granddaughter of Charles Darwin.

AV Hill is remembered chiefly for his mathematical formulations, both of the excitation of nerves by applied electric current, and especially of the relations between the force against which a muscle contracts, the speed at which it shortens, and the rates at which it liberates energy as work and as heat.

As a boy, David often acted as an assistant in his father's experiments. Like his father, he was an undergraduate at Trinity, Cambridge, which he entered in 1934 with a major scholarship. In his first two years, he studied physics and chemistry as well as physiology. He then registered as a medical student because in those days a medical qualification was a prerequisite for an academic career in physiology. After doing the necessary anatomy and the final-year physiology course, he had one year of research before the outbreak of the Second World War.

In that year he continued his father's work on isolated muscles from frogs, using for his heat measurements the equipment that AV had developed at University College London. He re-examined the absorption of heat that occurs during the first minute after a contraction, and showed that it is caused by the resynthesis of adenosine triphosphate (the immediate source of the energy dissipated during contraction) by transphosphorylation from phosphoryl creatine, and not by a stage in the formation of lactic acid from carbohydrates as had previously been supposed. He also measured the time courses of three other processes during recovery after a contraction that had not been previously measured because of their small size and slow time course: oxygen consumption, production of heat and changes in pH. This was a remarkable achievement for a young scientist in so short a time and on the strength of it David was elected to a research fellowship at Trinity College.

On the outbreak of war, he started clinical study but soon joined a group at the Postgraduate Medical School at the Hammersmith Hospital in London. Here he worked on the effects of crush injuries, which were expected to be among the most serious consequences of air raids. AV Hill had led the team developing anti-aircraft gunnery in the First World War, and it was on his advice that in 1940 the physicist Patrick Blackett was appointed as scientific adviser to Anti-Aircraft Command. AV then provided him with three physiologists as assistants, including his son David and myself. All of us had an adequate background in physics for our work, which involved adapting the gun-control equipment to operate with the crude data provided by the radar sets of that time, working on a wavelength of three metres. This entailed many visits to gunsites, both at practice firings and during air raids.

From 1942, David held various other posts in operational research for the Army, finally becoming personal assistant to Brigadier BFJ Schonland, scientific adviser to Field Marshal Montgomery. He was the first British scientist to examine an unexploded V2 rocket, and he obtained information about ballistic missiles that would have been launched by magnetic propulsion into Britain if the launching sites had not been overrun by Allied troops.

After the war, David returned to his research on muscle, first at Cambridge, then (1948–49) as physiologist at the laboratory of the Marine Biological Association in Plymouth, and finally as biophysicist back in Hammersmith (vice-dean, 1970–76). Here his prime duty was overseeing the development of electronics and of instruments for observations on human patients, but he had time to continue his research.

Until 1971 he continued in the same general field as his own and his father's pre-war work, using physical techniques on isolated muscles and nerves but with an emphasis on the intracellular structure of muscle (neglected by AV) and using many original techniques. A group of his papers reported optical changes in nerve and muscle. Another series of investigations on muscle used ultraviolet microscopy and radioactive tracers both to localize the adenine nucleotides and phosphoryl creatine in relation to the muscle-fibre striations and to follow the intracellular tubular system that communicates with the external fluid. This system serves to conduct the influence of excitation inwards from the surface membrane of the muscle fibre to activate the contractile material. He discovered a 'short-range elastic component' in the response of resting muscle to stretch, which implied that a number of cross-bridges between the thick and thin filaments exist even in the resting state but are broken when the relative

displacement of the filaments exceeds a few nanometres. Almost all of his papers up to 1971 were under his authorship alone.

From 1971 until 1977, David collaborated with RHT Edwards and his group in studies on human muscle, measuring force, heat production and chemical changes, the latter research requiring samples taken from their own muscles by needle biopsy. From 1977, he continued his work on muscle with PA Merton, activating their own muscles by heroic procedures such as stimulating them with electric shocks through the skin and by strong magnetic fields applied to the brain.

In 1949, David had married Stella, sister of the immunologist John Humphrey, and they had three daughters. Following his retirement in 1982, David experimented in photography, and, after he and his wife made their final move to Yorkshire, he made himself extremely skilled in woodwork. He died after a long illness in which he became progressively less mobile, though he retained his faculties and remained cheerful until the end.

I got to know David Hill well as an undergraduate: my own career followed his closely from my arrival at Trinity College one year after him. After he left Cambridge in 1948 we kept in touch until his death. His friendship was of great importance to me, especially when I first arrived at Trinity, younger than most of my contemporaries and very shy. He was exceptionally kind, gentle, modest and generous. He will be greatly missed.

Andrew Huxley
Grantchester, Cambridge

Reprinted by permission from *Nature*, 24 October 2002

Professor Mary Pickford

1902 – 2002

Mary Pickford started her career when there were few women doctors and considerable prejudice against women scientists; she went on to make her mark on medicine and physiological science. She became determined when told by Sir Cooper Perry, superintendent of Guy's Hospital and later Principal of London University, that 'women are no good at that sort of thing'.

Lilian Mary Pickford was born on 14 August, 1902 in Jabalpure, in the centre of India, where her father was a successful planter of indigo and tobacco. In the 17th century her forebears had started the Pickford transport service. Her father's cousin, William Pickford, was Master of the Rolls, created Baron Sterndale in 1918. His younger daughter, Mary Ada Pickford, became one of the first women members of Parliament. The Marquis of Bristol was a great-grandfather.

At the age of six, Mary Pickford was left 'at home' in England with her aunt. The aunt's husband was an engineer who specialized in work for hospitals, especially for Guy's. As a child Mary was forever asking questions and her relations were tireless at finding appropriate responses. At first she wanted to be a doctor, later to do research; she ended up being both, a renowned medical teacher and research worker.

When she arrived in England she was at first taught privately, sharing a governess with a cousin. In 1914 she was sent to Hamilton House, Tunbridge Wells, and in 1916 to Wycombe Abbey School. She enjoyed school and was impressed by the person who taught her the rudiments of playing the cello, but her school record was unremarkable. In 1921 she went to Bedford College, London University, where she read science, obtaining a first class general honours in 1924.

In 1925 she went to University College London and began part-time work in pharmacology with the famous scientist AJ Clarke and then with EB Verney, with support from a Medical Research Council grant; she enjoyed working on the kidney and the heart-lung preparation. While working part-time, she started clinical studies, this having become practicable as her godmother had left her an income of £120 a year.

Verney became ill and for a while Pickford held the fort in the Pharmacology Department, keeping one page ahead of the students. She gained a 'conjoint' medical qualification in 1933 and at University College Hospital met some of the great medical figures of that era – TR Elliot, Sir Thomas Lewis, Wilfred Trotter and Sir Francis Walshe – whilst amongst her contemporaries were George (later Sir George) Pickering, and Harry (later Sir Harold) Himsworth, who became Secretary of the Medical Research Council. The medical school had only 60 entries annually and so, said Pickford, 'One could know everyone and feel the influence of great men. This was an untold blessing and the place could be enjoyed.' Is the present, politically driven, passion for numbers, rather than standards, not a retrogressive step'

After qualification Pickford undertook some junior hospital jobs but Verney moved to Cambridge University

and she soon joined him there, becoming a Beit Memorial Research Fellow. In 1939 she became a lecturer in the Physiology Department of Edinburgh University. During the Second World War, staffing levels were minimal, and in some departments the arrangements were wholly unsatisfactory. An Egyptian medical student with a wife and a number of children to support, who repeatedly failed his clinical examinations, saw 'a gap in the market'. He ran cram courses for the students en masse, in the Odd Fellows Hall, a stone's throw away from the medical school; there they learnt, it appears, by chanting strings of facts.

Mary Pickford kept the flag flying for physiology in this difficult period. She also helped in outpatients at the Royal Hospital for Sick Children. She spent one Christmas in London during the Blitz, saw the city burning, did locums for hard-pressed general practitioners and inspected the vast underground shelters. On returning to Edinburgh, on occasions she sang in the Usher Hall to entertain the troops.

Pickford published extensively; her work was endocrinological and related to the hypothalamus and pituitary. She made observations on dogs; some needed substantial surgery, many only trivial procedures. Some she trained to urinate on command. The dogs enjoyed her company and she was very concerned with their welfare so that the observations would be as physiological as possible. If, on some mornings, a dog was not taken up to the lab the animal would bark to draw attention to himself and to register his disappointment. On her door there was sometimes the notice *Go Away! Do Not Even Knock*. The knock would upset the dog and hormone levels would vary unpredictably. The picture so widely portrayed of terrified animals in research could not have been further from the mark. Much of Pickford's work was concerned with the relationship of two hormones, the anti-diuretic hormone that controls water balance by its action on the kidney, and oxytocin that acts on the uterus.

She gained a DSc in 1951 in Edinburgh and later was given an Honorary DSc by the Heriot-Watt University. In 1954 she became a Fellow of the Royal Society of Edinburgh, in 1977 of the Royal College of Physicians of Edinburgh, in 1966 of the Royal Society of London and in 1966 was the first woman to hold a chair in the Edinburgh Medical Faculty.

She was always utterly straightforward in her dealings; this was alas not true of everyone in high places. She was especially concerned about the welfare of the women students; at the end of a class in physiology she would sometimes ask the women to stay behind after the men had left; she would then give them some advice about, for instance, the advisability of learning ju-jitsu to protect themselves should the need arise.

At one time there was a 'Regency' scheme for the students; as a regent Pickford would have had five students allotted to her. She would invite them individually to her house for a sumptuous tea and was interested in their lives; she was motherly and protective, a very caring person. The regent system collapsed and now that the university is swamped with numbers, this civilized arrangement could not be revived.

In 1963 and 1964 she attended the 'Two Way Traffic in Ideas Seminars' organised in Edinburgh by Tam Dalyell MP for Dick Crossman, then Shadow Cabinet Secretary of State for Education and Science, and contributed in her gentle and authoritative manner valuable and constructive ideas about medical education. At meetings of learned societies, she sometimes asked questions. If a paper had been given by a young, nervous person or by someone from abroad, the questions were couched in the gentlest manner and might contain helpful advice for further studies. If, however, an experienced person had blundered, and should have known better, she would start the question in the most polite manner but a few sentences later, using perhaps the phrase 'you did not say… did you?', the flaw in the argument would be exposed.

Pickford made a number of lecture tours in both North and South America. She had wit and a sense of fun. She enjoyed being mistaken for her namesake, the star of the silent screen, when checking into American hotels, especially when this meant receiving bouquets of flowers or baskets of fruit. This happened when she attended a Physiological in Boston Congress in 1929; she had sailed across with other scientists on the liner Minnekahda.

After a day's work in the lab she sometimes gave a dinner party in her home. In 1951 she drove a 1933 Rover saloon car, the shock absorbers of which had become non-functional; she found that travel over the Edinburgh cobbles was more comfortable when the car was full of passengers. The increased mass would lower the resonant frequency of the vehicle and tune it away from the rhythmic percussive drive from the impact of the seats.

After she attended an evening class run by a most stimulating artist, George Garson, in a cellar in the Royal Mile, painting became an important pastime for her. One year she went high up in the Andes and painted some of the indigenous people. She exhibited annually with The Edinburgh Women Artists, a group that she had started. In retirement she went annually to a painting school in Mull and painted elephants from her childhood memo-

ries. She learnt about the techniques of the silversmith, and about lapidary.

In 1972 she moved for family reasons to Derbyshire and worked three days a week at Nottingham University, where she was appointed Special Professor of Endocrinology. She moved back to Edinburgh in 1983 and was still driving in her nineties. She joined the Senior Fellows Club of the Royal College of Physicians of Edinburgh (alias the 'Old Buffers' Club') and came to the lunches. Having trouble with both hips, she needed help from two people to get up the steps into the building.

She was for many years a member of St John's Episcopal Church in Princes Street, Edinburgh. The Right Rev Neville Chamberlain, Bishop of Brechin, who was formerly the Rector of St John's, in 1994 said of her: 'To be in Mary's presence is to step back several generations and wallow in marvellous, intelligent conversation, savour the smells of India, learn the intricacies of animal physiology and marvel at the speed of technology in the 20th century (she remembers seeing the first man to fly in an aeroplane across the Channel!).'

Mary Pickford never had television, loved Turner's paintings and enjoyed the music of Mozart, Beethoven and Britten. She wrote short poems and whilst she never talked in the lab about religion, she had theological discussions with the rabbi who lived in the other half of her house.

In 1995 she moved south again, needing by then to be in a nursing home. Her health was fairly good until about three months before her death, on her 100th birthday. She never married.

E Geoffrey Walsh

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Laurence Malcolm

1913 – 2001

Laurence Malcolm was the son of Professor John Malcolm, who held the Chair in Physiology at the University of Otago, New Zealand from 1905 – 1943. He studied medicine at Otago from 1931, with a break in 1932 for a family sabbatical in Britain, during which time he attended classes at St Andrews and Edinburgh universities. After completing his preclinical studies in 1934, back at Otago, he took the opportunity to enter a science-based course and achieved B Med Sci in 1935, probably a substantial contributor to his interest in fundamental physiological research. Following his graduation with MB ChB in 1938, Laurence Malcolm completed his house jobs in clinical medicine and then joined the Department of Physiology at Otago, where JC Eccles arrived in 1944.

In 1944 Dr Malcolm came to work as an exchange lecturer at St Thomas's Medical School and subsequently was appointed as Reader in Physiology at St Mary's Medical School. After a year spent working with Professor Chandler Brooks in New York, he was appointed to a post working with Professor W Feldberg at the National Institute for Medical Research, Mill Hill in 1953. During his time at Mill Hill he published many neurophysiological papers in collaboration with Sydney Hilton, W Feldberg and many others; his particular field was that of evoked potentials and their basis in spinal cord and brain. His mastery of experimental technique was so precise that it was an exquisite 'art form' to watch and learn by.

In 1959 Laurence Malcolm was awarded the Regius Chair in Physiology at Marischal College of the University of Aberdeen, where he introduced many innovative projects. One was the intercalated science degree for medical students, which continues today as BSc Med Sci, based on his own experience in Otago. He was also instrumental in building a well-respected BSc degree in physiology, the first graduates coming in 1963, and incorporated in the final year an original research project – this has given many students a 'launch' into research careers over the years.

In Aberdeen, Professor Malcolm was concerned for the welfare and enhancement of both staff and students. He believed that colleagues sharing their coffee break could also share ideas and solve problems in both teaching and research. His hospitality at parties at his home, House of Minmundy, was generous and warm, providing for good relations between staff and postgraduates in the department.

Professor Malcolm served as Dean of the science faculty at Aberdeen in the early 1970s, and was instrumental in developing more 'modular' course structures to increase the range of possibilities for students. The foundation course in physiology was designed on the basis 'What do we expect them to know?' for detailed analytical study in more senior years. During his time in Aberdeen

Professor Malcolm welcomed a variety of visitors from other countries – particularly South America, Stefan Mellander from Sweden and Pavel Hnik from Czechoslovakia – to the neurophysiological laboratories. He supervised a number of research assistants and postgraduate students working particularly on neurotransmitter actions as identified from evoked potential studies. Both staff and postgraduates were encouraged to travel to conferences and to work in other laboratories.

In 1975 Professor Malcolm retired early, returning to his native New Zealand, but settling in the north island with plans to grow an orchard of kiwi fruit. While his trees developed he worked at the new University of Auckland in both neurophysiological teaching and research, publishing his last paper in 1980.

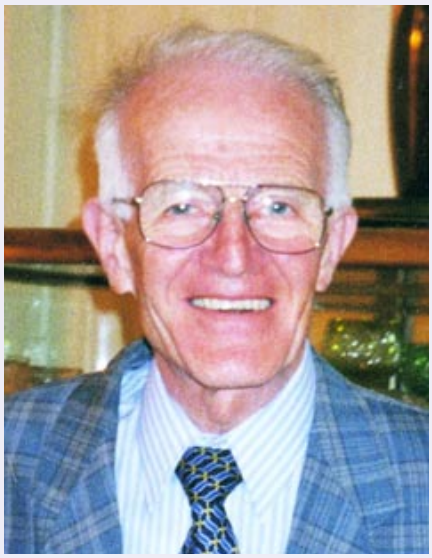
Professor Malcolm maintained his interest in physiology to the end. His keen intellect ensured his enjoyment of IUPS meetings in Glasgow, UK, Prague, Czech Republic and, last of all, in Christchurch, New Zealand where he appeared delighted to meet old friends and full of life and energy, despite celebrating his 88th birthday at the Congress.

Laurence Malcolm had a wide range of interests – including hill walking and Rotary Club activities. He was actively involved as a lay preacher and vestry member in the Anglican church of New Zealand, working to form a New Zealand 'sea of faith' group.

Ruth Payne
Old Aberdeen, Scotland

Stanislav Tuček

1932 – 2002



Many readers will be saddened to hear that Stan Tuček died in Prague on 27 September, 2002. For the last three years of his life he had suffered uncomplainingly from leukaemia. Although not a Member he was known to the Society from his attendance as a Foreign Guest at UK meetings and as a co-organizer of our joint meeting with the Czech Physiological Society in 1998. Recently he held a grant under the Society's Centres of Excellence Support Scheme. He had a worldwide reputation as a neurochemist and was involved in arranging and editing numerous important symposia on the cholinergic nervous system. In the mid-1960s he worked with Catherine Hebb at Babraham, and later with S-C Cheng in New York.

Despite the constraints on research in iron-curtain days, his laboratory in the Institute of Physiology in Prague was extremely productive as can be seen from the bibliography in his 1978 monograph *Acetylcholine Synthesis in Neurons*. His productivity continued unabated to the end of his life: he was still working on a paper during his final spell in hospital.

Friends throughout the world will want to extend their sympathy to his widow Dana, his son Martin and his daughter Lenka, in the loss of a charming, caring and courageous man.

Ann Silver
The Physiological Laboratory
University of Cambridge

Eberhard Buhl

It is with deep regret that we announce the untimely death of Professor Eberhard Buhl. After a long period of ill health his condition took a devastating turn for the worse over the New Year and he died of heart failure in the early hours of Saturday, 18 January in the Leeds General Infirmary. Eberhard was a young man, but at 43 he had achieved more than many academics whose lives have not been cut so tragically short. After gaining medical qualification in Germany he enjoyed many fruitful years as a neuroanatomist working in institutions within Europe and as far afield as Australia. He came to the UK to work at the MRC Anatomical Neuropharmacology Unit in Oxford. In 1999 he came to the University of Leeds to fill the chair in Neurobiology. At Leeds he rapidly established one of the world's leading neuronal network research groups and took over the reins as Head of the School of Biomedical Sciences in January 2002.

His demise is an immense loss to the University, his friends and colleagues throughout the world and his family. We extend our heartfelt condolences to his wife Dora Lozsadi.

The Neuronal Oscillations Research Group
University of Leeds

A full obituary will be published in the next issue of *Physiology News*

Reginald James Whitney

1914 – 2001

Reg Whitney, outstanding for his research in biomechanics and human physiology and distinguished as an inventor, died on 1 November 2001, aged 86.

Born at the beginning of WWI, he lived through difficult times during the Depression and WWII, but he persisted in his academic career in the 1930s, eventually obtaining a doctorate in zoology at the University of Birmingham. He had an addiction for developing new methods and apparatus, which was put to good use in 1941 when he was directed into Army operational research engaged in problems arising for men operating tanks. Later, his focus was in gunnery which he began to develop as multi-disciplinary personnel research, an early link to ergonomics. As a senior scientific officer with the War Office his ideas and interests became more clearly defined in the study of posture and motion during normal human activities, particularly those of extreme activities such as lifting and handling heavy loads.

In 1948 he joined the MRC Climate and Working Efficiency Unit in Oxford. It was here, studying human muscle action in the forearm, that he developed the mercury-in-rubber strain gauge which has become known worldwide as the Whitney strain gauge plethysmograph used for quantifying human peripheral blood flow. He established the technique over the next two years, exploring how, for example, blood flow could be measured simultaneously in muscle and skin. His next major contribution at Oxford was the development and construction of a force analysis platform suitable for investigating whole body activities, impulsive actions, ballistocardiography and centre of mass, and studying a wide range of subjects from world class athletes to his infant son. By the late 1950s it had become apparent that the force records required to be interpreted in association with photogrammetry and electromyography, and further, by the use of data logging and computer analysis techniques, the availability of which at the time were hardly dreamt of. In 1958, he moved from Oxford to the MRC Institute for Medical Research at Hampstead to set up a laboratory in human biomechanics where he continued to analyse human posture and motion with applications in the Services, industry, sports and clinical medicine. Whole-body activities such as in sports proved too difficult to record adequately, but a more likely situation was presented by the Royal Navy with a request to investigate the effects of ship motion on human performance. Thus he embarked on the construction of a simulator which imposed conditions of a ship's pitch and roll. When the Hampstead Unit was disbanded in 1974, he continued this work at the RAF Institute of Aviation Medicine, Farnborough and from where he retired from the MRC in 1980.

Reg's wife, Joan, died in 1966 and he was then faced with the task of bringing up his still young family alone. For the rest of his life his overriding concern was for the happiness of his four children and six grandchildren in all of whom he took immense pride. During retirement at his home in Barnes he continued to retain his interests and activity in biomechanics as well as indulging in his inherent constructional skills. Reg was an affable and modest man with unique intellectual talents, and he will be remembered with affection and admiration by all those who had the privilege of knowing him.

Ken Collins
Joe McGlade

Emmeline Lesly Jervis

Elected 1960
Died 9 October, 2002

New developments in hearing and balance

Scientific Editors: Brian CJ Moore, Jonathan Ashmore & Mark Haggard

British Medical Bulletin Volume 63, 2002
Oxford University Press. ISBN 0-19-851625-8.
247pp, £42.50

When I was a student there were two periodicals which I used to read, but did not particularly like reading. These were *Annual Reviews* and the *British Medical Bulletin*. I disliked *Annual Reviews* because they seemed to be all turgid data and references, with hardly any pictures and little or no attempt to provide perspective. The *British Medical Bulletin* also struck me as a pictureless wasteland of facts, but with the added disadvantage that it was printed in a font size of about 4, so that you needed a magnifying glass simply to read it, let alone figure out what it was going on about.

Twenty years later, *Annual Reviews* still seem exactly the same as far as I can tell. However, I have both some good news and some bad news regarding the *British Medical Bulletin*, as judged from this present volume. First the good news. The size 4 font has now been banished from the text and replaced with one that, even now, I can read comfortably without mechanical aid. Not quite such good news, however, is that – as if in deference to a venerable tradition – the mini font has been retained for tables, figure legends and references, so I was not able to dispense with my magnifying glass altogether.

Now for the bad news. There are still hardly any illustrations, resulting in page after page of densely referenced text. I am sure this will delight card-carrying afficionados of the field, but the disadvantage is that anyone else is likely to suffer rapid and strong sedation. Personally, I still find the relative lack of serious attempts to provide a wider context for the contributions both surprising and fundamentally inexcusable. If anything, with the recent trend towards increasing sub-specialisation and researchers focusing on finer and finer molecular detail, this tendency is even more noticeable today than it was 20 years ago. Providing an abstract, a brief introductory paragraph and a brief conclusion does not, in my opinion, suffice.

I was amused to note that an attempt to engage the 'Medical' in *British Medical Bulletin* has been made by including a brief 'Key points for clinical practice' section in some of the chapters. However, when key points are deemed to include 'There is now little doubt that cochlear structure allows the inner ear to perform like a multichannel mechanical spectrum analyser', I doubt that the volume is likely to be taken off the shelf in many clinics.

Lest anyone thinks that I am being too negative, I should at this point state that I do find this current volume of the *British Medical Bulletin*, as previous volumes which I have consulted in the past, to be a useful compendium of information. The editors have done a good job in marshalling a wide variety of contributions which do indeed survey new developments in hearing and balance. I am sure many researchers in the field will find individual contributions helpful and informative. But I can't help feeling that review compendia such as these end up being quoted more than read. In today's wired world, where finding scattered information is easier than ever before, the purpose of reviews which are mere compendia of facts, rather than creative digestions, becomes a more prominent question than ever.

John A Lee

Making sense of science – SuperCell

Fran Balkwill and Mic Rolph

Portland Press, London.
ISBN 1 85578 093 3.
£6.99, paperback

This book is the latest in the *Making sense of science* series from Portland Press Ltd. The books have been edited for children, teenagers and families by prominent scientists. The series editor is Fran Balkwill and the series illustrator is Mic Rolph. To date the books have all been well received and have sold very well.

For reasons that I find hard to fathom *SuperCell* does not gel as well as others in the series. It attempts to cover a wide readership, but fails to do it as well as the rest of the series. This is unfortunate since the book is very well produced, as would be expected from Portland Press, and is profusely and colourfully illustrated.

Early on the concept of cells (and that we are all made up of cells) is introduced, but it is not done well. Many different cell types are shown as early as page 4, but no idea of their likely functions is shown and an idea of their size does not appear until page 15. In addition there are sudden jumps in both the style and level of approach, as when introducing the concepts of the plasma membrane, ribosomes, the Golgi system, cytoskeleton, mitochondria and chromosomes in just two pages, albeit facing pages!

For me this particular book does not work well, but the rest of the series is very good and Balkwill and Rolph are to be praised for the overall concept. Hopefully, further books in the series will be as good as the previous ones.

Bill Winlow

The Benevolent Fund of the Physiological Society

PO Box 11319, London WC1V 6YB
Telephone 020 7269 5713 Fax 020 7269 5720

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PHYSIOLOGICAL SOCIETY SCIENTIFIC MEETINGS

(For further details, please visit http://www.physoc.org/Meetings/future.html)

2003

Newcastle upon Tyne – 3-4 April
Dublin – 8-10 July
Manchester – 10-12 September
Cambridge – 17-19 December

2004

Glasgow – March
Babraham Institute, Cambridge – May
Cardiff – July
Cork – September
King's College, London – 20-22 December

2005

Bristol – July

The Benevolent Fund of the Physiological Society

NOTICE OF ANNUAL GENERAL MEETING

The Trustees hereby give notice that the Annual General Meeting of the Benevolent Fund will be held at 1 p.m in the Eisai Lounge, University College London on Tuesday, 8 April 2003.

Jo Hancock
Benevolent Fund Administrator, for and on behalf of the Committee

Tel: 020 7269 5713
Email: jhancock@physoc.org

YOUNG PHYSIOLOGISTS' SYMPOSIA 2003

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

University of Coventry

May/June 2003

Whole body human physiology

Main contact:
Douglas Thake (d.thake@coventry.ac.uk)

BENCH TO BEDSIDE SYMPOSIA
ION CHANNEL DISEASE

Royal Society of Medicine, London
28 March, 2003

Further details from:

Royal Society of Medicine
1 Wimpole Street, London W1G 0AE
Tel: 020 7290 2965
Fax: 020 7290 2977
Email: events@rsm.ac.uk

*

SOCIETY FOR EXPERIMENTAL BIOLOGY ANNUAL MEETING

Forty years of invertebrate neuropharmacology – a tribute to Professor Robert Walker

Southampton
April, 2003

Further details from:

Professor Roddy Williamson

Email: rwilliamson@plymouth.ac.uk

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40th SPRING MEETING OF THE BRITISH MICROCIRCULATION SOCIETY

University of Bristol
7 – 8 April, 2003

The meeting includes a symposium on *Lymphatic Research*

UK Organiser: Dr Dave Bates

Further details from:

BMS Secretary
Microvascular Research Laboratories
Department of Physiology
University of Bristol
Southwell Street
Bristol BS2 8EJ

Tel 0117 928 9818
Fax 0117 928 8151
Email: dave.bates@bris.ac.uk

www.microcirculation.org.uk

Abstract and registration deadline
7 March 2003

**

7th ANNUAL MOLECULAR TECHNIQUES WORKSHOP

University College, Cork
7 – 16 April, 2003

A 10-day residential workshop, sponsored by the Physiological Society and the Wellcome Trust, for the training of physiologists in molecular biological techniques. The course is appropriate for physiologists who are reading for a PhD or are at the post-doctoral level and who have little or no previous experience of molecular techniques. The course will be limited to 16 students, who intend to follow a career in the physiological sciences. Preliminary enquiries to:

Dr Maggie Leggett
The Physiological Society
PO Box 11319
London WC1V 6YB

Email: mleggett@physoc.org

*

NEUROLOGY FOR NEUROSCIENTISTS IV

Magdalen College, Oxford
7 – 8 April, 2003

The Guarantors of Brain have kindly agreed to sponsor a ninth symposium on *Neurology for Neuroscientists*.
The aim of this symposium is to provide neuroscientists with the clinical background to neurological diseases, and with insights into how neurological problems can illuminate basic neuroscience. Further details, including a full programme listing and application forms are available from:

www.ion.ucl.ac.uk/neurochemistry/N4N/index.html

*

BRITISH NEUROSCIENCE ASSOCIATION ANNUAL MEETING

Harrogate
13 – 16 April, 2003

Details from:

Dr Richard Ribchester
Email: rrr@ed.ac.uk

*

22nd ALTERNATIVE MUSCLE CLUB

University of Leeds
15 – 17 April, 2003

The Alternative Muscle Club is an informal meeting organised *by* young scientists *for* young scientists and is now in its 22nd year after the organisers hand over the torch of responsibility to a new institution every year. The AMC is a special meeting that encourages young research students, postgrads, postdocs and those with an interest in muscle biology to participate and develop communication skills as well as meet other scientists working in the field. The event will feature guest speakers at the cutting edge of muscle research.

Such a unique blend of fun and science in such a relaxed atmosphere is a great advertisement for muscle biology and the scientific world itself and should not be missed.

The cost of the event for the three days is £100 (includes accommodation, entertainment and all meals including the legendary AMC Conference Dinner).

Email: amc2003@bms.leeds.ac.uk

www.leeds.ac.uk/bms/amc2003

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Noticeboard entries continue on page 52

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 2003 edition of Physiology News should reach the Publications Office by 12 March, 2003.

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

BIOCHEMICAL SOCIETY FOCUSED MEETING ON CALCIUM OSCILLATIONS and 5th UK MEETING ON CALCIUM SIGNALLING

University of Liverpool
1 – 2 May, 2003

Calcium is a ubiquitous second messenger involved in variety of physiological functions.

Day one of this two-day meeting is a Biochemical Society focused meeting on calcium oscillations honouring the retirement of Professor Cobbold (University of Liverpool).

Day two is the 5th UK meeting on Calcium Signalling where more general aspects of calcium regulation will be discussed.

Speakers

Day 1
Sir Michael Berridge *Babraham, UK*
Peter Cobbold *Liverpool, UK*
Anne Green *Warwick, UK*
Richard Lewis *Stanford, USA*
Ole Petersen *Liverpool, UK*
Trevor Shuttleworth *Rochester, USA*
Alec Simpson *Liverpool, UK*
Andy Thomas *UMDNJ, USA*
David Yule *Rochester, USA*

Day 2
Martin Bootman *Babraham, UK*
John Carroll *UCL, UK*
Dermot Cooper *Cambridge, UK*
Tomoko Kamishima *Liverpool, UK*
John McCarron *Glasgow, UK*
Steve O'Neill *Manchester, UK*
Steve Pennington *Liverpool, UK*
Rosario Rizzuto *Ferrara, Italy*
Alexei Tepikin *Liverpool, UK*

*

SECOND WORLD CONGRESS ON FETAL ORIGINS OF ADULT DISEASE

Brighton Centre, UK
7 – 10 June, 2003

www.foad2003.org/

*

3rd CONGRESS OF THE FEDERATION OF EUROPEAN PHYSIOLOGICAL SOCIETIES

Nice, France
28 June – 3 July, 2003

Further details from:

FEPS2003, CNRS UMR 6548
University of Nice – Sophia
Antipolis, Faculté des Sciences
06108 Nice Cedex 2, France
Tel 33 4 92 07 68 51
Fax 33 4 92 07 68 50

Email: FEPS2003@unice.fr
www.unice.fr/FEPS2003/

*

INTERNATIONAL SOCIETY FOR AUTONOMIC NEUROSCIENCE (ISAN)

Calgary, Alberta, Canada
4 – 8 July, 2003

Special features of this meeting will include a relatively inexpensive registration fee (about Canadian $550) and reduced registration fees for postdoctoral fellows and students. The fee will cover the cost of the meeting banquet and some meals. Economical accommodation is also available. There will be opportunities for junior faculty members to present major lectures in addition to posters.
www.fp.ucalgary.ca/isan2003/

ISAN Satellite Symposia

ENTERIC NEUROSCIENCE

Banff, Alberta, Canada
9 – 13 July, 2003

Email: hsharkey@ucalgary.ca
www.med.ucalgary.ca/webs/ENS/

AUTONOMIC DYSFUNCTION AFTER SPINAL CORD INJURY: MECHANISMS, PREVENTION AND TREATMENT

Banff, Alberta, Canada
10 – 11 July, 2003

Email: bpettypiece@rri.ca
lcweaver@rri.ca

www.isanweb.org/meetings/satellite2003a.html

*

SIXTH IBRO WORLD CONGRESS OF NEUROSCIENCE

Prague, Czech Republic
10 – 15 July, 2003

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MICROELECTRODE TECHNIQUES FOR CELL PHYSIOLOGY

20th Workshop 3-17 September 2003
Laboratory of Marine Biology 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 specialised topics. A copy of the Plymouth Microelectrode Handbook will be provided.
- Accommodation (for 14 nights – arrive and depart on Wednesday) is close to the laboratory and includes breakfast. Lunch is provided in the department each day and an allowance 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 2003. 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. Please note that printed and emailed copies are required.

1 Please give a concise description of your research, your reasons for wishing to attend and your experience of techniques taught on the workshop. 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 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 is usually available for young scientists 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 funding the full fee please indicate in your application.

Paper and email copies of the application 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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THE CONGRESS OF THE LATIN-AMERICAN ASSOCIATION OF PHYSIOLOGICAL SOCIETIES (ALACF) AND BRAZILIAN PHYSIOLOGICAL SOCIETY (SBFIS)

Ribeirao Preto, State of Sao Paulo, Brazil
1 – 4 September, 2003

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IUPS 2005 – 35th CONGRESS OF THE INTERNATIONAL UNION OF PHYSIOLOGICAL SCIENCES

San Diego, CA, USA
31 March – 5 April, 2005

IUPS 2005 is being organised by the six member societies of the US National Committee of the IUPS, the American Physiological Society, the Society for Neuroscience, the Microcirculatory Society, the Society of General Physiologists, the Biomedical Engineering Society and the Society for Integrative and Comparative Biology, under the auspices of the US National Academy of Sciences.

www.IUPS2005.org/

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