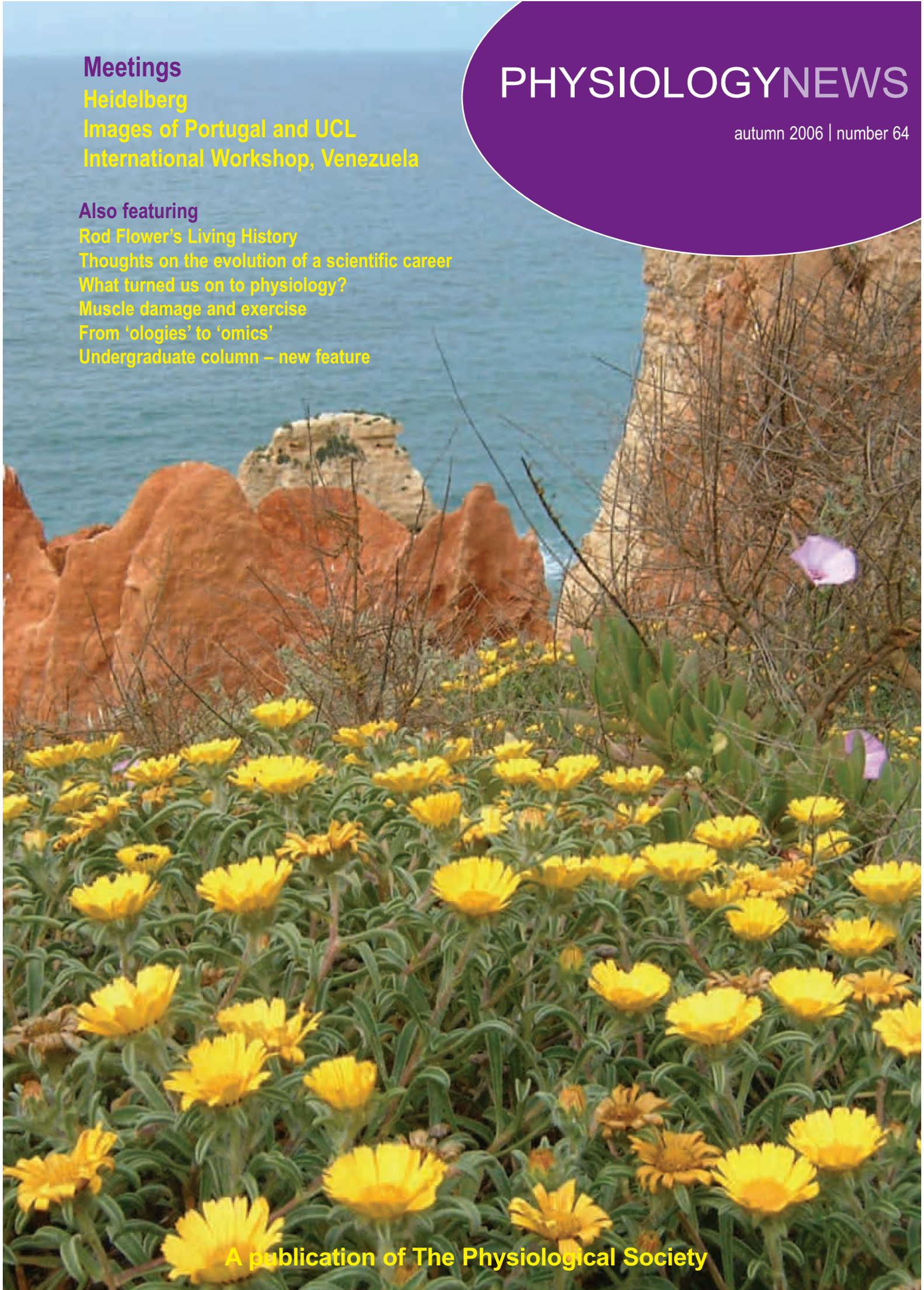

PHYSIOLOGYNEWS

autumn 2006 | number 64

Meetings
Heidelberg
Images of Portugal and UCL
International Workshop, Venezuela

Also featuring
Rod Flower's Living History
Thoughts on the evolution of a scientific career
What turned us on to physiology?
Muscle damage and exercise
From 'ologies' to 'omics'
Undergraduate column – new feature

A publication of The Physiological Society

PORTUGAL FOCUSED MEETING

Basic science of cystic fibrosis

20 April 2006

Tivoli Almansor, Algarve

(*photos by Mike Gray*)

More photographs from the Portugal Meeting on the inside back cover

Clockwise from above:
Seagull – 'visitor' or 'participant' (note chess set behind)
View of pool/bay from hotel bedroom
Dancing (young and old) at the symposium dinner
Pink flowers!
A nice cliff view
Richard Olver (Dundee) and his wife, Susan
Marie Johannesson (Sweden), President of the European Cystic Fibrosis Society, at the symposium dinner

The Society's dog. 'Rudolf Magnus gave me to Charles Sherrington, who gave me to Henry Dale, who gave me to the Physiological Society in October 1942'

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Cover photos




Clockwise from top left:

Portugal, UCL, Heidelberg and Portugal

PHYSIOLOGYNEWS

Action points

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Physiology News

Deadlines

Letters and articles and all other contributions for inclusion in the Winter 2006 issue, No. 65, should reach the Publications Office (lrimmer@physoc.org) by 21 September 2006. Short news items are encouraged and can usually be included as late copy if space permits.

Suggestions for articles

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

Physiology News Online

Physiology News is now available on The Society's web site: http://www.physoc.org.

Guidelines for contributors

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

Format of articles

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

Length of articles

This will be determined by the subject matter and agreed with the Executive Editor.

Submission of articles

Authors should submit articles as a Word document attached to an email. Illustrations should be sent as separate attachments (see below) and not embedded in the text.

Illustrations and authors' photographs

Authors are encouraged to submit diagrams, drawings, photographs or other artwork with their articles or to suggest appropriate illustrations. A photograph of the author(s) should also accompany submissions, if possible. Illustrations and photographs may be colour or black and white, prints, transparencies or tif/jpeg files with a **minimum resolution of 300 dpi**. Electronic colour figures should be saved 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 2005* at http://www.physoc.org)

In this issue

Welcome to the Autumn issue of *Physiology News*. The words I think best describe this issue are 'colourful' (or 'visual') and 'varied'. We have quite a focus on people. Apart from photographs from the recent UCL meeting, and of various physiologists enjoying themselves in the tropics (p. 30), we have a Living History, three long-standing Members of The Society telling us how they got started, and our new Chief Executive Mike Collis telling us about himself and his scientific career so far.

This issue also exemplifies how physiology as a subject is looking forward, while acknowledging and celebrating its rich past. Among the 'future-gazing', open access continues to make waves (p. 33), while Ian McGrath offers a perspective on 'whither physiology' (p. 43), and Donna Brown asks 'Where next' for physiology graduates (p. 38). Rod Flower's Living History (p. 7) looks at early research into inflammatory mediators, while Traces of the Past (p. 35) heralds the re-launch of The Society's History and Archives Committee.

Physiological experiments *in vivo*, both in humans and animals, provide one clear link through the 130 years of The Society's history. As Ann Silver explains (p. 18), physiology undergraduate students were once a main source of willing (mostly) experimental subjects, and experiments on man still have new things to tell us, as the articles by Dwain Eckberg and Tom Kuusela (p. 26) and Simon Gandevia and colleagues (p. 21) exemplify. Finally, Thelma Lovick makes the case for more engagement with the media and the public over animal experimentation in the editorial (p. 3).

Austin Elliott

See 'A risky course' (p.18).

Exploiting the media for animal research

The Physiological Society has been in existence now for over a century. One of the issues that prompted The Society's foundation was the question of animal research and the need to protect the interests of scientists. Even in the 19th century, as a nation of animal lovers, the British had reservations about the use of animals for scientific research purposes. Indeed, legislation to regulate the use of animals for scientific research has been in place since 1876. The need to protect the researchers also arose and the Research Defence Society (www.rds-online.org.uk) was founded in 1908. Since that time, in a rational and measured way, it has defended the use of animals for medical research purposes and explained the long-term benefits that have been gained from animal experimentation.

An uneasy harmony between scientists and the 'antis' has thus existed, based on the fundamental right to protest that is enshrined in the British way of life. We are a tolerant lot on the whole. We smile at men (or women) ranting from soap boxes and we warm to eccentricity. Most of us quite like the idea of being able to put forward outrageous views, however misguided. But maybe this benevolent attitude has a downside.

In the face of the anti-vivisectionist lobby most physiologists put their heads down and got on with their work. Even as late as 2005, some major universities in the UK appeared ashamed of their involvement in animal research with obscure corners of their web sites admitting to 'occasional' use of animals. Surely the 'antis' were just a small irrational minority and the Great British Public would see reason? To their great credit some high profile academics have been putting their heads above the parapet at not inconsiderable personal risk, in order to put the case for animal experimentation. There is no doubt that these measures have been influential in Government circles, and at a personal level individual physiologists almost always win their arguments. But, although we may be winning the battles, are we winning the war?

We are still seeing the disastrous consequences of the activities of the anti-vivisectionist lobby. All of us must know one or more colleagues whose work on animals has precipitated the hate phone calls, who have had their house daubed, their neighbourhood leafleted, their family threatened or, in the most extreme cases, been physically attacked in the name of animal welfare. We are careful, these days, regarding what we say about our work in public places. We are instructed to be wary of opening packages of unknown provenance. We receive tuition from our institution's security teams on spotting terrorist activity. We learn what to do in an emergency. And all of this is accepted as part and parcel of being a physiologist. When we react we do so rationally, lobbying the Government through the accepted channels, producing appropriate literature to distribute to schoolchildren, acting as the voice of reason in debates. But somehow it has only worked up to a point. Why?

In the past few years the activity of the animal rights protestors has got completely out of hand, with unacceptable acts of intimidation and violence being perpetrated against individual scientists, the staff of animal breeding establishments and their families and even construction workers linked to the building of new laboratories. How can this have been allowed to happen? Essentially we run a personal risk every day just by doing our job.

Maybe it is time for a different approach. We would do well to reflect on the efforts of two individuals who have made a significant impact in promoting the benefits derived from research on animals. In 1991 a member of the public, Andrew Blake, set up the pressure group Seriously Ill for Medical Research (SIMR) with the object of supporting the humane use of animals and the ethical use of biotechnology in medical research. A Freidrich's ataxia sufferer, Andrew succumbed to the disease in 2002, aged 29. SIMR has now been re-branded as the Patients Voice for Medical Advance (www.patientsvoice.org.uk) and it is encouraging that the current Minister for Science and Innovation has now publicly pledged his support, alongside high profile Members of The Physiological Society.

The most recent success in galvanising public support for animal experimentation was initiated by an Oxford schoolboy. Laurie Pycroft had become frustrated by the furore surrounding the building of the University of Oxford's new Biomedical Research Facility and the way those opposed to research on animals were dominating the public debate. With a clarity of vision reminiscent of the fable of The Emperor's New Clothes, he set up the organisation Pro-Test with the simply-stated aim 'to counter the irrational arguments of anti-vivisectionists by raising public awareness of the benefits of animal research and create an environment where scientists can speak out' (www.pro-test.org.uk).

It worked. An initial demonstration in Oxford early in January this year escalated to a massively successful demonstration in the town in February by an estimated 1,000 supporters and was followed in May by a public debate in Oxford. This unprecedented show of support for animal research attracted worldwide media attention.

So what can we learn from all this? Unfortunately perhaps, we should accept that rational argument is not the only effective method for swaying opinion. Or at least that the right forum is as important as the right argument. Using the media is the way it's done these days. After all, until you read about the benefits of work on animals in the Sun, it's simply not going to register in the popular consciousness. But perhaps the tide of public opinion really is starting to turn. On 24 July the BBC broadcast a *Newsnight Special* devoted to the question of animal research. This was followed 3 days later by a *Newsnight* debate on the issue. Included, was a live demonstration by a Parkinson's disease sufferer of the dramatic improvement in his quality of life that has resulted from deep brain stimulation, a technique developed almost exclusively as a result of research on animals. This media exposure has been a great boost. Our duty now is to seize the moment and make the best use of the media to educate the public.

Thelma Lovick

A Science Media Centre Seminar *Making the case for animal research in the media* will be held in London on 14 November, 2006. For more information contact smctemp@ri.ac.uk.

Heidelberg Focused Meeting

Control and modification of excitation-contraction coupling in health and diseased muscle

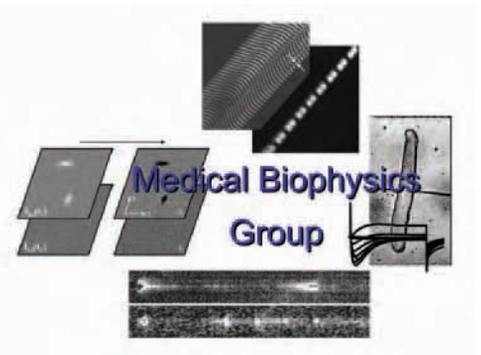
The Meeting

Excitation-contraction coupling in both healthy and diseased muscle is the topic of this one day Physiological Society Focused Meeting to take place at Ruprecht-Karls-Universität, Heidelberg, Germany on 13 September 2006.

There has been a flurry of progress from different groups in the area and it is intended that this Meeting will provide new insights and future collaboration. The preceding meeting of the European Society of Muscle Research in Heidelberg means that there are likely to be a lot of basic and applied muscle physiologists around.

The Hosting Group

The Meeting will be hosted by the Medical Biophysics Group at the Institute of Physiology and Pathophysiology that was founded by Rainer Fink in 1990 (http://www.medbiophysics.uni-hd.de). The Group's work covers various aspects of methodological developments and techniques for life science applications ranging from electrophysiology to linear and non-linear fluorescence microscopy with a special focus on muscle. Studying specific changes of the excitation-contraction coupling process in muscle under various pathophysiological conditions bridges the gap between basic science and clinical application.



Organisers

Joseph Bruton (Karolinska Institute, Stockholm), **Rainer Fink** and **Oliver Friedrich** (Ruprecht-Karls-Universität, Heidelberg)

Invited speakers

Martin Schneider (University of Maryland, MD, USA)
Werner Melzer (University of Ulm, Ulm, Germany)
Eduardo Rios (Rush University, Chicago, IL, USA
Godfrey Smith (University of Glasgow, Glasgow, UK)
Angela Dulhunty (Australian National University, Canberra, Australia)
George Stephenson (La Trobe University, Melbourne, Australia)
Manuela Zaccolo (Venetian Institute for Molecular Medicine, Italy)

35th European Muscle Conference

The E-C coupling Meeting will be preceded by the 35th European Muscle Conference, also hosted by the Medical Biophysics Group in Heidelberg from 9–12 September. The EMC meeting covers general aspects of muscle physiology and pathophysiology ranging from molecular motors to gene therapy of Duchenne muscular dystrophy. Further information on that meeting will be available at http://www.emc2006-heidelberg.de

The University

In 1386 Count Ruprecht I founded Heidelberg University, Germany's oldest institution of higher learning (right, bottom). It played a leading role during the age of Humanism and the Reformation.

The City

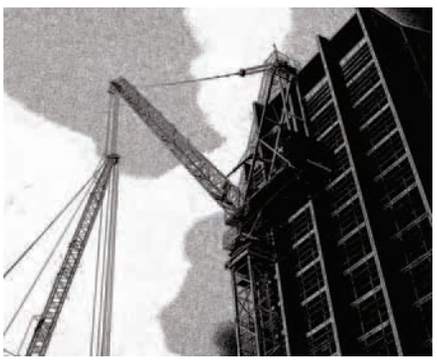
Located on the Necker River amidst mountains, woods and sloping vineyards, Heidelberg is perched high above the barrow lanes and picturesque roofs of the Old Town (right, top) and the ruins of the red sandstone Heidelberg Castle (right, centre) that crowns the city. For five centuries it was the glamorous residence of the Electors Palatine.

We look forward to welcoming you to Heidelberg in September.

Joseph Bruton, Rainer Fink and Oliver Friedrich

For further information and online registration please visit:
http://www.physoc.org/meetings/heidelberg2006.asp

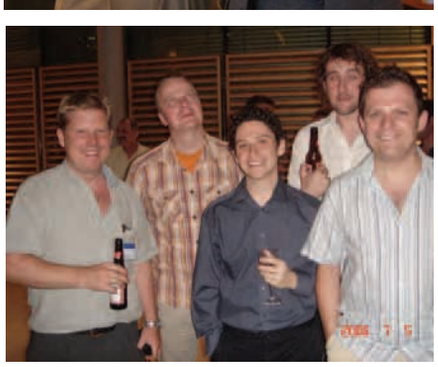
The Physiological Society Main Meeting, UCL 4–7 July 2006

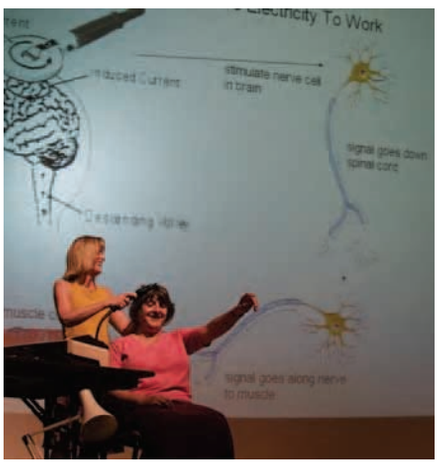


Top, right: UCL heads past and present, Tim Biscoe (left) and John Carroll.
Above, left: John Henderson and Richard Creese
Above, right: new Meetings Secretary Prem Kumar enjoys his *J Physiol* cover photo.
Third row, left: Otto Hutter with retiring President Alan North. Third row, right: Tea and trade show.
Fourth row, left: David Patterson, new Chair of *Experimental Physiology*, with his predecessor John Coote. Fourth row, right: Elfa Wilmot and Ann Silver at The Society's Benevolent Fund stand.
Bottom, left: Society staff Nick Boross-Toby, Simon Kellas, Liam McKay, David Bennett and Casey Early.

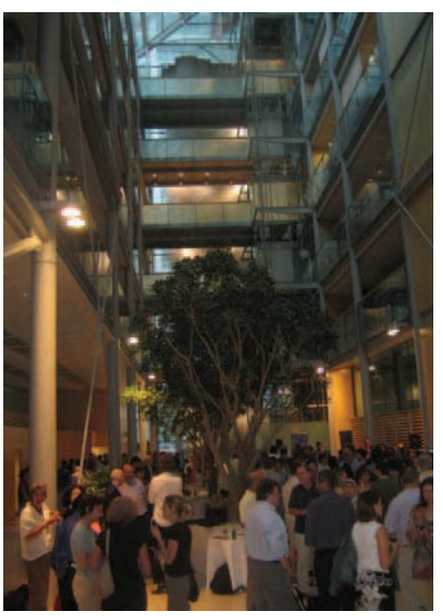
(*UCL photos on pages 5,6 and 47 kindly provided by Nick Boross-Toby, Austin Elliott, Jonny Goodchild, Prem Kumar, Giovanni Mann and Ken Wann*).

The Benevolent Fund raffle at UCL was won by new Society Chief Executive Mike Collis (a case of wine) and Giovanni Mann (*Trust and deceit* by Gerta Vrbova, reviewed by Thelma Lovick on p. 50). The raffle at The Society dinner (book tokens) was won by Tracey Mills (Manchester).





Top, left Plaque in the old University College hospital commemorating Joseph Lister. Top, centre: UCL entrance with The Society in occupation. Top, right: Cabinet in the UCL cloisters commemorating the work of Nobel Laureates Andrew Huxley and Bernard Katz. Above: David Attwell's 'helpers' at The Society's Public Lecture. Below: A musical welcome for the audience at the Public Lecture.
Third row, left: Hog roast at the Regent's College BBQ. Third row, right: Reception in the foyer of the Wellcome Trust building.
Bottom, left: The BBQ in full swing. Bottom, right: The party's over.



‘Second messengers’ of glucocorticoid action

John Vane’s observation that aspirin blocked the generation of those odd, fatty acid derived-mediators, the prostaglandins, set Rod Flower’s feet firmly upon a track that he has followed throughout his career. He looks back here at a question that had puzzled researchers since the end of the 19th century

In 1971 I had just completed my undergraduate training in physiology at Sheffield University and was about to commence my postgraduate studies with John Vane in the Department of Pharmacology at the Royal College of Surgeons in London. If it is true that the planets do influence our fate, then all I can say is that they must have been very favourably aligned at this moment! John’s observation that year, that aspirin blocked the generation of those odd, fatty acid derived-mediators, the prostaglandins (PGs), was important for two main reasons; it provided pharmacologists with a convincing explanation for how these drugs produced their triple analgesic, anti-pyretic and anti-inflammatory effects (because PGs were known at that time to be pro-inflammatory and to cause fever and hyperalgesia) and it also gave physiologists a useful tool with which to probe the role of these local hormones in virtually any physiological model. On top of all that, it set my feet firmly upon a track that I have followed throughout my career.

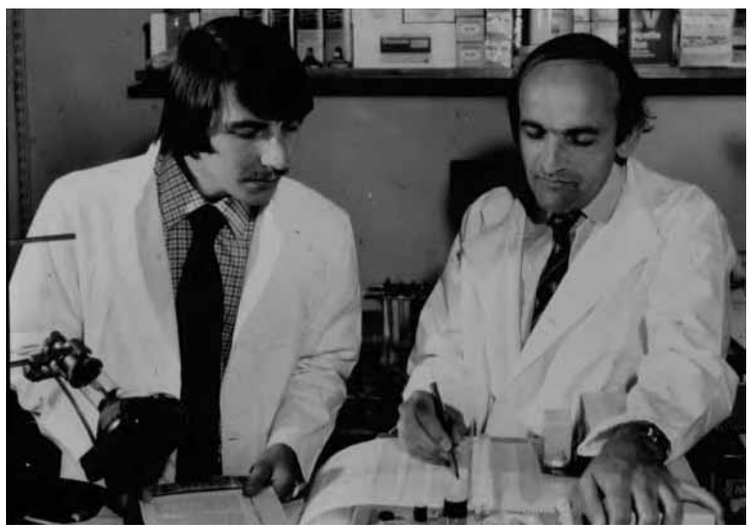


Figure 1. The author (right) with Geoff Blackwell at the Wellcome Foundation *circa* 1990.

The ‘aspirin question’ had puzzled researchers since the end of the 19th century but John’s solution had, like many others in science, begged several further questions. For example, did the many other ‘non steroidal anti-inflammatory drugs’ (NSAIDs) in the formulary behave the same as aspirin in this respect? For that matter, did other anti-inflammatory drugs, such as the glucocorticoids, or analgesic drugs, such as morphine, act in the same way? These questions formed the first part of my PhD studies.

John was heir to the ‘physiological’ tradition in pharmacology and our research tools were the bioassay techniques of Dale, Gaddum and Burn. Our first experiments, using strips of smooth muscle to assess PG formation by cell-free preparations of the PG-forming cyclooxygenase enzyme, suggested that the inhibition was a specific and almost universal property of the NSAIDs. This was good news in some ways, because it supported the notion that this effect underpinned NSAID pharmacology, but it also posed an intellectual dilemma too: if, for example, the glucocorticoids (far more potent anti-inflammatories than aspirin) didn’t act by inhibiting PGs, how did they work?

Looking back on it now, it seems strange that we attached so much importance to PGs and their actions, but in those days (the mid 1970s) the number of known mediators was small and researchers had little inkling of the existence of that vast network of cytokines and chemokines, which have since been shown to regulate many important aspects of the inflammatory response.

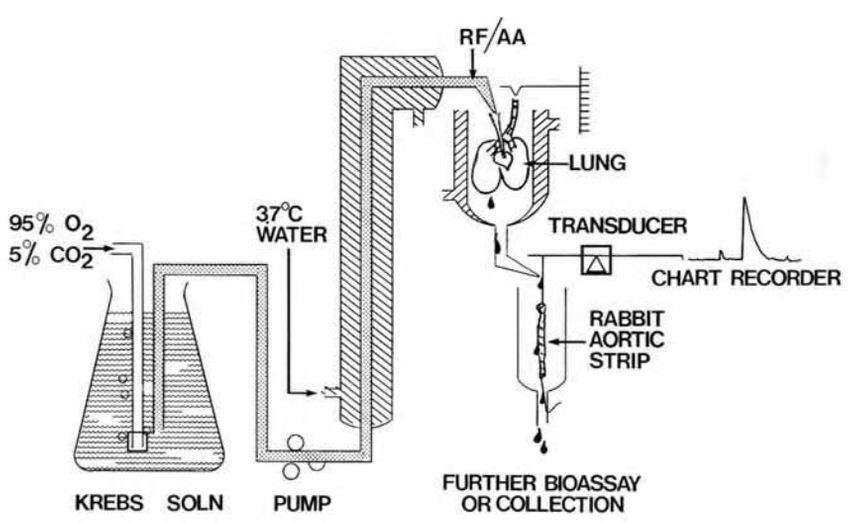
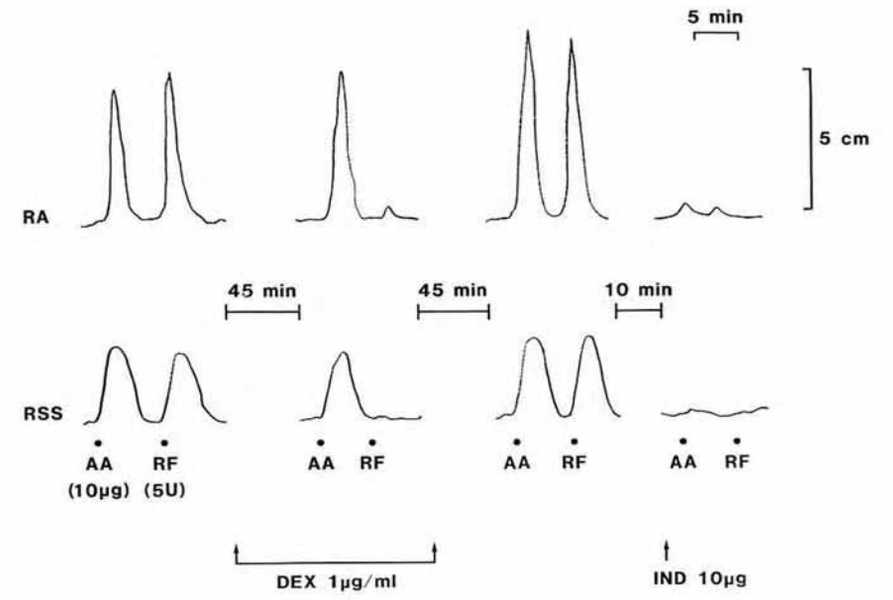


Figure 2. Basic apparatus for measuring prostaglandin release from the guinea-pig isolated perfused lung. Warmed Krebs’ solution is pumped through the pulmonary artery and the effluent allowed to superfuse a rabbit aortic strip which is highly sensitive to thromboxane A_2. Two types of agent can elicit the release of thromboxane: ‘AA’, arachidonic acid, which is the substrate for the cyclooxygenase and which is converted directly into thromboxane on its passage through the pulmonary circulation; and ‘RF’, releasing factors, which include substances which trigger the release of endogenous arachidonic acid thus producing the release of thromboxane A_2 by an indirect route.



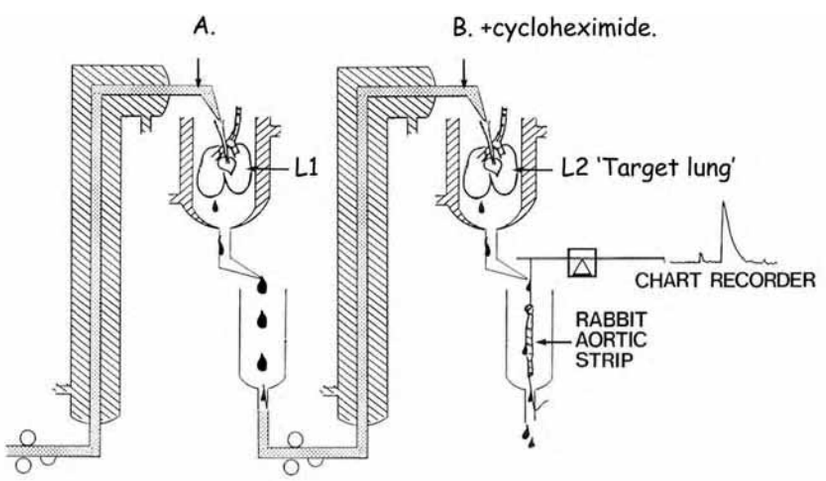


Figure 3 (top). A trace showing the release of thromboxane A_2 and prostaglandin E_2, as detected by contractions of the rabbit aortic strip (RA) and the rat stomach strip (RSS) induced by injections of arachidonic acid (AA) and a "releasing factor" (RF) before, during and after an infusion of the glucocorticoid dexamethasone. It can be seen that the glucocorticoid selectively blocks the indirect action of RF but not the direct conversion of AA into PGs. The onset of this effect is only about 30-45 min, but is also short-lived as the effect has virtually worn off within 45 min of the infusion being discontinued. (*Note that a single injection of the cyclo-oxygenase inhibitor, indomethacin (IND) completely blocks the release of eicosanoids in response to either stimuli.*)

Figure 4 (bottom). The apparatus used to detect 'second messengers' of glucocorticoid action. Two guinea pig isolated perfused lungs were set up in series. Lung 2 (L2, 'target lung') was rendered insensitive to the direct actions of glucocorticoids by a consistent infusion of cycloheximide such that infusions of glucocorticoids at point B did not have a blocking action on thromboxane A_2 release illustrated in Figure 3. However, if the glucocorticoids were infused at point A, such that the drug first passed through lung 1 (L1), the synthesis of thromboxane A_2 in the 2nd lung was blocked as usual.

John's lab moved to the Wellcome Research Foundation at Beckenham in 1973 and whilst there, I became interested in the way in which the substrate for PG synthesis (arachidonic acid) was generated and released. The models I used included 'biochemical techniques' such as tissue slices labelled with radioactive fatty acids, but also a favourite bioassay preparation, the guinea-pig isolated perfused lung. The organ was perfused with warmed Krebs' solution and the effluent allowed to superfuse banks of bioassay tissues chosen for their sensitivity to PGs. Injection into the lung of arachidonic acid led to an immediate release of PGs and their half-brother, thromboxane (Tx) A_2, that was easily detectable because it produced contractions of the superfused rabbit aortic strip. We also observed that other substances such as the mysterious 'RCS-RF' (subsequently identified as a leukotriene mixture) also caused a massive release of TxA_2 even though it wasn't a cyclo-oxygenase substrate.

Oddly, it soon became evident that, contrary to our intial observations, the glucocorticoids actually *could* block PG generation in this preparation, but only because it contained intact cells – they were inactive in the cell-free enzyme systems prepared from this tissue. Working with my PhD student Geoff Blackwell, and a visitor from the Netherlands, Frans Nijkamp, we observed that when infused into this preparation, glucocorticoids could selectively inhibit the stimulation produced by RCS-RF without affecting the direct conversion of arachidonic acid into TxA_2. This experiment therefore suggested a more complex mechanism than straight forward cyclo-oxygenase enzyme inhibition. We had already speculated (as had others too) that the glucocorticoids were somehow acting on a process that liberated free arachidonic acid in the lung tissue and thought that this might be an enzyme of the phospholipase A_2 family (although little was then known about these enzymes.

In those days the consensus opinion was that the anti-inflammatory effect of glucocorticoids was brought about by the physico-chemical stabilization of lysosomal membranes, but experiments by endocrinologists interested in sex hormone action suggested there may be another mechanism involving an intracellular 'receptor' with a nuclear localisation, and it was these findings which prompted us to see if such a mechanism also obtained in our guinea-pig perfused lung system.

Geoff Blackwell and I were able to demonstrate that a receptor for glucocorticoids was indeed involved in that action and that the glucocorticoid effect on TxA_2 release required on-going protein and RNA synthesis. This was important for it replaced the concept of a 'monolithic' anti-inflammatory mechanism for these drugs with the possibility that there may be many effects produced as a result of gene modulation. It was an idea whose time had evidently come as

I remember that several other similar papers appeared in the literature at about the same time.

Further developing this idea, I speculated that there may be a factor generated in response to glucocorticoids which was responsible for the PG blocking effect. As an undergraduate, I remember being thrilled by Otto Loewi's experimental ingenuity when he demonstrated that *'vagusstoff'* could be released from one perfused heart and act upon another and I decided I could apply a similar type of thinking to the glucocorticoid problem. Using a modification of our perfused lung model we demonstrated that infusion of gluocorticoids into one lung produced a factor that blocked PG generation in another in which the direct effect of gluocorticoids was prevented by the use of inhibitors of protein/ RNA synthesis.

This was the start of a project which has consumed my colleagues and I for many years. The isolation and characterisation of this factor took a long time and much of the initial work was done with colleagues such as Luca Parente who was visiting from the University of Naples. It was the mid 1980s before the protein (originally termed 'macrocortin' or 'lipocortin', now called annexin A1) was cloned (by Biogen). With the recombinant protein in our hands, Pippo Cirino (another visitor from the University of Naples) and I were at last able to confirm its anti-inflammatory and PG inhibitory properties. Much of my subsequent work, done in collaboration with many other colleagues, has been to investigate its role in mediating other effects of glucocorticoids in the immune, neuroendocrine and other systems.

It has been a most exciting journey and it is not over yet. A few years ago, we generated, here in my Institute, an annexin A1 null mouse and were delighted to find that its phenotype supported many of our early ideas as well as pointing up some new fruitful research directions for us to explore. Working, over the years, with so many superb scientists (only a few early colleagues are mentioned here) from around the world has been a privilege as well as a tremendous joy and the Wellcome Trust's financial support was absolutely crucial to this project.

Such was the weight of opinion in the 1970s regarding the probable mechanism of action of glucocorticoids that our first papers attracted many adverse comments and several referees doubted that a genomic (as we now call it) mechanism was at work (partly because of the speed of the response). Ironically, we have recently shown that the liganded glucocorticoid receptor can actually have very rapid signalling effects within the cell, which are *independent* of any genomic action, and that these play an important role in modulating annexin A1 release (and no doubt other important cellular effects). However, it then proved difficult to get *this* work published because of the cumulative weight of observations from all those groups who have demonstrated the primacy of genomic actions! Such is science!

R J Flower

Biochemical Pharmacology, William Harvey Research Institute, Charterhouse Square
London, UK

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Where are they now?

Geoff Blackwell remained at the Wellcome Foundation working as a research pharmacologist until the company merged with Glaxo.

Pippo Cirino worked with the author at the University of Bath. He later returned to the University of Naples to complete his academic training. He currently holds the Chair of Pharmacology there.

Rod Flower is a Wellcome Trust Principal Research Fellow and, together with his colleague Mauro Perretti, jointly heads the Centre for Biochemical Pharmacology within the William Harvey Research Institute at St Bart's and the Royal London School of Medicine and Dentistry in London.

Luca Parente left the Wellcome Foundation and returned to work at the University of Naples before taking the Chair of Pharmacology at the University of Salerno.

Frans Nijkamp left the Wellcome Foundation in 1977 to return to the Netherlands. He gained a Chair of Veterinary Pharmacology in 1983 and is currently Head of the Department of Pharmacology and Pathophysiology at the University of Utrecht.

John Vane (below) left the Wellcome Foundation in 1986 and founded the

William Harvey Research Institute on the Charterhouse Square campus of the (then) St Bartholomew's Hospital Medical School in London. He was awarded the Nobel Prize for Physiology or Medicine in 1982 for his work on the mechanism of action of aspirin-like drugs and was knighted in 1984. He passed away in November 2004 leaving behind him a vibrant Institute which is dedicated to perpetuating his scientific ideals.

Thoughts on the evolution of a scientific career

Mike Collis looks back at the decisions which led him to his role as the new Chief Executive of The Physiological Society

My first month as Chief Executive of The Physiological Society has just finished and it has been a stimulating and enjoyable learning experience. I don't know if there will be a 'typical' day to furnish an article for *Physiology News* in the future, but I thought it would be more appropriate to write something about my background and career path, to give you an insight into my motivation and vision for The Physiological Society. You are probably wondering what a pharmacologist who has spent most of his career in the pharmaceutical industry thinks about physiology!

I have always been passionate about science and fascinated by how biological organisms function. As a child I spent many happy hours looking down a microscope at simple specimens like pond water, and I was fascinated by the strange organisms that inhabited that micro-environment. Indeed, I consider myself lucky to have been educated at a time when performing experiments was key to school science lessons. I have vivid memories of the excitement I got from biology and chemistry practicals and the fascinating experience of dissecting a rat. The loss of practical science from today's classroom should be a major concern to us all as scientists. How will young people be inspired to become scientists if they don't experience the excitement of doing experiments?

As well as being fascinated by biology, I have always been motivated by the potential to use science to solve problems and improve health and welfare. This influenced me to choose one of the first Applied Biology courses available for my degree. I was particularly attracted by the 'sandwich course concept', where students spend periods working outside the university in laboratories, because it allowed one to sample a variety of scientific areas in depth. During my undergraduate days I actively sought variety and had my first work placement at Kew Gardens, studying plant physiology. My next placement was at the Ministry of Agriculture Veterinary labs where I learnt about various animal parasites. Despite the less savoury aspects of some field experiments, I found parasitic organisms fascinating examples of evolutionary adaptation to a very novel and challenging environment – in or on another organism. My final placement was in the pharmaceutical industry where I was given a project to develop a more relevant model of rheumatoid arthritis than the Freunds adjuvant model used then in screening. I greatly benefited from these work experiences. Indeed, throughout my career I have found that students who spend time working in the 'real world' of a research laboratory benefit hugely, and are much more motivated and employable than those without such experience.

> **'Nothing endures but change'**
> **(*Heraclitus 540 BC*)**

With this in mind, it is sad that the lack of practical science in schools is also mirrored these days at university level. Pressures to increase student numbers, without the necessary increase in the staff and financial support for science courses, have led to this unfortunate situation. In my experience, newly graduated scientists these days are ill-equipped to work in a research environment, unless they have gained real laboratory experience through a work placement or a significant practical project in their final year.

Mike Collis as a post-doc in Antwerp

My first real job was in the pharmaceutical industry in a small cardiovascular group. The leader of the group was a vet and I benefited greatly from his experience in performing *in vivo* experiments as well as a range of *in vitro* preparations used as quantitative pharmacological assays. Although the majority of my own subsequent research has been using *in vitro* systems, it has always been obvious to me that bio-medical advances require high-quality *in vivo* experiments performed by scientists who have been trained by experts with a genuine concern for animal welfare. This is another area of research and training that has seen significant erosion in recent years. Many of you will have read the survey performed by The Physiological Society in collaboration with the British Pharmacological Society (Maggie Leggett in *Physiology News* **60,** 39-40) which quantified the extent of this problem. I am very pleased to have lead the joint initiatives between the pharmaceutical industry and a number of other research funders to reverse this trend (Collis. *Nature Reviews Drug Discovery* 5, 377-380).

I studied for my PhD part-time, during my first employment within the pharmaceutical industry. The project I wanted to pursue concerned changes in the responsiveness of blood vessels from hypertensive animals. There was a great debate at that time between those who felt that these alterations were due to functional changes in the contractile machinery (e.g. David Bohr) and those, led by the eminent Swedish physiologist Bjorn Folkow, who suggested that these were a

consequence of structural changes involving an increase in vessel wall to lumen ratio. I wanted to test these different hypotheses by examining the way vessels responded to agonists which utilised different signal transduction mechanisms to evoke contraction and by performing a longitudinal study as hypertension developed. My research found that both hypotheses were correct, but that changes in signal transduction occurred early in the development of hypertension and were then followed by evidence of structural vascular changes. For me, studying for my PhD developed my passion for scientific research and allowed me to work in the laboratories of the eminent cardiovascular scientists who had inspired me with their work.

I have always thought that one of the great privileges of being a scientist is that one can work in different countries and in the labs of those who you admire and respect. I was awarded a Royal Society research fellowship to work with Paul Vanhoutte in the Department of Physiology and Pharmacology at the University of Antwerp. One of the many benefits of working in Paul's lab was the stream of eminent cardiovascular physiologists who visited. I found that the scientists who were the true leaders of the scientific area were always genuinely interested in the work of a humble post-doc like me. Living in Antwerp also gave me a lasting affinity for the area and its gastronomic and alcoholic delights!

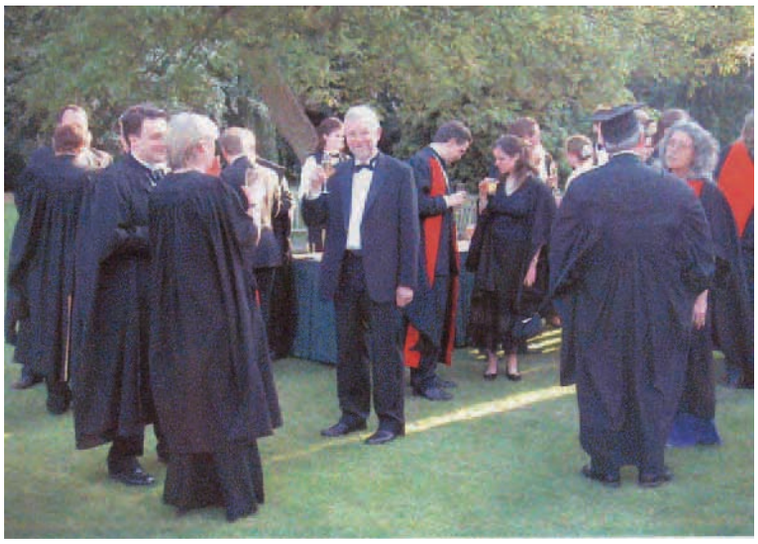
The proud owner of an aged Buick Wildcat in Rochester, Minnesotta

My next opportunity took me across the Atlantic to work with John Shepherd in the Department of Physiology at the Mayo Clinic. Being a post-doc at the Mayo was a challenging and exciting experience. Looking back, I view the quality of the research at the Mayo to be the equivalent of the best champagne. Post-doctoral training in the Department of Physiology was, however, rigorous and intended to develop you as a scientist. I recall vividly the often painful 8 a.m. Monday morning meetings where each post-doc had to present their work and respond to critical comments from some of the top physiologists in the US. The objective of this rigorous and critical environment was to develop independent scientists who could compete for grants. Feedback and peer review are the only real way we develop as scientists, but sometimes the experience is painful for the young scientist who finds it hard to realise that the criticism is directed towards improving the science and not at you personally! I feel that an essential role of a learned society such as The Physiological Society is to maintain the highest standards of scientific rigour and the peer review that nurture good science and good scientists.

John Shepherd at the Mayo Clinic

The next change in my career was to return to the UK and to the pharmaceutical industry. I wanted to use my cardiovascular expertise in a drug discovery environment and was fortunate enough to get a position at ICI Pharmaceuticals working for the renowned cardiovascular physiologist, James Conway. I had 12 very happy years at ICI and progressed a number of drug candidates into clinical development. I also had the good fortune to work with Mike Snow, an outspoken member of The Physiological Society who came from the Cardiovascular Research Group at Leeds. I learnt a great deal from Mike who has an intuitive understanding of haemodynamic control mechanisms and doesn't 'mince his words'.

In 1991, Pfizer approached me to move to Sandwich and manage their cardiovascular group, I accepted the challenge and started yet another phase of my research career. When I joined Pfizer, their aim was to be the number one pharmaceutical company in the world – they now are. Pfizer really hit the headlines with Viagra which was, of



Working hard at Downing College, Cambridge

course, originally a cardiovascular drug targeted for angina. Viagra was probably the most highly publicised launch of a new drug ever. What many people don't realise though is that Pfizer also markets the world's leading lipid lowering drug and the most successful calcium channel blocker.

After running research groups at Pfizer for about 10 years, I felt the need for a change and took on the new role of Scientific Director for collaborations and liaison. This role put me on the interface between the biological science going on at Pfizer in the UK and the UK/EU academic research environment. This was a very stimulating and enjoyable job in which I interacted and collaborated with scientists in many leading physiology and pharmacology departments, with the major learned societies involved with mammalian biology and with the research councils and industry associations such as ABPI/CBI. One of my most enjoyable 'duties' was to attend Physiological Society Meetings to judge abstracts and award Pfizer prizes to exceptional young physiologists at the start of their careers. Regrettably, following the downturn in the fortune of the pharmaceutical industry, I found my operating budget being cut dramatically and then my group closed down. I will not pretend that I found this a particularly pleasant experience, although I understood the business rationale for the decision. But all changes bring new opportunities and this one lead me to a new and stimulating role with The Physiological Society.

My own career has been characterised by change and adapting to new experiences. I believe in natural selection and appreciate the parallels between the natural world and that of human organisations. Continual adaptation and evolution to new circumstances are required for the long-term success of organisms and of organisations. This is certainly the situation at The Society as we go through a re-branding exercise, design a new web site and embark on the first joint meeting with the British Pharmacological Society and the Biochemical Society in 2007. There are some major threats to physiology and to The Society, such as the potential financial impact of open access publishing, the submersion of physiology departments into larger biomedical science clusters and the lack of understanding by the public of what physiology is all about. I feel that one of the challenges for The Society is to maintain its strong tradition of scientific excellence and quality publications, whilst engaging effectively with the public and the Government to ensure that physiology is seen as the exciting science that is fundamental to translating the explosion of genomic information into benefits to mankind.

In this article I have attempted to highlight some of the experiences and people (particularly the physiologists) who have facilitated and enhanced my scientific career. I feel I have been incredibly lucky to have a career in science and want to ensure that the new generation of aspiring young scientists have similar opportunities. I have also raised some of my concerns about the training and mentoring environment of the future. Who will teach science and medical students an integrative approach to biology in the 21st century? The Physiological Society has played a key role in shaping the scientific environment, both in the UK and abroad, and I hope that it will continue to fulfil this role. I feel that one of my missions as Chief Executive is to increase the profile of physiology as the basis for all life science and medical advances.

I would welcome your thoughts on the key issues for The Society and hope that many of you will respond to this article with your thoughts and proposals for future initiatives.

Mike Collis
Chief Executive, The Physiological Society

Special Interest Groups

From 2007, each of The Society's Special Interest Groups (SIGs) will be required to have two Convenors serving overlapping terms of office. This initiative, agreed with our current incumbents, has been introduced in order to ensure continuity of expertise and to provide the membership with further representation at SIG level. The Society is therefore currently seeking nominations for individuals to act as Co-Convenors (one each) for Cellular Neurophysiology, Cellular Signalling, Comparative Physiology, Epithelia & Membrane Transport, Heart & Cardiac Muscle, Human Physiology, Locomotion, Microvascular & Endothelial Physiology, Muscle Contraction, Renal Physiology, Respiratory Physiology, Sensorimotor Control, Sensory Functions, Somatosensory Physiology and Teaching and Co-Convenors (two each) for Cardiovascular, Respiratory and Autonomic Control, Blood-Brain Barrier, Comparative & Invertebrate Neuroscience, Ion Channels and Smooth Muscle.

The deadline for nominations is 1 December 2006. Further details and nomination forms at http://www.physoc.org/sig/index.asp

Through the looking glass – the state of Indian physiology and pharmacology

As a UK delegate at the 51st Annual Conference of the Association of Physiologists and Pharmacologists of India (APPICON) held in Pondicherry in December 2005, I was surprised by a prominent Indian scientist in his opening remarks lambasting Indian physiology and pharmacology in general, but particularly the quality of doctoral theses. This outburst contrasts starkly with commonly held views of Indian biochemistry and information technology.

Having attended APPICON and visited a number of departments within India over a 9 month period, I feel that much of the work appeared to fall into one of four camps.

Research generated from an idea without an appropriate web-based literature search

Whilst the information contained within the abstracts provided by Medline is, of course, limited, it should at least serve to prevent unnecessary duplication. Whilst acknowledging that access to journals may be limited, no study in the 21st century should be initiated let alone reach the stage of data presentation.

Many of the 'ideas' were intellectually worthy, however this is not enough. I am yet to meet a scientist who has not had a 'great' idea only to find their hopes dashed as they learn that a similar or identical publication already exists. Pursuing such work without scientific justification is a waste of precious time, intellect, energy and resources.

Some of the work appeared to be a repetition of published work upon an Indian population

This is entirely justified when significant population differences may exist, for instance where genetic or nutritional factors are relevant or if this information aids the application of a particular theory or practise within India. However, this is not always the case and it must be recognized that the international academic appeal of such work may be limited.

David Green speaking at the closing ceremony of the annual conference of the Association of Physiologists and Pharmacologists of India.

Yoga – the 'key' to health

Similar accusations could be levelled at the significant emphasis on yoga and naturopathy-related healing. Whilst both areas represent niches for Indian science and offer significant opportunities for low cost community based care, it is important for the perception, strength and growth of biomedical science that it is not limited to such enterprises.

The fourth type of work was that which possessed an international perspective

This may have resulted from an appropriate knowledge of the international literature with, or without an active collaboration. Even if the work was collaboratory in nature, often the work was conducted in India by Indians. Therefore the talent is present within India, however on occasions it may be wasted, or at least not maximised. Of course, the 'brain drain' entices particularly the talented, and those possessing a broad horizon. In fact the widespread use of English as the language of scientific teaching and interaction offers a poisoned chalice. However, if the conditions are right, personnel and investment flow can be inward; unfortunately, this is not the case for the biomedical sciences.

In order to reverse this trend and recognize the talent that India possesses action needs to be taken. Obviously retaining talent by improving facilities, providing career incentives for research and increasing the financial rewards are expensive and difficult to justify. Particularly when it could be argued that the quality in depth is not present and that basic health care is not a right given to all. I, however, propose a simpler and, I believe, a more cost affect initiative.

The way forward?

Access to Medline and an email address for each member of academic staff could be provided. In this way, even in medical colleges with little or no current ability to conduct research, there can be interaction with the wider scientific world. This would open the lines of communication and create opportunities for collaboration, initially within India. The Indian scientific community is spread across the nation; therefore communication has traditionally been extremely difficult. Hopefully this can serve to strengthen the opportunity, resolve, ability and ultimately quality of research. Then an annual conference could serve as a place to put a face to a name, and a spring board for new and stronger ties that operate all year round.

Currently, much good work remains under the radar of the international scientific community as some Indian journals do not possess a citation index. The improvement of submissions to the *Indian Journal of Physiology and Pharmacology*, for example, would then increase the possibility of obtaining a citation index. Subsequently, this and other interactions could then provide a spring board to broader international collaboration.

Of course, the 'rest of the world' needs to be willing to grasp the mantle. In addition to personal or organic collaborations, institutions such as Imperial College London are actively starting to formulate more formal links; however, ultimately they succeed or fail on personal interaction. Funders also have a pivotal role to play. International grants should highlight the potential role of work originating in the developing world in order to overcome the belief that they are not entitled to apply and also to encourage so that time and effort is spent with at least some degree of hope.

When encouraging medical research in developing countries one should not consider it an opportunity to 'do it on the cheap'. In fact in my experience technical equipment costs are not considerably different from the developed world. Furthermore, any studies should have the same regard for ethics and the rights of subjects as Europe or the USA. Advantage should not be taken of potential poverty or lack of knowledge that may result in participation in studies unattractive in developed countries. A vital point is that the aims and potential benefits of a project must be consistent with the needs and desires of that particular country and its people.

If a more complete spectrum of funding opportunities were presented to the developing world, Indian scientists in some areas may be well placed to compete. In this age of globalisation developing nations cannot be expected, or expect to support, international quality research alone; however, by taking bold steps to facilitate interaction research can improve.

Greater incorporation of Indian scientists would benefit not only India, but international science as a whole drawing on the reservoir of talent. India is a vast country and it would be a travesty of a missed opportunity if the revolution taking place in other industries and disciplines fails to be extended into the biomedical sciences before it is too late.

David A Green
Department of Movement & Balance, Department of Clinical Neurosciences, Imperial College London, Charing Cross Hospital Campus, London, UK

Society Member Subrata Tripathi responds

Dr Green's account of his experience in India is accurate in its description of the contemporary state of affairs in Indian medical colleges, and this has in general been true for the last three or four decades at the very least. At a time when physiology departments around the world have long separated from pharmacology and are in fact themselves being subsumed, the 'Association' of Physiologists and Pharmacologists of India (APPICON) appears anachronistic. I am not a member. Indeed it is not the adhering body' to the International Union of Physiological Sciences (IUPS). IUPS is linked by the Indian National Science Academy; in contrast, neighbouring countries like Pakistan and Sri Lanka have direct links to IUPS through their national physiological societies.

It is heartening to see Dr Green's concern in suggesting possible ways forward, but I feel that he has not fully grasped the realities of funding of higher education, not just medical education, that come in the way of a sustainable improvement in the teaching (and research activities) of basic biomedical sciences in India. First and foremost, physiology, with one or two exceptions, is not part of mainstream university education, and thus outside the purview of the University Grants Commission. Because a career in medicine is easily among the most sought after in India, most physiology teaching is done in medical colleges, *affiliated to Universities*, but funded by the Health Ministries of the central or state Governments, where fiscal outlay is nominally above payroll. Private medical colleges, with a couple of exceptions, are much worse. Thus there is very little funding for basic biomedical sciences in general and certainly does not attract the better graduating doctors for a career in teaching or research. Health and medical education are not electoral issues and the budgetary outlay at both central and state governmental level is directed at clinical care. The other ministries like Biotechnology and Science and Technology fund investigator initiated projects, but that is a small fraction of what is needed.

The magnitude of the problem is so large that it is not possible for 'outside' help to compensate for the lack of direct investment by the Government in medical education. Indeed, there is a move afoot to expand medical education and research rapidly by opening about half a dozen institutes like the All India Institute of Medical Sciences, along the lines of the more successful Indian Institutes of Technology. However, the political will to generate resources with a 'Health Cess' like the recently introduced 2% 'Education Cess' is yet to emerge. Most physiologists already have internet access and cellular phones at rates among the cheapest in the world, and with the growing list of free online journals are certainly not as badly connected as it might appear. However, very little initiative can be expected without a solid scientific support base and fiscal outlay by the State and the Central Governments. This is compounded by a lack of appreciation of the circumstances under which a handful of Indian physiologists and pharmacologists have made outstanding contributions to the world literature and APPICON could still be the forum to convey that inspiration to younger entrants to these subject areas.

Subrata Tripathi
Tata Institute of Fundamental Research, Colaba, Mumbai, India

European consultation on animal research

The European Commission has started a public consultation about the revision of Directive 86/609 which regulates animal research within the EU.

The consultation is in two forms:

- a set of questions for the general public about broad issues
- a much more detailed questionnaire aimed at experts.

The Society encourages Members to make individual submissions (numbers count!) and will also be making a formal response to the Consultation. If you wish to contribute to The Society's response, please contact Liz Bell (ebell@physoc.org).

For further information please visit
http://www.physoc.org/news/full_details/index.asp?ID=313

Three long-standing women Members of The Society, Olga Hudlická, Gerta Vrbová and Lynn Bindman, reveal what turned them on to physiology

Olga as a newly qualified doctor in 1950 (top) and Olga as she is today

Olga Hudlická, Emeritus Professor of Physiology in Birmingham, found genetics a turn on ...

Whilst I was still at grammar school in Czechoslovakia, I read a book about genetics and was really fascinated by it. At that time the only places where genetics was taught was in medical schools, so I decided I had to study medicine. However, by the time I had started to make progress with my studies, genetics in general, and the professors who taught it in particular, were under heavy criticism from the communist party, so it would have been hard to pursue my interests in this area any further. But I wanted to have some experience in science, so as a student I worked for almost 2 years in the Department of Experimental Pathology, gathering sera from patients with cancer and analysing them for special binding of Cu^{2+} with proteins. My supervisor was hoping to discover a new method for the early diagnosis of cancer. When I finished the analyses, and presented him with the results, he asked me what I suggested could be done with the data! I was so disappointed by the fact that he did not have any hypothesis, and that all my work was for nothing, that I decided not to have anything more to do with so-called science and I made up my mind to specialise in cardiology.

But I was persuaded, I think against my better judgement, to do something else.

Czechoslovakia was under German occupation from 1939 until the end of World War II and the universities were closed. Many university teachers, scientists as well as doctors, had perished in concentration camps. So after the war, there was a tremendous shortage of doctors, enormous numbers of students (there were 3,000 students in the first year when I started to study, and we had lectures in the biggest concert hall in Prague) and too few university teachers who were overworked with teaching, writing textbooks, or giving oral examinations.

Of course, they had no time for research. As a result, in the late 1940s the government created special institutions where a few selected scientists would train young graduates to pursue a career in research. I was asked to be a part of this programme whilst I was finishing my studies for my medical degree and I agreed to start immediately afterwards. At first I was very unhappy about the whole thing, particularly because my supervisor was a neurologist who was interested in epilepsy and conditioned reflexes and asked me to work out a method to produce spasm of cerebral arteries as a conditioned response and then to de-condition it.

As a galvanometer and a kymograph were the only pieces of equipment I had, some lateral thinking was required and I decided to measure the temperature in the rat brain as an indicator of blood flow. It took me 6 months to realize that the whole thing was absurd. Fortunately, Ernest Gutmann, who had worked for his PhD at Oxford during the war, was in the same department and advised me to assess cerebral circulation by direct observation of pial vessels through implanted windows in the skull. After several months I had three cats with well-healed windows ready for observation. However, the lab moved to a different part of Prague and the cats escaped, I gave birth to my daughter and my galvanometer and kymograph disappeared! I was able to work on the cerebral circulation later when I studied the role of sympathetic nerves in the regulation of cerebral blood flow and blood pressure in orthostatic collapse on rabbits. And I also asked for a transfer to Gutmann's group.

Gutmann's focus was muscle atrophy and regeneration. He taught me how to think and design experiments using the very limited equipment we had, but he could not teach me about methods in cardiovascular research. This was unfortunate since the task I was assigned within his group was to demonstrate the importance of blood flow in atrophic muscles. It was possible to travel to Hungary, so I went to learn some methods there, but the most important source of help came from the UK. Sidney Hilton, who was then working at Mill Hill in London, came to Prague for several weeks and helped to introduce me to some techniques needed to measure skeletal muscle blood flow. I was also fortunate to be able to spend 6 months at the Karolinska Institute in Stockholm where I learned much more about the ways of thinking about cardiovascular physiology and also started to have contact with Gene Renkin, with whom I later worked in the USA. I think his was the greatest influence in my rather convoluted career in physiology. But it all started with that genetics book.

Olga Hudlická
Department of Physiology, University of Birmingham, UK

For Gerta Vrbová, Emeritus Professor of Physiology at UCL, it was a combination of curiosity and a feeling of helplessness that got her started ...

When I was a medical student in Prague in 1948 I became fascinated by the newly emerging knowledge about how signals travel along nerves, and how nerve cells communicate with each other. I wanted to understand more about these events, and possibly expand the knowledge about them myself. Charles University had an Institute of Brain Research and in the fourth year of my medical studies I went to the Institute and presented myself to Ernest Gutmann, who at the time worked in the Institute where he studied peripheral nerve regeneration. When I first met Ernest and offered my services he asked me what I wanted to investigate and, of course, I had no idea. I had never seen a laboratory and had no experience with research of any kind. I told Ernest that I was interested in how nerve cells communicate with each other.

'to improve on the lack of equipment, I was presented with an old oscilloscope and asked to put it in working order'

At that time the department had no equipment other than a balance, some equipment to study morphology and an oven to dry tissues. In order to improve on this lack of equipment for physiological studies an old oscilloscope was presented to me and I was asked to put it into working order.

I had never seen an instrument like this, but I bravely struggled to get this machine to work. After much effort and waste of time when I was getting nowhere I discovered that the oscilloscope I had been given had no cathode ray tube! This was a real setback so I decided I would use the equipment that we already had that I knew worked. The balance and oven for drying tissues seemed to be the best

Gerta Vrbová in 1948 (top) and now

equipment available, so we had to design a project that could be accomplished using it. Together with another student in the Institute, Ivan Rychlik, we decided that we could study an important clinical problem – brain oedema and its control. This project was quite successful, and taught me to design experiments that could be accomplished with very simple equipment.

Shortly afterwards Ernest Gutmann moved to the new Institute of Physiology and became Head of one of the divisions. Our Division consisted of three people: Ernest Gutmann, myself and Radan Beranek. Ernest believed that physiological problems should be tackled using a multidisciplinary approach and this concept appealed to me tremendously, although we were a little short staffed for this approach! The central question that our little group set out to study was trophic interactions between motor nerves and muscle, and this was closer to my original interest of studying communications between cells. We still had little equipment, and lacked in training and experience, but we made up for these shortcomings with enthusiasm.

Even so, I was still not sure that I wanted to do full time research. After I qualified and became a medical doctor I accepted a full time job at the Department of Neurology at the Charles University. It was an excellent Neurology Department and I enjoyed learning the tricks needed to diagnose

'we had to design a project that could be accomplished using the equipment we knew worked'

the neurological deficits in my patients. However, after having accomplished this, there was, in most cases, little that could be done to treat the patient. It was this helplessness and curiosity about how the nervous system and muscles work that finally drove me back to do basic research. I have always hoped that in the long run our understanding of the system will have an impact on treatment of neurological disorders.

So I suppose there were four main reasons for my becoming a physiologist:

- reading about the mechanism how signals are conducted along nerves;
- the enthusiasm of Ernest Gutmann;
- curiosity;
- helplessness when faced with treating most neurological disorders.

Gerta Vrbová
Department of Anatomy and Developmental Biology, University College London, UK

Gerta's book *Trust and Deceit*, a story of her wartime experiences in Czechoslovakia and Hungary, is reviewed on p. 50.

Until 30 September 2006, Readers of *Physiology News* may obtain copies of the book at the reduced price of £13 including postage and packing. To order your copy see details, also on p. 50

... and for Lynn Bindman, Emeritus Reader in Physiology, UCL, it was a blind date ...

A mixture of chance, ignorance and fascination led me to become a physiologist.

A friend asked me to look after a visiting American. I arranged to meet my blind date outside Foyle's second-hand bookshop in the Charing Cross Road. Misplaced among the novels outside the shop was Bainbridge and Menzies' *Textbook of Physiology*. I picked it up out of curiosity, realised that physiology was the aspect of zoology I most enjoyed, and bought the book.

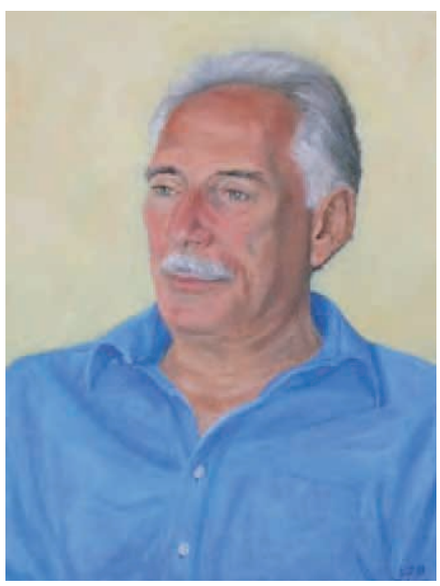
I had thought of studying art and english at A Level, but my father pointed out I should be able to earn a living. 'You won a science prize,' he said 'so why not study science and get a job as a laboratory technician?' My school told me I needed physics as well as A Level botany, zoology and chemistry, but I didn't enjoy physics lessons. The teacher had appalling body odour. When I found I couldn't enter university without the subject, I went to a tutorial college for a 9 month A Level course. The Principal looked up university physiology degrees for me. I didn't fancy living in a women's college at Oxbridge. King's College London only offered physiology as an intercalated degree in the medical course in those days, so University College London (UCL) was the only place to which I applied. I knew nothing about the quality of the teaching or research there.

At my first interview, Sir George Lindor Brown asked me why I wanted to study physiology and not medicine? I quoted my parent's view that medicine was an unsuitable career for a woman to combine with marriage and children. He looked over his spectacles at me and murmured 'Ah. Both my wife and daughter are doctors'. I wasn't offered a place. However, I was put on the waiting list; one of the accepted applicants went to Cambridge, so I did get into UCL, in 1957.

Dr Laurence Smaje by Lynn Bindman, 2006.

The Physiology Department at UCL was a wonderful place to be a student. I had weekly tutorials with Otto Hutter or Jim Pascoe, and their enthusiasm for the subject was contagious. In the Easter vacation I worked for three weeks in Alan Ness' lab. 'Why do you think the rat's lower jaw incisors can be independently moved laterally?' he asked. 'Is there a cutting edge in the midline?' I enquired. 'Good' he replied, but no, there wasn't. We didn't find the answer in spite of hours of observation, and measuring the angles between the incisors' tracks when the rat scraped the edge of a block of cheese. A paper published subsequently described how rats use the lower incisors for grooming and crushing insects in their fur. Alan's enquiring mind was stimulating and I felt that for the first time in my life I was being asked to think creatively instead of learn facts.

Dr Howard Jacobs by Lynn Bindman, 2005.



The third undergraduate year trained us for research. We often experimented 4 full days a week. We interacted with postgraduates and staff informally in the teaching labs. and in the Starling Room. We went to lectures given by eminent visitors. I remember being cross with Jim Pascoe for sending us to a boring lecture on somatosensory cortical mapping in a variety of animals. That's anatomy, not physiology, I complained.

Meanwhile, a boyfriend, Geoffrey, had gone to Chicago as a teaching fellow in law for a year. He asked me not to marry anyone else while he was away, and we corresponded weekly by airmail. He was invited to work in Boston. Would I come over? I found a poster in the corridor offering a postgraduate fellowship at Harvard, to work with Steven Kuffler. I went to ask Bernard Katz if he'd give me a reference. 'Certainly not', he replied kindly. I was summoned to see G L Brown. 'It's no good you going to the States until you have a PhD' he explained. I was conditionally offered an MRC scholarship, to do my PhD with Olof Lippold, who became a lifelong friend.

Geoffrey decided to return to the UK and work as a solicitor. We married the next April, during my PhD. Olof collaborated with a psychiatrist, Joe Redfearn, and once a week we drove to Graylingwell mental hospital near Chichester to research the effects of weak polarizing currents passed through the human brain. The current had remarkable success in a catatonic patient who became able to talk, and in alleviating depression in other patients. We tried the procedures on ourselves before applying them to the patients. Unfortunately, one day the technician set the control to 10 times the normal value; we didn't notice, and the excessive current caused my mouth and hands to contract in a spasm. I hope there are no long-term after-effects. At UCL we examined the effects of polarizing currents on the cerebral

cortex of anaesthetised rats. Weak direct currents that increased firing rates, and enlarged cortical evoked responses, produced effects that lasted hours after the current ceased. That was my first paper in *Nature* in 1962, but I was very much the junior author.

Our first child was born in May 1963 before I completed my PhD. I finished writing it in the autumn, I think, because our then Head of Department, Andrew Huxley, asked my permission to take it to Stockholm with him, to read on the journey to collect his Nobel prize. After our second son was born, Andrew suggested I worked part-time, which I did for the next 8 years, until our daughter started school full time. When I was experimenting for up to 20 hours a day, I often thought of my parents' advice that medicine was not a suitable career for a married woman with children. My parents ended up helping me look after them, because physiology was much too exciting a career to give up.

Now in retirement, I have started painting again. Rather than provide photographs of myself for this article, I submit two paintings of friends. Would anyone else like to be a model and get a free portrait?

Lynn Bindman
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Potential sitters may contact Lynn at
l.bindman@ucl.ac.uk

A risky course

Hugh De Wardener's account of being his own experimental subject (*Physiology News* **63**, 13) reminded me of the hazards facing biomedical students in the 1950s. If any sort of Safety at Work or Human Rights legislation existed in those days it didn't extend to the Departments of Physiology, Biochemistry or Pharmacology in the University of Edinburgh.

My first year was spent doing zoology, chemistry and physics. This was risk free with no unscheduled excitements except when a physics lecturer ignited his gown by draping a sleeve on the glowing rheostat while demonstrating Wilson's Cloud Chamber. The second year was more challenging: I combined zoology with the physiology and biochemistry course taken by the medics for 2nd MB. In a physiology practical on the difference between oxygen consumption when resting and standing, I was attached to a spirometer, with CO_2 absorber, and told to lie still until instructed to stand. All of a sudden the lights were much brighter, the lab was much noisier and the rest of the group were grumpily complaining that I hadn't stood up when told to. Luckily for me, someone noticed I'd gone blue and had disconnected me from the faulty spirometer. Though none of us had any values to put in our practical books it was, at least for me, an unforgettable demonstration that the onset of anoxia is completely undetectable but senses are heightened in recovery. Another experiment, on the pH of urine, required us to take an ammonium chloride pill at regular intervals during the 18 hours preceding the practical. One subject who had forgotten to do this obligingly swallowed the lot all at once. She passed out but lived to tell the tale.

For one of the biochemistry practicals we kept a week-long record of everything we ate, then worked out the calorific value, and the proportion of protein, carbohydrates etc. (no interest in unsaturated fats and fibre at that time). Obviously it saved a lot of effort to eat (or claim to eat) the same menu every day, or even for every meal. I have kept my menu and can truthfully say that the frequent appearance of bread and jam is a reflection on my landlady, not my honesty. The lecturer's main reaction to our tabulated results was surprise at our survival. In another practical we extracted stomach contents from each other via a nasally-inserted stomach tube; release came only when blood was detected in a sample. Possibly the most dubious biochem practical involved the injection of insulin followed by frequent blood sampling. As a sop to safety, or possibly to shift responsibility, the injections were given (reluctantly) by a medically qualified lecturer in the Pharmacology Department. At the end of an afternoon of finger pricks we crossed the road for coffee at 'Medical Martins' where it was exceptionally warm. Before long I noticed my left leg felt damp – blood was trickling from my fingertips into my shoe.

It was ironic that the biochemists considered the Pharmacology Department as 'better qualified' given that the third year pharmacology course included the injection of cocaine. Since the instructions warned that intravenous injection should be avoided we chose the intercalating veterinary student to do the job. He inserted the needle painlessly, drew back expertly – and the syringe filled with blood. This so unnerved him that on his second attempt he went in at a very shallow angle thereby rolling up a fold of skin: the needle came out the other side and the cocaine shot across the lab.

I don't remember any thing particularly alarming in 3rd year physiology, but the final year had its moments. In one of Mary Pickford's practicals we were injected subcutaneously with vasopressin (it was excruciatingly painful), then told to drink a litre of water. We felt pretty nasty and were all thankful to shed our water load peacefully at home during the evening. All, that is, except Mike Brush – he had gone to the theatre and his frequent visits to the Gents were not popular with his neighbours. Mike also suffered more than the rest of us in Reg Passmore's exercise experiment in which we did step tests on blocks of different heights. Since he was a cross-country runner, Mike was made to exercise on higher steps, and at a greater rate, with a brick-filled ex-Army haversack on his bare back. Reg's only response to Mike's head shakings and agonised expression was to urge him on. The experiment ended abruptly with Mike desperately disconnecting himself from the Douglas bag, then revealing a back rubbed raw by the canvas haversack. In another of Reg's experiments we had to establish our residual volume, i.e. the amount of air remaining in the lungs after maximal expiration. This involved being weighed under water in an enormous tank. To get in, we climbed a ladder, then swung across to a seat that was lowered to the point of total immersion. I remember nothing of the science but a lot of the accompanying alarm.

We were the last year to suffer this experiment because the lab was demolished soon afterwards. Reg's intention to install a sunken, possibly less intimidating, tank in his new lab was thwarted by the impenetrability of the Edinburgh granite – something our successors should have been grateful for.

Ann Silver
Honorary Member, Cambridge, UK

Autoregulation of neuronal activity by presynaptic $GABA_A$Rs

Presynaptic $GABA_A$ receptors have recently been identified in several cell types. Alain Marty and Sheyla Mejia-Gervacio present evidence showing that these receptors are able to shape neuronal firing patterns and discuss the role of this regulatory process for the maturation of synaptic networks in the cerebellum

Alain Marty (left) and Sheyla Mejia-Gervacio

It has been known for decades that $GABA_A$Rs exist in presynaptic terminals and in axonal locations of crustacean nerve-muscle preparations, as well as in the mammalian spinal cord. However, their exact functional role remains poorly understood. Presynaptic $GABA_A$Rs presumably sense ambient GABA, which remains in the interstitial fluid after synaptic activity from neighbouring neurons. An alternative, recently explored, possibility is that GABA is released by the neuron containing the receptors. In this case, presynaptic $GABA_A$Rs act as autoreceptors.

Due to the technical difficulties of recording the currents generated by activation of presynaptic $GABA_A$R in axons, studies showing clear functional $GABA_A$R-mediated presynaptic conductances have remained scarce. Recent examples include the suprachiasmatic nucleus, where axonal $GABA_A$Rs have been proposed to be involved in the modulation of neurotransmitter release (Belenky *et al*. 2003). In hippocampal mossy fibers there is evidence for the co-release of GABA and glutamate after seizures (Gutierrez, 2000), and axonal $GABA_A$Rs have been identified (Ruiz *et al*. 2003) but their functional significance remains unexplored. In the interneurons of the molecular layer of the cerebellar cortex (MLIs), Pouzat & Marty (1999) showed that, following an action potential, it is possible to record $GABA_A$R-mediated currents which are generated in the axons. These currents could be differentiated from those of somatodendritic origin on the basis of their slower kinetics and small amplitude fluctuations. These axonal $GABA_A$R-mediated conductances act as autoreceptors, since GABA binds back to the cell from which it was just released (Fig. 1*A*).

In a recent study we addressed the functional consequences of $GABA_A$ autoreceptor activity in MLIs. Our experiments showed that the activation of this axonal conductance produces a slow afterspike potential that could be recorded in the soma (Mejia-Gervacio & Marty, 2006). When using a physiological intracellular concentration of Cl^-, which in MLIs is above equilibrium (15 mM: Chavas & Marty, 2003), this afterpotential is depolarizing. As shown in Fig. 1*B*, both the autoreceptor current (i) and the afterdepolarization (ii) are sensitive to $GABA_A$R blockers (Pouzat & Marty, 1999; Mejia-Gervacio & Marty, 2006). The $GABA_A$ autoreceptor-mediated afterdepolarization lasts about 150 ms and its peak amplitude reaches from 5 to 20 mV. Its activation increases the presynaptic afterspike excitability, sometimes producing afterdischarge.

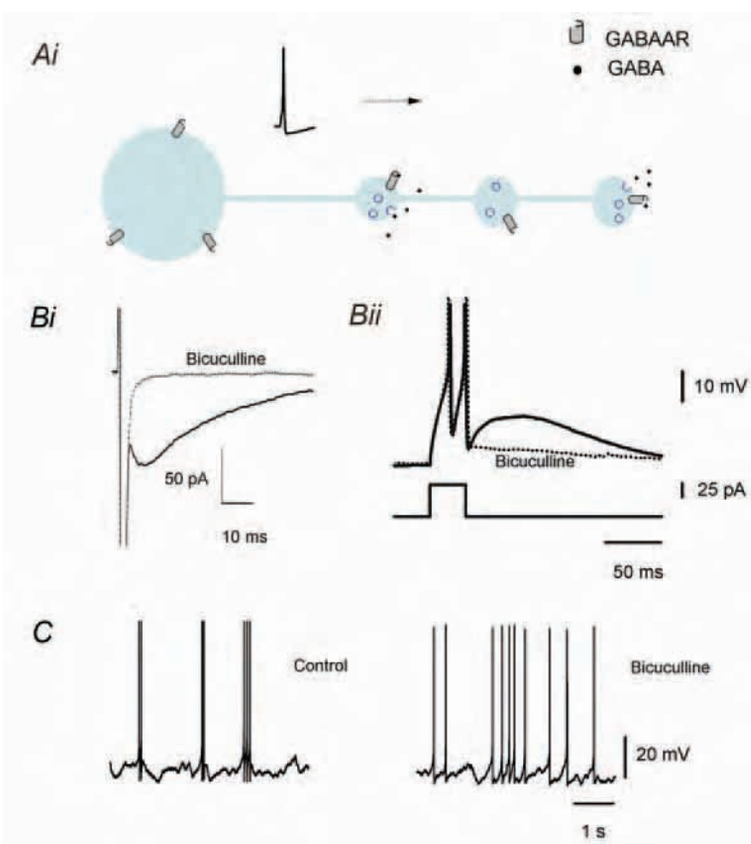

Figure 1. *Ai*, Schematic representation of a gaba-ergic neuron with self-activating axonal $GABA_A$R-mediated conductances. The depolarization of the axon induces GABA release which binds back to receptors located near the release site in the axon. *Bi*, The activation of $GABA_A$R-mediated conductances in the axon produces a slow inward current which follows the Na^+ current responsible for the action potential. This inward current is sensitive to bicuculline (from Pouzat & Marty, 1999). *Bii*, In current clamp, MLI firing produces a slow afterdepolarization, which is also sensitive to bicuculline. *C*, The application of bicuculline switches the spontaneous firing pattern of a MLI from bursting to regular firing in this postnatal day 13 (PN 13) neuron.

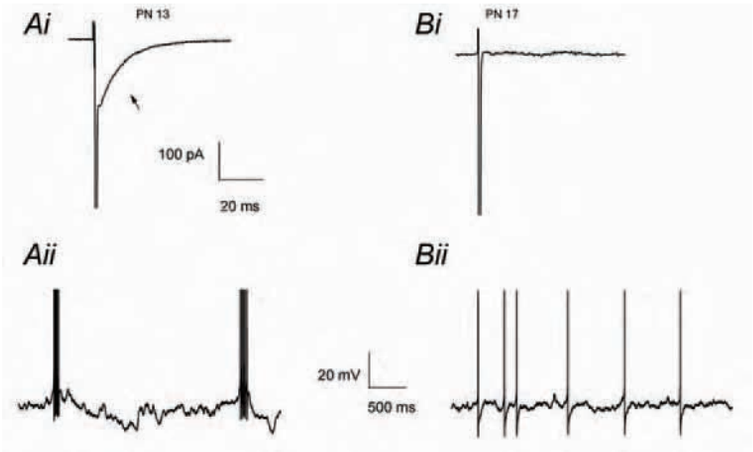

Figure 2. Transient expression of autoreceptor $GABA_A$R-mediated current shapes the firing pattern of cerebellar MLIs. *A*, At PN 13 the expression of autoreceptor current (arrow in *Ai*) coincides with a bursting' firing pattern (*Aii*). *B*, At PN 17, the disappearance of autoreceptor current (*Bi*) coincides with a shift to a regular firing pattern (*Bii*). Recordings in *Ai* and *Aii* (respectively *Bi* and *Bii*) were done in the same cell.

The increase in afterspike excitability, mediated by $GABA_A$ autoreceptor currents, shapes the firing pattern of MLIs, promoting discharge in short 10-20 Hz bursts. Conversely, blocking these conductances leads to a more regular firing pattern, as shown with pharmacological blockers (Fig 1*C*), or following washout of autoreceptor currents after long periods in whole-cell configuration (Mejia-Gervacio & Marty, 2006). Spontaneous activity in bursts was found in MLIs during the developmental stage immediately following the establishment of MLI-PC synapses, namely PN 8-15. This bursting pattern gradually fades with the $GABA_A$ autoreceptor conductance, until both phenomena disappear completely at PN 17 (Fig. 2). Thus, the expression of the autoreceptor current and its regulation of firing pattern, coincide with the period in which the synapse MLI-PC shows an immature phenotype (PN 8-15). It seems likely that the transient expression of axonal $GABA_A$R, and possibly of other presynaptic receptors as well, influences the establishment and maturation of synaptic contacts. Specifically, repetitive presynaptic firing could help synapse stabilization by enhancing the release probability of the neurotransmitter. Moreover, the control of neuronal excitability by axonal $GABA_A$Rs makes this process susceptible to modulations affecting both axonal conductance and membrane potential, since the size of the afterspike depolarization diminishes at values approaching E_{Cl}.

Presynaptic $GABA_A$Rs thus seem to be involved in the autoregulation of neuronal activity. The sign of this regulation is likely cell type-specific, and will depend on factors such as E_{Cl} (see above), as well as some other unexplored ones. In periglomerular cells of the olfactory bulb, GABA is released from dendrites, and binds back to dendritic autoreceptors (Smith & Jahr, 2002). In this case, the activation of $GABA_A$Rs inhibits firing, even though the position of E_{Cl} is quite depolarized in these cells, as it is in MLIs. The reason why dendritic autoreceptors of periglomerular cells are inhibitory, while the axonal autoreceptors of MLIs are excitatory, is uncertain, but may be related to the timing of GABA release, which may be more precise in the latter case.

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New Editor for *The Journal of Physiology*

David N Sheppard (University of Bristol), pictured right, has joined the Editorial Board of *The Journal of Physiology*.

David and his colleagues investigate the relationship between the structure and function of the cystic fibrosis transmembrane conductance regulator (CFTR) Cl- channel, with the goal of developing rational new therapies for cystic fibrosis and related diseases. After obtaining his PhD from the University of Cambridge with Francisco V Sepúlveda, David undertook postdoctoral research with Fernando Giraldez (Universidad de Valladolid) and Michael J Welsh (University of Iowa). Returning to the UK, David was a BBSRC Advance Research Fellow at the University of Edinburgh before becoming a Lecturer, then Senior Lecturer, at the University of Bristol. David is Co-ordinator of EuroCareCF, a European Commission-funded project to integrate cystic fibrosis research in Europe. The BBRSC and CF Trust generously support the research of David and his colleagues.

Muscle damage and exercise: does the brain contribute to muscle weakness?

Some forms of exercise lengthen contracting muscles. This damages the myofibrils when we are not accustomed to the exercise, and full recovery takes some days. Recent studies by Simon Gandevia and colleagues have looked not only at the peripheral changes in the muscle but at the changes in the central nervous system. Voluntary activation of the muscle is impaired after eccentric exercise and contributes to muscle weakness. This impairment depends on the length of the muscle

Most of us have, at some time, experienced the sensation of muscle pain, stiffness and weakness the day after some unaccustomed exercise, such as running or hiking. These symptoms typically last for several days, and indicate that our muscles have been temporarily damaged. Studies into this phenomenon go back more than 100 years (Hough, 1902). The damage is greater when the exercise involves contractions in which the muscle has been actively lengthened and used as a brake or shock absorber. These are termed eccentric contractions. During exercise we use our muscles as both motors and brakes, and they are more prone to damage when used as brakes.

A characteristic property of skeletal muscle is its length-tension relation. A muscle produces its maximal isometric tension or force at a specific optimal length, and this force decreases when the muscle operates at lengths longer or shorter than the optimum. In humans when muscle is damaged after eccentric contractions, the length-tension relation and optimal length actually shifts to the right, in the direction of longer lengths (e.g. Prasartwuth *et al.* 2006, see Fig.1). Hence the exercise induces different degrees of weakness at different muscle lengths.

Research into exercise-induced muscle damage has largely focussed on peripheral factors responsible for the prolonged weakness, in particular the muscle fibres themselves, as morphological evidence of damage to myofibrils has been reported in humans after eccentric contractions (for review see Proske & Morgan, 2001). But what about central factors – is it possible that a reduced ability of the brain to drive the muscle contributes to the weakness? It certainly contributes to reduced maximal force in some acute bouts of fatiguing exercise (for review see Gandevia, 2001). Our recent evidence suggests that the answer is also 'yes' when muscle is damaged by exercise.

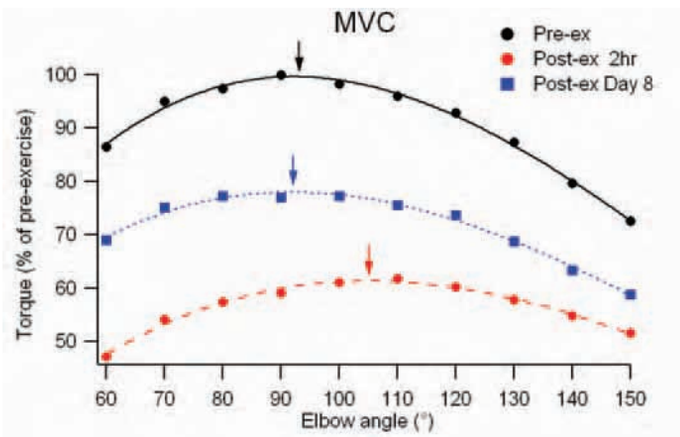

Figure 1. The relationship between maximum voluntary strength of elbow flexors and joint angle (muscle length) before and after a period of damaging eccentric exercise (mean of 8 subjects). There is both a prolonged voluntary weakness in the muscle, and a short-term shift in the length-tension relation towards longer muscle lengths. Recovery of force is not complete 8 days after exercise. Data from Prasartwuth *et al.* (2006).

We tested for changes in voluntary activation of elbow flexors after a series of eccentric contractions, using twitch interpolation (Prasartwuth *et al.* 2005). This technique is used to estimate how effectively the muscle is being driven by the central nervous system during a maximal voluntary contraction (MVC). The amount of 'extra' force (if any) produced by an electrically-evoked twitch during a MVC is compared to the force produced by the same stimulus in a resting muscle. If, for example, the extra force produced by a twitch during a MVC is 10% the size of the resting twitch, voluntary activation is calculated as 90% (Gandevia, 2001).

We first found that after the elbow flexor muscles performed eccentric exercise until maximal voluntary force had fallen by ~40%, there was a significant reduction in voluntary activation by 19% (from 97 ±1% to 79 ±7%), when measured at 90° elbow angle (Prasartwuth *et al.* 2005). This reduction persisted for 2 days after the exercise, suggesting that the decrease was not simply due to a short-term effect such as metabolic fatigue. Eccentric muscle damage is more prominent if the muscle is lengthened from a length beyond its optimum (Morgan, 1990), but we wanted to know whether changes in voluntary activation also showed a major dependence on muscle length. As a follow-up, the study was repeated, but this time maximal voluntary force and voluntary activation were measured across a wide range of elbow angles, between 60° (short length) and 150° (long length). Again, eccentric exercise was performed until MVC force dropped by 40%.

After exercise, the optimal angle for MVC torque had shifted to the right (by ~16°). Voluntary activation was reduced significantly at all test angles in the early stages after exercise (2 hours, 1 day), and had not fully recovered after a week (being still impaired at the shortest test length of 60°). Interestingly, the size of the reduction showed a length-dependence, being more impaired at shorter muscle lengths (Fig. 2). Subjects did not report muscle pain until a day after the

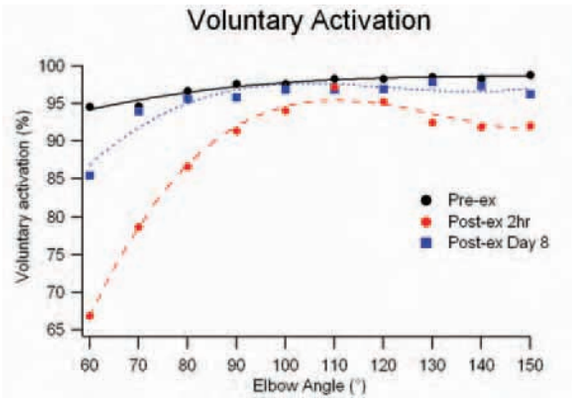

Figure 2. Voluntary activation of elbow flexors for different joint angles (muscle lengths), determined using twitch interpolation (mean of 8 subjects). Notice the slight reduction in voluntary activation for short muscle lengths (60° and 70°) even before exercise. After damaging exercise, there is a significant reduction in voluntary activation across all angles that is more pronounced at shorter muscle lengths. Voluntary activation is still impaired 8 days post-exercise.

exercise, so that, at least initially (2 hours post-exercise), pain was not responsible for the impaired voluntary activation. An additional finding (supported by our initial study), was that the force produced by a twitch had decreased by ~80%, about twice as much as that of the voluntary contraction. This deficit in twitch force remained well below control (~50%) after 1 week.

So what do these findings mean? First, the weakness after exercise was not just due to damage to the muscle, but also to a reduced ability of the brain to drive the damaged muscle, and this central contribution to weakness was more pronounced at short muscle lengths. Second, the prolonged and much greater relative force loss for twitch contractions (compared to MVCs) suggests that 'weakness' for more commonly performed submaximal contractions may be more pronounced than for the maximal ones. Finally, the results highlight the short- and long-term changes in the relation between the mechanical output of the muscle motor and the output of the spinal motoneurones needed to drive the motor.

It is not clear what caused the impairment in voluntary activation. It could mean that the brain reduced its drive to the damaged muscle, or that the damaged muscle changed in such a way that the brain was no longer as effective in producing force. The latter possibility is supported by the finding that voluntary activation was length-dependent both before and after damage, implying that it is influenced by the muscle's inherent length-tension properties. Muscle fibres require a higher frequency of activation to produce tetanic fusion at a short than a long length. However, the finding that voluntary activation was impaired across the full range of muscle lengths after exercise suggests that a true reduction (or change) at the level of the brain may also be occurring.

This is indeed an exciting area to investigate further. Future studies will aim to gain more insight into the interaction between central and peripheral factors limiting force output of skeletal muscles.

Trevor Allen, Jane Butler Simon Gandevia, Orawan Prasartwuth, Janet Taylor

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LETTERS TO THE EDITOR

A century of physiology online

I have just received my copy of *Physiology News* and read your announcement about the archiving project (**63**, 40). Congratulations to *The Journal of Physiology* team for what I suspect has been a considerable challenge.

We must look to the future but in doing so we should not lose sight of those and their work who have gone before us and upon whose shoulders we now stand. Initiatives such as this enable teachers, like me, to direct students to historical documents and so develop scholarship in our charges.

Of course, even though the archive goes back a century and more, that is still comparatively recent in the history of how humans function and, as regards my particular interest, respond and adapt to exercise.

Nevertheless, in the context of the history of formal scientific investigation, the archive makes an outstanding contribution.

This achievement deserves acknowledgement and adds to the celebration held on May 11. I hope I am not the only one to register appreciation.

Edward M Winter

The Centre for Sport and Exercise Science, Sheffield Hallam University,, Sheffield, UK

In *Physiology News* **63** (p. 40) Carol Huxley mentions some of the intriguing titles she'd noticed in the online archive of *The Journal of Physiology*. She didn't include my own favourite 'The obese mosquito' (E Van Handel (1965). *J Physiol* **181**,478–486). Apparently the author (or possibly the reviewer) had suggested 'The fat gnat' as a running title but, sadly, this was deemed superfluous. Rather than let this splendid wording go to waste I resurrect it now, 41 years on.

Ann Silver

Honorary Member, Cambridge, UK

Neuronal lactate metabolism

The first piece of the jigsaw falls into place

In a recent article we described the potential of systemic lactate to act as an energy substrate for the brain under specialised conditions (Brown & Prior, 2004), and suggested that MRI could be used to answer key questions regarding this issue. We have now carried out some preliminary experiments and present the essential findings here. However, it is perhaps expedient to backtrack and provide some background on brain energy metabolism in order to present our data in the appropriate context.

That glucose is the main energy support of the brain is in no doubt, as previously described (Brown & Prior, 2004). Key facts of brain energy metabolism are as follows:

(1) although it comprises only 2% of body weight, the brain takes up 20% of available oxygen and 40% of available glucose via 10% of the cardiac output, thus contributing to 20% of the basal metabolic rate, i.e. resting brain has a very high metabolic demand.

(2) the respiratory quotient (RQ) of the brain, the ratio of the CO_2 produced to O_2 consumed, is close to 1.0, implying that efficient oxidative phosphorylation of carbohydrate (glucose) is the predominant energy generating process in the brain.

(3) the metabolic ratio of the brain (the cerebral metabolic rate of oxygen consumption (CMR_{O2}) versus cerebral glucose utilisation (CMR_{glc}) at rest is close to 6 (~5.7), which signifies almost complete oxidation of glucose.

$$\text{Glucose } (C_6H_{12}O_6) + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$$

The requirement of integrated brain function for oxygen has been amply (if not altogether ethically) demonstrated (Rossen *et al.* 1943). During the Second World War, Anderson's group persuaded the authorities in the USA to allow them to carry out experiments on some 140 prisoners in the Stillwater State Prison, Minnesota. They implemented a Mae West type lifebelt, which could inflate a pneumatic cuff to

Figure 1. Apparatus for inducing cerebral ischaemia in humans worn by its designer, J P Anderson.

occlude the carotid arteries, while leaving the trachea unobstructed (Fig. 1). They found that in all 'volunteers' consciousness was lost 6 to 8 seconds after occlusion of the carotid arteries, thus demonstrating the absolute dependence of higher cognitive function on a continuous delivery of oxygenated blood to the brain. Thus the conventional view of brain energy metabolism can be summarised as follows: the brain requires a constant uninterrupted supply of both blood borne glucose to fuel brain energy metabolism, and oxygen as a means to efficiently metabolise the glucose.

In recent years there have been two main challenges to this dogmatic view. The first concerns the coupling of glucose utilisation and oxygen uptake in the brain during activation. It was shown by Raichle's group that during increased brain activation the metabolic ratio decreases, implying that glucose utilisation is not matched by increased oxygen uptake. This leads to the conclusion that there is a significant increase in glycolytic metabolism in activated brain areas (Fox *et al.* 1988). Given the dependence of brain function on an adequate supply of oxygen it may appear puzzling that a small amount of glucose is not oxidised completely at rest (metabolic ratio ~ 5.7). This may be due to:

(1) biosynthesis – glutamate and GABA, the two most common neurotransmitters in the brain, are formed via the Krebs cycle intermediary α-ketoglutarate, but are ultimately derived from glucose.

(2) at rest glycolysis exceeds the oxidative capacity of the brain, thus lactate produced in excess of demand is lost from the brain.

(3) there is a lack of mitochondria at synapses, dictating glycolytic metabolism at these sites.

Additionally, not all brain tissue requires oxidative phosphorylation. Astrocytes are widely believed to be glycolytic (see later), but some central tissue such as the optic nerve axons can survive in the absence of oxygen (Baltan Tekkök *et al.* 2003). However, during activation of brain areas the uncoupling of glucose and oxygen is too great to be due to the above explanations, and it remains an intriguing mystery.

The second challenge to the dogmatic view of brain energy metabolism relates to the compartmentalisation of glucose once it has crossed from the circulation into the brain parenchyma. It has been argued that astrocytes may take up glucose and glycolytically metabolise it to lactate, before passing the lactate the neurones. This is the essence of the 'astrocyte neurone lactate shuttle' (ANLS) hypothesis (Pellerin & Magistretti, 1994; 2003). They argue that the system is activated during synaptic activity where astrocytic reuptake of synaptic glutamate (coupled with Na^+ uptake) promotes activation of the Na^+ pump and conversion of

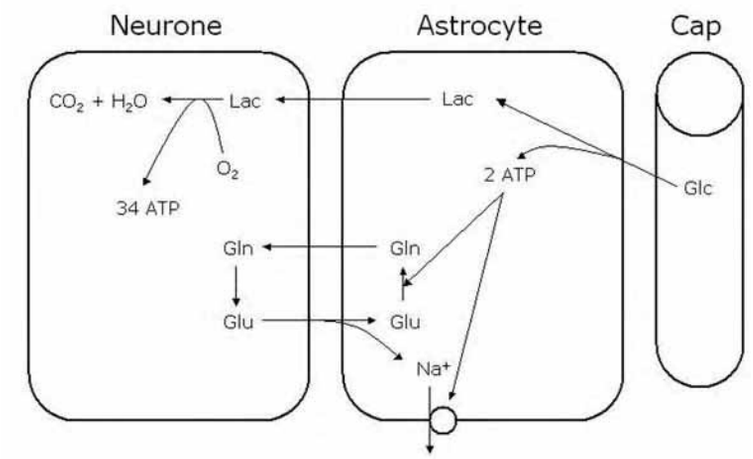

Figure 2. A schematic diagram of the mechanism by which synaptic activity is coupled to increased glucose uptake and glycolytic metabolism in astrocytes. This mechanism is the basis of the ANLS hypothesis. Glc - Glucose, Lac - Lactate, Gln - Glutamine, Glu - Glutamate, Cap - Capillary.

glutamate to glutamine. Both these processes require ATP, which could be provided by glycolytic metabolism of glucose. The end product of this astrocytic glycolysis is lactate, which is subsequently transported to neurones for oxidative metabolism (Fig. 2). Such a system does have an appeal, namely:

(1) it correlates well with the coupling of glucose consumption to glutamate cycling.

(2) increasing glutamate levels leads to increased glucose uptake by astrocytes.

(3) it explains the disproportionate uptake of glucose into glial cells (50%) relative to their metabolic rate (5%).

(4) lactate is released from astrocytes.

The ANLS is hypothesised to be activated during increased brain activity. Thus basal brain activity is adequately served by glucose metabolism, but increases in tissue demand require that lactate is metabolised by neurones. This ANLS hypothesis has caused a major spar in the brain energy metabolism community, and has essentially polarised the field, with the interested parties taking pot shots at each other at monthly intervals via reviews published in the *Journal of Cerebral Blood Flow and Metabolism*. It would seem logical, if this issue is so contentious, to design a simple experiment(s) to directly measure cellular substrate metabolism. It is here that the divergence between desire and reality has led to great confusion. This can be summarised as follows:

Desire – to measure energy metabolism in a single cell (or even different regions of a single cell) in the brain in real time.

Reality – the heterogeneous nature of the cellular organisation of the brain, coupled with the limited spatial and temporal resolution of currently available monitoring techniques, makes this impossible.

Compromise – devise experiments using currently available techniques whose results can be used to infer unknown aspects of metabolism that cannot currently be measured directly.

It is this compromise that has led to confusion, as groups have clashed over interpretation of data. However, a key issue raised by both challenges to the dogmatic view of brain energy metabolism is neuronal metabolism of lactate. That brain tissue can use lactate as an energy substrate has been known for over 50 years, although these experiments were carried out on *in vitro* brain preparations (McIlwain, 1953). More recent studies have shown that, although lactate can support energy levels in brain slices, the electrophysiological indices of function (the EPSP and population spike) are not fully supported, implying an absolute requirement for glucose that lactate cannot provide (Bachelard *et al.* 1984). This has recently been substantiated by studies showing that synaptic mechanisms require glucose, and that lactate cannot act as a substitute (Bak *et al.* 2006). This may be due to the positioning of glycolytic enzymes at the cell surface adjacent to Na^+ pumps, or due to the lack of mitochondria at synapses. That lactate can at least partially support function implies that all the necessary transporters and enzymes are in place for efficient lactate metabolism by neurones.

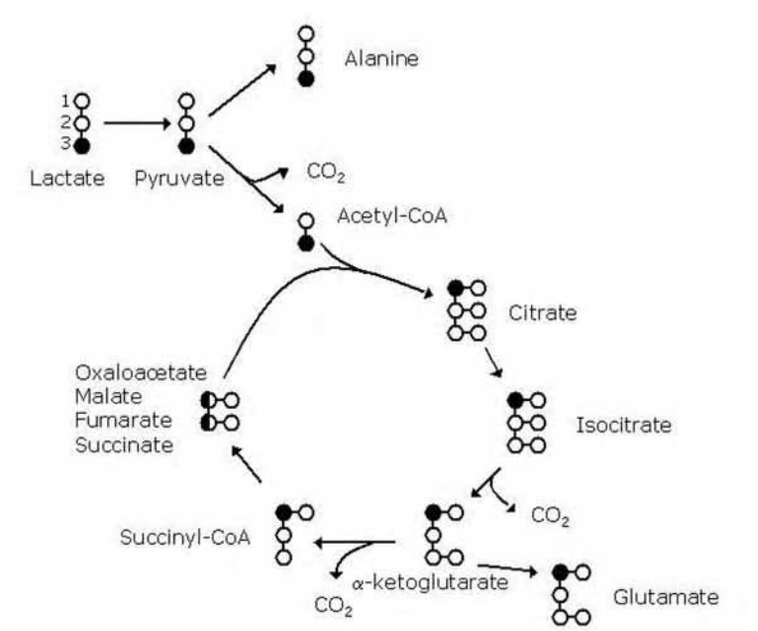

Figure 3. Labelling pattern for metabolism of [3-^{13}C] lactate by NMR spectroscopy for the first turn of the tricarboxylic acid cycle. Conversion of lactate to pyruvate is followed by conversion to Acetyl CoA then incorporation into the cycle. Glutamate derived from α-ketoglutarate is labelled in the C4 position.

Indeed, studies on rodent optic nerve have demonstrated that glycogen-derived astrocytic lactate is shuttled to fuel axons both during aglycaemia and during increased tissue energy demand under normoglycaemic conditions (Brown *et al.* 2003).

An interesting and seemingly unrelated series of studies have revealed that, under certain conditions, it appears that lactate in the systemic circulation can act to fuel the brain. During extreme exercise blood glucose levels fall while blood lactate levels can increase dramatically, resulting in a net uptake of lactate into the brain (Dalsgaard *et al.* 2004). However, a net uptake of lactate, although suggestive of lactate metabolism, does not definitively show that lactate is metabolised by the brain. Sonnewald's group has addressed this issue where labelled lactate (^{13}C) was systemically injected in control animals under normoglycaemic conditions resulting in an increased labelled alanine in the brain (Qu *et al.* 2000). We have taken this idea a step further and have injected labelled lactate into rats that were rendered hypoglycaemic by injection of insulin. We hypothesised that under these conditions there should be minimal gluconeogenesis of lactate in the liver as there is no excess systemic glucose for storage. Transient blood lactate levels of 10 mM were reached while glucose levels fell to about 2 mM. NMR spectroscopy was used to determine enrichment of metabolite ^{13}C from brain extracts. We detected labelled lactate and glutamate, but a complete lack of labelled glucose (Fig. 3), indicating that no glucose from gluconeogenesis was present in the brain tissue. This implies that the labelled glutamate, an indicator of oxidative metabolism, must have originated from lactate.

The uptake and metabolism of systemic lactate by the brain can be seen as an extension of the cell-to-cell signalling concept to include peripheral tissue. The data from studies on vigorous exercise have revealed the ability of muscle cells to convert glucose to lactate, which is then extracted by the brain from the systemic circulation and metabolised. This highlights the ability of tissues to partially metabolise glucose, then pass on the energy rich intermediary metabolites to different cells or even tissues. This ensures an efficient use of glucose, a concept that has been summarised as 'activity-dependent and temporal-spatial partitioning of brain metabolism' (Dienel, 2004).

As we go to press, another *J Cereb Blood Flow Metab* review by Shulman's group (Hyder *et a*l. 2006), leading advocates of the ANLS hypothesis, proposes an updated model of glial-neuronal metabolic trafficking to incorporate oxidative glucose metabolism in astrocytes as well as significant neuronal uptake of glucose. The plot thickens!

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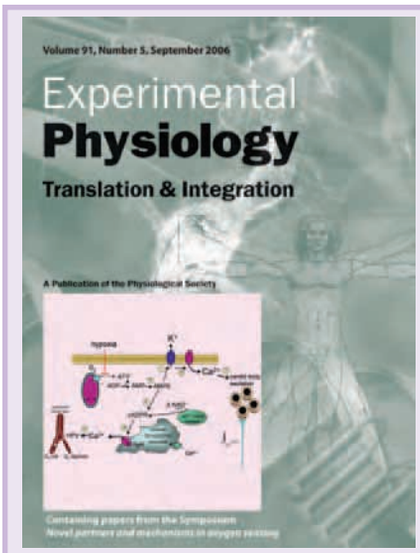

The September issue of *Experimental Physiology* contains reports from the *Novel partners and mechanisms in oxygen sensing* symposium held at Experimental Biology 2006. Gregg Semenza presents important observations on cardio-respiratory responses to chronic continuous and intermittent hypoxia in heterozygous mice partially deficient in HIF-1α, the O_2 regulated subunit of the HIF-complex. Paul Schumacker elaborates on the importance of complex III of the mitochondrial electron transport chain and reactive oxygen species in HIF-1 activation by hypoxia. A Mark Evans presents exciting new data on the role of AMP-activated protein kinase as a potential O_2 sensor that couples mitochondrial metabolism to pulmonary vasoconstriction as well as carotid body activation by low O_2. Paul Kemp focuses on the critical role of protein-protein interations in conferring the O_2 sensitivity to the carotid body chemoreceptors. Specifically, he discusses interactions between heme oxygenase-2, the enzyme that catalyzes generation of endogenous carbon monoxide and Ca^{2+}-activated K^+ channels in the hypoxic response of the glomus cells of the carotid body.

For more details see p. 34 or visit http://ep.physoc.org/content/vol91/issue5

Variability of human vagal baroreflex responses

In 'steady-state' resting humans, baroreflex gain fluctuates hugely and rhythmically at very low frequencies

Dwain Eckberg (left) and Tom Kuusela

The arterial baroreflex occupies a central position in physiology: in healthy people, ever-present arterial pressure fluctuations lead to nearly instantaneous, usually reciprocal, changes of vagal and sympathetic neural outflows, which in turn modulate function of the heart and blood vessels.

Before 1969, there was no quantitative way to gauge the effectiveness of human baroreflex control. However, in that year, Smyth, Sleight & Pickering (1969) reported that brief systolic pressure elevations following bolus intravenous pressor injections provoke parallel prolongations of the intervals between heart beats. The regression of cardiac responses on pressure changes yields a slope, expressed in ms $mmHg^{-1}$, which represents the 'gain' of the vagal, or heart rate, portion of a subject's baroreflex responses. Subsequent research (Bertinieri *et al*. 1985; Fritsch *et al*. 1986) showed that baroreflex gain also can be calculated from simple regression analysis of (small) spontaneously-occurring systolic pressure and heart period changes.

Wesseling and Settels (1985) mused about a conundrum that besets baroreflex research: If highly sensitive (Eckberg, 1977) baroreflex mechanisms are functioning properly, why is blood pressure so variable? We sought answers to this question by analysing the baroreflex function of supine healthy young adults on three separate days, using a cross-spectral method (Badra *et al*. 2001) which is based on correlations between power spectra of spontaneously-occurring systolic pressure and heart period changes. We estimated baroreflex gain over 15 s windows, moved every 2 s through 20 min periods of frequency- and tidal volume-controlled breathing (Eckberg & Kuusela, 2005).

Figure 1 shows an example of our results. The top and middle left panels indicate that this resting subject, who was to all outward appearances in a 'steady-state', was actually changing profoundly: for unknown reasons, his blood pressure, heart period (R-R intervals), and R-R interval variability increased steadily. The lowest left panel indicates that, during a 19 min period, this subject's baroreflex gain, estimated from baroreflex sequences [red (Bertinieri *et al*. 1985; Fritsch *et al*. 1986)] and cross-spectra (black), more than doubled. Cross-spectral baroreflex gain fluctuated profoundly and ranged from 5 to 68 ms $mmHg^{-1}$, a 14-fold difference! The right panel of Fig. 1 indicates that baroreflex fluctuations were periodic, with a peak frequency of about 0.009 Hz, or one cycle every 110 s.

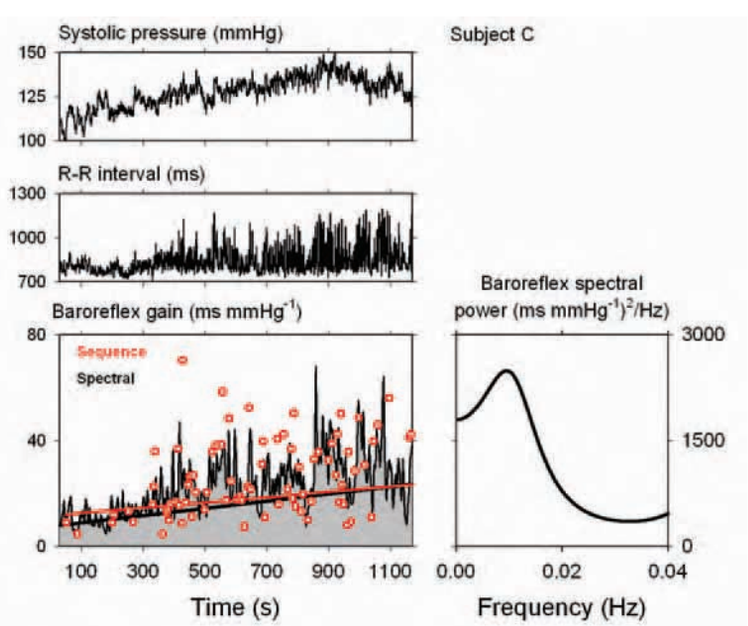

Figure 1. Data from one subject. Individual and average baroreflex slopes drawn from sequence analysis are shown by red circles and the red line, and baroreflex gain drawn from cross-spectral analysis is shown in black. For unknown reasons, this resting subject experienced major increases of all measurements during the recording period. The autoregressive spectrum on the right indicates that the periodicity of cross-spectral baroreflex sequences fell in the very low frequency range.

Although other volunteers did not have such a striking steady increase of baroreflex gain, they all had major fluctuations of baroreflex gain. In the nine subjects studied, minimum, mean, and maximum baroreflex gain averaged 5, 18, and 55 ms $mmHg^{-1}$, and the ratio of maximum to minimum baroreflex gain ranged from 4 to 35 (average: 14). The centre frequency of baroreflex fluctuations averaged 0.011 Hz, or about one cycle every 90 s. Thus, baroreflex gain periodicity falls in the very low [arbitrarily, 0.003 to 0.05 Hz (Berntson *et al*. 1997)] frequency range.

Figure 2 provides a different perspective on variability of baroreflex gain. In this and all other subjects, baroreflex distributions were skewed to the right, such that all subjects experienced infrequent, but major, augmentations of gain above their more prevalent levels. This figure also illustrates heretofore unrecognized complexities of human baroreflex function; it documents major differences in the distributions of baroreflex gain from day to day. Although this subject's average baroreflex gain on days 2 and 3 were similar, 52 and 45 ms $mmHg^{-1}$, their distributions were vastly different. Baroreflex gain was concentrated at lower levels on Day 2 than Day 3.

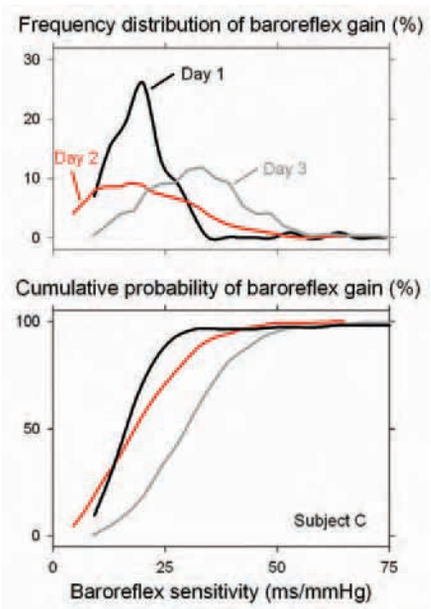

Figure 2. Frequency distribution and cumulative probability of baroreflex gain from the same subject whose data are shown in Fig. 1, as recorded on three different days.

Figure 3 suggests that fluctuations of baroreflex gain may have functional significance. In these two. and several other, subjects, spikes of baroreflex gain (shown in red) seemed to occur in response to troughs of blood pressure – that is, brief pressure reductions ratcheted up baroreflex responsiveness. The right panels of Fig. 3 show the reverse side of the same coin. Here, systolic pressure was signal-averaged on average baroreflex gain (black), and at 2, 4, 6, and 8 mmHg ms^{-1} below the average (illustrated by gradations of gray from the highest (lightest), to the lowest (darkest) level of baroreflex gain. These data suggest that reductions of baroreflex gain are followed by elevations of arterial pressure.

These findings may have clinical significance. Patients with cardiovascular diseases have reduced vagal baroreflex gain in proportion to the severity of their diseases (Eckberg *et al*. 1971). Moreover, the prognosis of cardiac patients is poor when vagal baroreflex responses (La Rovere *et al*. 1998) or vagally-mediated heart rate fluctuations (Bigger Jr *et al*. 1992) are low. Subnormal heart rate variability at very low frequencies is particularly ominous. Our research provides a significant link between prognostically-important baroreflex gain and prognostically-important very low frequency heart rate variability. The import of this association is unknown; however, it may be that cardiac patients do not have the 'baroreflex reserve' we report in healthy people, and thus may inadequately mount reflex responses to the major haemodynamic challenges that occur in daily living.

In conclusion, our work shows that in ostensibly 'steady-state' resting healthy people, vagal baroreflex responsiveness fluctuates in a major way at very low frequencies. These results suggest that the key dimension of time should be included in characterizations of human baroreflex function.

Acknowledgements

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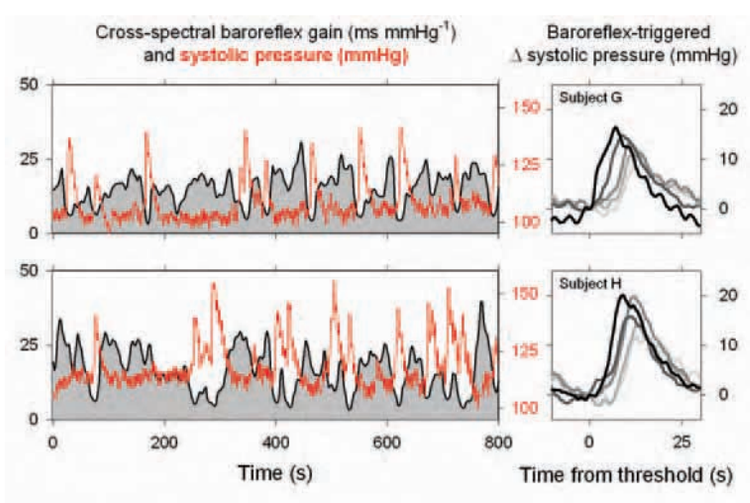

Figure 3. Cross-spectral baroreflex gains and systolic pressures from two different subjects. In these volunteers, spontaneous dips of pressure seemed to provoke major increases of baroreflex gain. The right panels show systolic pressure, signal-averaged on average, and 2, 4, 6, and 8 ms $mmHg^{-1}$ below average baroreflex gain. The gray scale indicates measurements obtained with the highest (lightest) to lowest (darkest) baroreflex threshold crossings. Taken together, these analyses suggest that pressure reductions trigger increases of baroreflex gain, and baroreflex gain reductions trigger increases of arterial pressure.

Vitamin D and disease prevention

Vitamin D, produced by sunlight exposure of the skin, is essential in mineral metabolism and skeletal health. The high prevalence of vitamin D insufficiency and its association with increased risk for osteoporosis, diabetes, tuberculosis, autoimmune diseases, and cancer have prompted the re-evaluation of daily requirements

Alex Brown (above, left), Eduardo Slatopolsky (above, right) and Adriana Dusso (left)

Vitamin D was discovered early in the 20th century as the component of fish oil essential for the prevention and cure of rachitic bone disease. Vitamin D_3 or cholecalciferol can be produced in adequate amounts by skin exposure to sunlight. Vitamin D_2 or ergocalciferol, a related compound with very similar activities, is found in a few plants (Dusso *et al.* 2005).

Vitamins D_3 and D_2 have little intrinsic activity and must be metabolised to exert biological effects (see Fig. 1). Hydroxylation of carbon 25 occurs primarily in the liver. 25-hydroxyvitamin D [25-OHD], the most abundant vitamin D metabolite in circulation, is used as the index of vitamin D status. 25-OHD is further metabolized by the 1α-hydroxylase to 1,25-dihydroxyvitamin D [$1,25(OH)_2D$], the active (hormonal) form. Although the kidney is the primary source of the circulating $1,25(OH)_2D$, 1α-hydroxylase is also found in many cells throughout the body. Nonrenal $1,25(OH)_2D$ production serves cell-specific functions (Dusso *et al.* 2005). In fact, the association between vitamin D deficiency and higher susceptibility to tuberculosis (Zasloff, 2006) and cancer (Zittermann, 2003) results from inadequate production of $1,25(OH)_2D$ by nonrenal sources rather than systemic $1,25(OH)_2D$ deficiency .

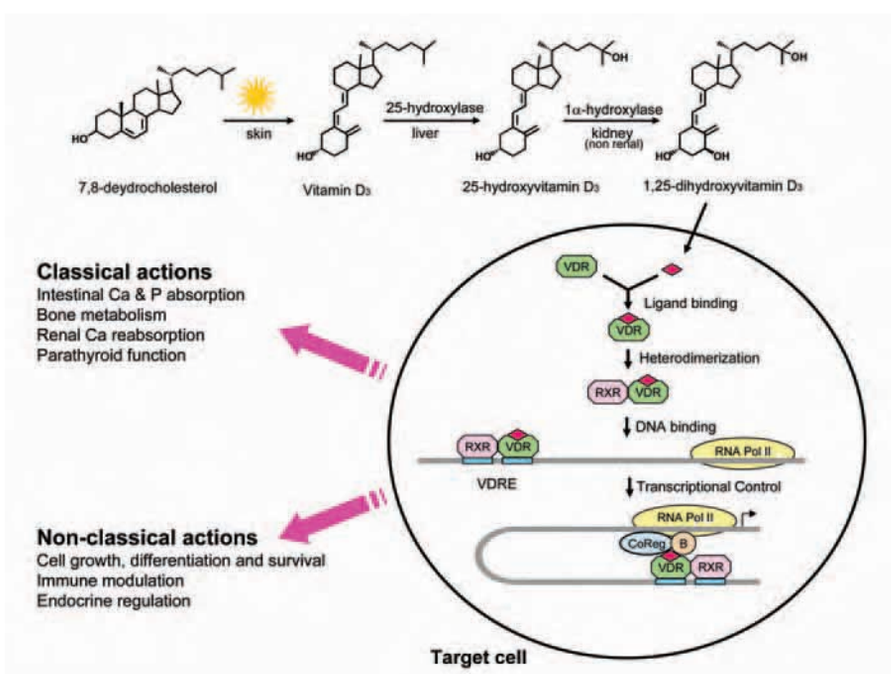

Figure 1. Vitamin D activation, mechanism of action and biological responses

$1,25(OH)_2D$ acts as a steroid hormone. It binds with high affinity to a specific intracellular receptor, the vitamin D receptor (VDR), a member of the steroid receptor family. Upon $1,25(OH)_2D$ binding, the VDR undergoes a conformational change allowing interaction with a number of other macromolecules. Typically, the liganded VDR forms a heterodimer the retinoid X receptor (RXR), which promotes binding to specific DNA sequences in the promoters of regulated genes. The DNA-bound complex then recruits coactivators that unwind chromatin and facilitate gene transcription, or corepressors that suppress gene transcription. $1,25(OH)_2D$-VDR control of gene transcription mediates classical vitamin D actions on calcium homeostasis and skeletal integrity as well as nonclassical actions on cell growth, differentiation and survival, immunomodulation, and endocrine regulation (Dusso *et al.* 2005).

Classical $1,25(OH)_2D$/VDR actions in bone, intestine, the parathyroid glands and the kidney maintain serum calcium levels within the narrow limit required for normal cellular physiology and the development and maintenance of a mineralized skeleton. The impaired $1,25(OH)_2D$ production in chronic kidney disease decreases intestinal calcium absorption. The resulting hypocalcemia enhances the secretion of parathyroid hormone (PTH), which accelerates calcium release from bone in an effort to restore normal serum calcium. $1,25(OH)_2D$ also acts as a skeletal anabolic agent, necessary to sustain bone forming activity, matrix mineralization, and the normal coupling of PTH-induced bone remodeling (Dusso *et al.* 2005).

Interestingly, nearly 70% of the USA population with suboptimal levels of 25(OH)D has increased serum PTH,

despite normal $1,25(OH)_2D$. This suggests that adequate vitamin D supplementation should decrease the risk of osteoporosis and fracture in healthy individuals either by direct 25-OHD activation of the VDR, or as a result of local $1,25(OH)_2D$ production by bone and parathyroid cells expressing 1α-hydroxylase.

Nonclassical $1,25(OH)_2D$/VDR actions include regulation of cell proliferation, differentiation and survival, immunomodulation, suppression of the renin- angiotensin system and enhancement of glucose-mediated insulin secretion. Accordingly, abnormalities in the vitamin D endocrine system have been linked to hypertension, diabetes, disturbed muscular and cardiovascular function, susceptibility to infections, autoimmune diseases and cancer (Zittermann, 2003; Dusso *et al.* 2005; Garland *et al.* 2006). Intriguingly, however, the higher incidence of these disorders correlates to 25-OHD deficiency rather than insufficient serum $1,25(OH)_2D$. This suggests that increased local production of $1,25(OH)_2D$ upon adequate elevations in 25-OHD levels by vascular endothelial cells, immune cells, and pancreatic beta cells expressing 1α-hydroxylase could mediate the reduced incidence of hypertension, cardiovascular disease and diabetes in vitamin D-repleted individuals.

$1,25(OH)_2D$ /VDR actions in the immune system provide strong evidence of the contribution of adequate local $1,25(OH)_2D$ production by immune cells to the association between 25-OHD deficiency rather than $1,25(OH)_2D$ insufficiency with higher susceptibility to infections, autoimmune diseases and cancer (Hayes *et al.* 2003; Zittermann, 2003; Dusso *et al.* 2005; Garland *et al.* 2006).

The importance of adequate 25-OHD availability to the activated macrophage is evident in tuberculosis (Zasloff, 2006). As early as 1895, phototherapy was used to treat 'lupus vulgaris' (skin tuberculosis), but it was not until 2006, when local activation of 25-hydroxyvitamin D to $1,25(OH)_2D$ by macrophages infected with the mycobacterium tuberculosis was proven mandatory for the potent anti-tuberculosis properties of vitamin D. More important was the discovery that the low serum 25-OHD levels, a common occurrence in the African American population, limited the mounting of an adequate anti-tuberculosis response, a defect which could be corrected upon vitamin D supplementation. Similarly, in vitamin D deficiency, impaired local $1,25(OH)_2D$ production by dendritic cells appears to mediate abnormalities in the establishment and maintenance of immune self-tolerance, essential for prevention of autoimmune diseases as type I diabetes, multiple sclerosis, inflammatory bowel disease, encephalomyelitis and rheumatoid arthritis (Hayes *et al.* 2003; Zittermann, 2003; Dusso *et al.* 2005). Epidemiological studies associate vitamin D deficiency with the prevalence of these autoimmune disorders, and vitamin D supplementation can improve symptoms of rheumatoid arthritis and decrease relapse rates in multiple sclerosis (Zittermann, 2003).

Enhanced sunlight exposure is associated with lower death rates for breast, colon and prostate cancer (Garland *et al.*, 2006). $1,25(OH)_2D$/VDR control of DNA repair, induction of differentiation and apoptosis of malignant cells as well as enhancement of macrophage immune surveillance could mediate vitamin D efficacy in cancer prevention. In cancer, $1,25(OH)_2D$/VDR suppression of angiogenesis and cell proliferation, and induction of macrophage antitumoral properties, and tumor cell apoptosis may ameliorate the severity of cancer progression. In cancer cells expressing 1-hydroxylase, local $1,25(OH)_2D$ production could contribute to growth arrest since 25-hydroxyvitamin D, at concentrations insufficient to activate the VDR, suppresses cell proliferation. Tumor growth may also be suppressed by the $1,25(OH)_2D$ produced by activated macrophages in the vicinity of a cancer cell or in the tumor microenvironment. Indeed, vitamin D supplementation may prevent cancer and improve the efficacy of conventional anticancer therapy.

In summary, adequate vitamin D status could prevent the onset or ameliorate the progression of many prevalent diseases. New recommendations for daily requirements are mandatory. Dietary sources, including vitamin D-fortified food and vitamin supplements (400 IU/day) have only a minimal effect on 25(OH)D levels. Sunlight exposure is much more effective, but moderation is necessary to reduce skin cancer risk. Ten minutes of arm and face exposure per day is usually sufficient. The daily intake of vitamin D can be increased safely to 1,200 U/day (Zittermann, 2003; Garland *et al.* 2006). These relatively inexpensive measures to improve vitamin D status can have a major impact on the prevalence and severity of osteoporosis, diabetes, cardiovascular disease, hypertension, tuberculosis, autoimmune disease and cancer.

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BIOSCIENCES FEDERATION

The Biosciences Federation has elected the following new members of Council:

Professor John Coggins (Dean of the Faculty of Biomedical and Life Sciences, Glasgow University), Dr Pat Goodwin (Head of the Department of Pathogens, Immunology and Population Studies, Wellcome Trust) and Professor Frank Odds (Professor of Medical Mycology at the University of Aberdeen.

The International Workshop on membrane transport in health and disease

The first Workshop sponsored by The Physiological Society in Latin America

Rafael D García and María Elena Chemello (Instituto Venezolano de Investigaciones Científicas, Caracas, Venezuela) write:

Four participants, two from Venezuela and two from the UK, report on this event held on the beautiful Margarita Island, Venezuela, from 19–24 March 2006

As we got to Margarita, a Venezuelan island located in the Caribbean Sea, our expectations were growing; not just because of the paradisiacal environment that surrounded us but for the International Workshop on *Membrane transport in health and disease* which was about to start. On 19 March, 23 invited speakers from the UK, USA, Chile, Argentina and Venezuela, and about 50 students from Argentina, Brazil, Chile, Colombia, India, Mexico, Perú, Puerto Rico, the UK and Venezuela met in the Portofino Hotel. It was a perfect venue to hold a meeting for so many people, with adequate meeting rooms, nice gardens, restaurants, swimming pools and a very nice beach which provided the setting for a fruitful exchange of ideas and learning.

Welcoming speeches were given by the Organising Committee: Fabian Michelangeli, the local host, from the Latin American Centre of Biological Sciences (CLAB-UNESCO-IVIC); and David Eisner and Teresa Tiffert from The Physiological Society.

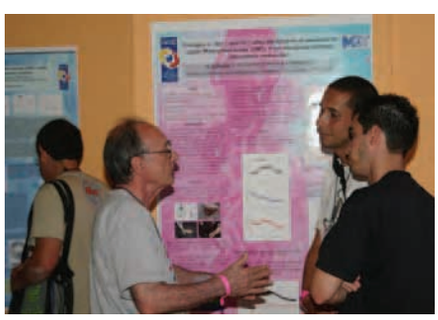
Above: Annette Dolphin (UK) and a Caribbean friend.
Below: Workshop participants.

Guillermo Whittembury, the prominent Peruvian scientist delivered the Introductory Lecture. With his charismatic personality, he brought us from the beginnings of transport physiology to the cloning era.

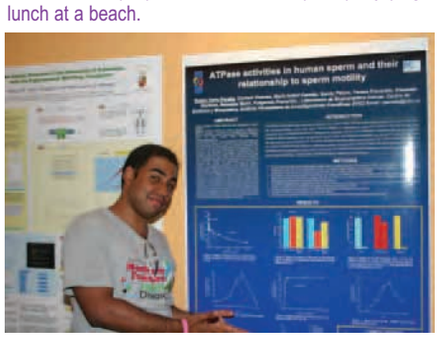
During the week, we had the chance to learn about all aspects of ion channels, transporters and ATPases including their involvement in muscle contraction, nerve conduction and in electrolyte and macromolecular secretion. The different methodologies covered molecular biology, electrophysiology, confocal microscopy and fluorescence. Additionally, during the course of the sessions we were able to understand the relationship between structure and function of membrane proteins responsible for ion transport and the important involvement of these proteins in several disorders such as cystic fibrosis, cancer, viral infections, cardiac arrythmias, hypertension, ischemia and heart failure, among others. Lectures were of the highest standard. One by one they astonished us by the level of complexity of the relationships in living cells and the way secrets are being unravelled by the scientists we had the opportunity to meet in our Workshop. We are sure that not just the students, but the speakers as well, learnt a lot about all the topics that were discussed during the sessions.

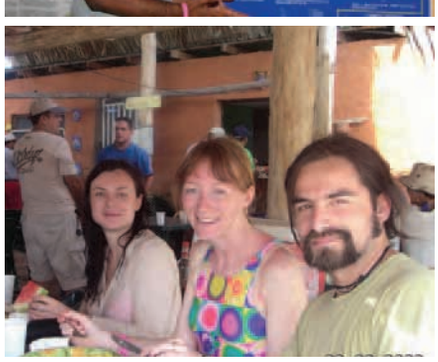
The presentation of posters by the students was also a very important activity. The informal discussions of the posters gave the students a chance to discuss their work and encouraged them to interact with the speakers. The best four posters were selected and the winners had to give an oral presentation the next day.

Socially speaking we had a welcoming dinner where people had the



Above
Top: Sofia Hernández (Venezuela) at the practical demonstration. Centre: Workshop organiser Fabián Michelangeli (Venezuela), left, with Guillermo Whittembury (Speaker). Bottom: Rafael Garcia (Venezuela), centre, discusses his poster with Luis Beaugé (Argentina), left.
Below
Top: Rubén Dario Peralta (Venezuela) at his poster
Bottom: Students (from left) Jenni Paynter (UK), Rachel White (UK) and Carlos Flores (Chile) enjoying lunch at a beach.





opportunity to meet and get to know each other. A nice break to ease the intensive work was an excursion to the beach of Punta Arenas and the Mangroves of La Restinga. However, even at this point sun and science were intermingled. To celebrate the end of the Workshop and its success, we had an enjoyable party where all the participants seemed to be thoroughly relaxed. This Latin American function was a reward after so much work.

Finally, we would like to thank the Organising Committee, the Faculty and the sponsors for this opportunity. We want to say that the Workshop was extremely valuable to students and speakers from developing countries where science is an uphill task. In some Latin American countries, science is not considered relevant for the development and progress of the country despite the fact that the work of their scientists can be compared to the highest standards reached by their counterparts in the UK or USA.

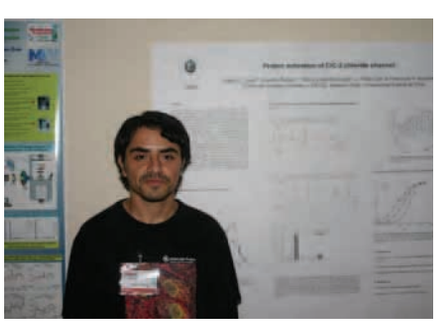
We hope there will be future similar meetings in Latin America, which will allow us to update and improve our understanding of the mechanisms that operate in living organisms.

Jenni Paynter (University of Oxford, UK) and Rachel White (University of Cambridge, UK) write:

The aim of the Workshop was to bring together young scientists and leading researchers from the international community to discuss their wide-ranging interests in the field of ion membrane transport. This was achieved through a series of lectures, round table discussions, demonstrations and poster presentations, which addressed the structure and function of ion channels, carriers and pumps responsible for the movement of sodium, potassium, chloride, calcium, protons and water in healthy and diseased tissue.

Throughout the week, a wide range of methodologies for investigating membrane transport were described in the lectures and presentations, including molecular biology, gene knockout

Above
Top (from left): Manuel Gasco (Peru) and Francisco Sepúlveda (Chile) at a poster discussion.
Centre: Workshop organisers Reinaldo DiPolo (Venezuela) and Teresa Tiffert (UK).
Bottom (from left): Speakers Virgilio Lew (UK), Luis Beaugé (Argentina) and David Eisner (Workshop organiser, UK).
Below
Top: Yamil Yusef (Chile) ready for a poster discussion.
Bottom: Carlo Caputo (Venezuela)



experiments, electrophysiology, radioisotopic flux measurements and kinetic studies, fluorescent measurements, confocal microscopy and mathematical-computational models. Using these techniques, the lecturers had investigated many disease states with altered ionic homeostasis, such as cystic fibrosis, hypertension, pre-eclampsia, absence epilepsy, ischemia, cardiac arrhythmias, cancer, viral infections and parasitic infections resulting in malaria or Chagas disease.

The participants, postgraduates and young postdocs, all came from Latin American countries except for one from India and two from the UK. For many, this was their first opportunity to attend and to present their work at an international meeting conducted entirely in English, posing an extra challenge for some! Active participation by all was encouraged, ample time being allocated for discussion after each lecture; this was well used by the audience who asked many enthusiastic questions. The lecturers were also very approachable and keen to discuss their work further. Informal poster presentations were also a key part of the schedule; authors of the four prize winning posters gave an oral presentation about their research; other students were selected to chair lectures. The enthusiasm of everybody who attended made it an extremely successful event and the opportunities provided to network will be helpful when new ideas are tried out when participants return to their laboratories. The Workshop location, on Isla Margarita was a definite highlight. For those of us from the UK it afforded a unique insight into scientific and cultural aspects of Venezuela and of other Latin American countries. It is hoped that the organisers will realise that the benefits of such a Workshop far outweigh the hard work of organising it and more of its type will be held in future years!

International Workshop
Cardiopulmonary function in health and disease
20–24 September 2006
The Department of Physiology, Charles University, Prague, Czech Republic
http://www.physoc.org/international/prague2006






Above
Top
Left: André Junqueira Zaharenko (Brazil). Right: Subrata Tripathi (India) charing a session.
Centre
Left: Cecilia Hidalgo (Chile) and Susan Wray (IUK). Right: Richard Vaughan-Jones (UK)
Bottom
Left: Silvana Del Mónaco (Argentina) and Right: David Gadsby (USA), chairing sessions

Below
Left: Reaching the Mangroves of La Restinga. Right: Poster winner Maria Elena Chemello (Venezuela).


THE JOURNAL OF PHYSIOLOGY

Symposia

The next *Journal of Physiology* symposium, *Physiology of brain-computer interface*, will take place on Friday, 13 October at the Society for Neuroscience Annual Meeting in Atlanta, Georgia, USA. This will be chaired by *Journal* Editor Leonardo Cohen and Niels Birbaumer. Speakers include Eberhard Fetz, Andrew Schwartz, John Donoghue, Jonathan Wolpaw and Bruce Dobkin.

During 2007 *The Journal* will sponsor two symposia at the Experimental Biology meeting in Washington DC *(Exercise hyperemia: are there any answers yet*? and *Obesity and the central nervous system*) and two at the IBRO World Congress of Neuroscience in Australia (*Brain adaptations for a successful pregnancy* and *Motor control*).

Full details of these and other symposia still under consideration will be available, as they are finalised, at http://jp.physoc.org/misc/symposia.shtml

2005 Impact factors

Experimental Physiology's impact factor rose for the 3rd year, against the general trend, from 1.83 to 2.05, validating the Editorial Board policies of a focus on translation and integration, an increase in the rejection rate to improve the quality of published papers and regular publication of symposium and themed review series. These policies will continue under the Chairmanship of David Paterson (see p. 34).

The Journal of Physiology's impact factor has dipped slightly from 4.34 to 4.27. The Editorial Board remains committed to raising the impact factor through publication of high quality papers that will make a significant contribution to the field. This year, as last, analysis of citations at article level will help inform Editors of how successful their policies have been. The Board also aims to raise the impact of *The Journal* through an increase in the number of themed issues containing invited reviews on emerging and exciting topics together with related research papers, some of which are based on *Journal*-sponsored symposia (see above) held at important meetings around the world. This programme will be coordinated by new Deputy Editor-in-Chief Brian Robertson. *J Physiol* is one of the 'super-tanker' journals publishing hundreds of articles each year, and the Board acknowledges that it will take time and careful judgment to adjust the impact factor to the level deemed appropriate by top research labs.

Open access – new developments

The spread of the open access ideology to funding agencies has been a concern

William Large (front row, left), Editor-in-Chief of *The Journal of Physiology,* hosted a unique dinner for past Chairmen in Cambridge on 23 June. Spanning 50 years of Chairmanship, those attending were: (Front row, seated from the left) Thomas Sears (Chairman from 1977–78), Sir Andrew Huxley (1956–57), Wilfred Widdas (1970–72), Ian Glynn (1968–70), Richard Dyball (1994–97); (Back row, standing from the left): Stewart Sage (2002–05), Nick Standen (1991–94), Barry Hirst (2000–02), Michael Spyer (1982–85), David Eisner (1997–2000) and Richard Boyd (1989–91).

to The Society over the last few years. If funding agencies demand that grant holders make their published work freely accessible on the internet immediately, or very soon after, publication subscriptions to the journals will be cancelled. The Society will not be able to function at its present level without subscription income – author publication charges may cover the cost of producing the journals but will not generate surplus income. Recent developments in funding agency policies are a mixture of good and bad news – there are signs that the agencies do recognise the effects their policies will have on societies and journals, but the message underlying the policies remains that public access to research output must be accelerated.

Up to 60% of papers published in *The Journal of Physiology* acknowledge funding from the US National Institutes of Health (NIH) so the activities of the NIH policy makers are of considerable interest. Last May the NIH began requesting that researchers should deposit papers based on funded research with PubMed Central. The number of articles deposited to date has been 'disappointing', only 4% of the total number published. Recently a new Bill was introduced which would require, as opposed to request, the deposit of papers no later than 12 months after publication. Fortunately, this formulation does not threaten subscription income, since The Society's journals make all their content free at 12 months. An earlier, more draconian version of the Bill set the latest time limit for deposit at 6 months, but a well-coordinated campaign by not-for-profit publishers and learned societies is thought to have influenced the NIH director, Elias Zerhouni, who is reported to have said that he did not wish to endanger the future of smaller journals.

Closer to home, the Research Councils UK have issued a revised statement of their policy on access to publicly funded research. The individual research councils will provide guidance on access to research output to their grant holders. The MRC has taken the most extreme position. Like The Wellcome Trust, they will require deposition of papers reporting funded research within 6 months with PubMed Central and will provide authors with funds to pay open access fees. The Blackwell Online Open author-pays option will allow MRC funded authors to submit papers to *Experimental Physiology* and *The Journal of Physiology*, but currently only 2% of accepted papers acknowledge MRC funding so in this case at least the policy is not likely to have a major effect on the content of the journals or The Society's subscription income.

Carol Huxley

Experimental Physiology
Translation & Integration

David Patterson, new Chair of *Experimental Physiology* (top), Deputy Chair Julian Paton (above, left) and Deputy Chair, USA, Nanduri Prabhakar (above, right)

New Chair

David Paterson was appointed as Chair of *Experimental Physiology* at the AGM last month. He takes over from John Coote, who retires after a 6 year term as Chair, during which time the impact factor his risen steadily.

David Paterson is Associate Head (with Kay Davies, FRS) to Sir George Radda, FRS in the Department of Physiology, Anatomy and Genetics (D-PAG) at the University of Oxford. He leads a team in the area of cardiac neurobiology and is Vice Chair of the Medical Research Strategy Group, Oxford, Joint Director (with Richard Vaughan-Jones) of the Burdon Sanderson Cardiac Science Centre, D-PAG, and Fellow of Merton College, Oxford. He also serves on the BHF Project Grants Committee and the National RAE Committee (Pre-clinical Medicine UoA 15).

Having served as Deputy Chair, David has been involved in the re-launch of the journal as *Experimental Physiology* with its sub title Translation & Integration and the move to Blackwell Publishing at the beginning of 2004. He helped formulate the new mission for the journal – to publish papers that focus on ascribing physiological function to genes and proteins in the wider context of integrative systems.

Future plans for the journal include maintaining its integrative nature (from cell to organ system), and positioning EP to receive papers in computational physiology that are underpinned by experimental data. This is an important and growing area that forms a part of systems biology. Julian Paton, Professor of Physiology at Bristol will become the new Deputy Chair of the Editorial Board and join Nanduri Prabhakar, our other Deputy Chair (USA).

Novel partners and mechanisms in oxygen sensing

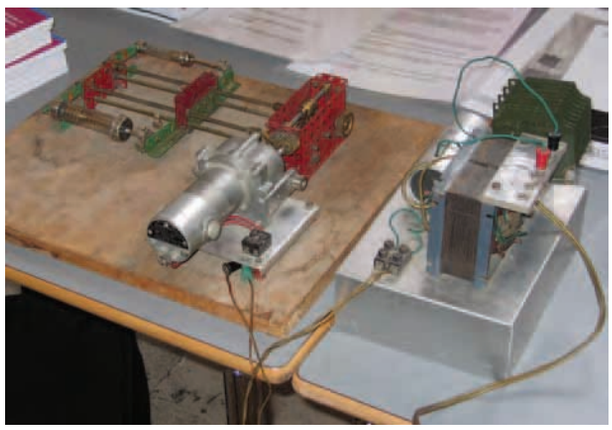
The September 2006 issue of *Experimental Physiology* contains four papers based on a symposium entitled *Novel partners and mechanisms in oxygen sensing*, which took place at the Experimental Biology meeting in San Francisco, USA in April (http://ep.physoc.org/content/vol91/issue5).

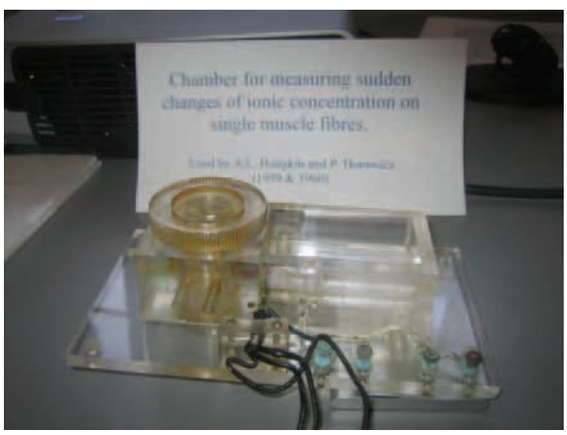
The aim of the symposium was to present recent views on the identity of oxygen sensor(s), interactions between various signal transduction pathways associated with cellular responses to hypoxia, and the importance of transcriptional activator, hypoxia-inducible factor (HIF) in physiological responses to hypoxia. Together, the presentations provided a broad range of perspectives outlining the role of transcriptional regulators in eliciting physiological responses to different paradigms of hypoxia and cellular and sub-cellular mechanisms associated with the fundamental mechanisms of hypoxic sensing. The symposium was sponsored by the Hypoxia Group of the American Physiological Society.

Nanduri R Prabhakar

Reactivating the History and Archives Committee

You may or may not have noticed these strange pieces of equipment, one partially constructed with Meccano, that were displayed on the History and Archives stand at the meeting in UCL. A far cry from today's sophisticated equipment but they provided some sophisticated results. One was in fact a unique chamber used by A L Hodgkin and P Horowicz in the late 1950s for measuring the effect of sudden changes of ionic concentration on single muscle fibres. Of the same vintage is the other pictured item, an infusion pump made by James Fitzsimons out of Meccano and an aileron motor from a World War II aeroplane (Meccano was invented by a Liverpool clerk, Frank Hornby, and first patented in 1901).



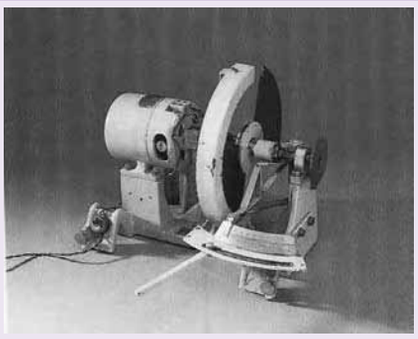


Top: James Fitzsimons' infusion pump
Above: Tissue bath used by A L Hodgkin and P Horowicz in the late 1950s
Below: History and Archives Committee members (from the left): Martin Rosenberg, Tilli Tansey and Dafydd Walters

The History and Archives Committee was initially established in 1989 prompted by the movement of The Society's archives from Churchill College, Cambridge to the Wellcome Institute. Tilli Tansey became The Society's Honorary Archivist, and a number of activities were established. These included supervising the cataloguing and conservation of The Society's printed and photographic records, organising an oral history programme, locating and copying films and videos belonging to The Society, and collaborating with the Science Museum in the collection of historical equipment. In recent years the Committee has been in a refractory state, but it has recently been reactivated and is now chaired by Dafydd Walters, a previous chairman of the Executive Committee. Members of the current Committee are Graham McGeown, David Miller, Martin Rosenberg, Ann Silver, Tilli Tansey and Saffron Whitehead with Amanda Engineer (Wellcome archivist) and a representative from *Physiology News* attending. We are all committed to preserving The Society's archival collections which include paper records, photographs, films and videos and, of course, historical equipment. We are currently conducting more oral history interviews with distinguished physiologists, collecting and identifying historic equipment, adding to The Society's photographic collection and digitizing the existing photographic collection for posterity. (Most of the archive is stored for us by the Wellcome Library in Euston Road.)

We want to preserve The Society's history so if anyone finds anything that may be an interesting addition to the archive please get in touch with a member of the History and Archives Committee rather than committing anything valuable to waste collection.

Saffron Whitehead
St George's University of London, UK
For the History and Archives Committee



Millikan's spectrophotometer

In the summer of 1994, Tilli Tansey, The Society's Archivist based at the Wellcome Trust, wrote to all Society Members seeking information about papers, photographs, films and equipment that might usefully be acquired for The Society's collections. One response came from Sir Andrew Huxley, who wrote*:

There is in my lab at Cambridge a piece in which you might be interested. It is a key part of a spectrophotometer that was being developed just before World War II by Glenn Millikan, one of the sons of the American physicist R A Millikan, famous for the oil-drop experiment. Millikan was then a lecturer in physiology at Cambridge and he had been a research fellow of my College (Trinity) and was living in the College. He was a most lively and attractive person who was extremely good to many students of my generation, taking us out in his car at weekends, interesting us in his research, etc. and was one of the influences that led me to switch from my original interest in physics into physiology. Both he and Britton Chance (who was in Cambridge, I think in 1938) worked with Jack Roughton, improving his rapid reaction apparatus, etc. Millikan used photoelectric methods to record the change in oxygenation of myoglobin in a cat muscle during work. Through contact with Keilin, he appreciated the value that a spectrophotometer would have for biochemists, and began to develop one in collaboration with the Unicam company, then recently started by a Mr Stubbings who I believe had previously worked for the Cambridge Instrument Company.

Just before the war, Millikan married Clare, the elder of the two daughters of the Mallory who was killed on Everest, and returned to the USA, where he developed his photoelectric device for recording the oxygenation of the blood in aircraft pilots. He asked me to take over the collaboration with Unicam, which I did as I stayed in Cambridge for the first 6 months of the war as a clinical student; the development did not progress very far, however, as Unicam had to concentrate on war work. Very sadly, Millikan was killed in a climbing accident shortly after the end of the war, and for that reason his name is less well known to physiologists than it deserves to be.

The part of the spectrophotometer that is in my room is the device for reducing the intensity of the reference beam so as to match that of the beam that had traversed the specimen. It is a rotating disc, opaque except for a sector whose angle can be adjusted while the disc is rotating. Its size is that it would probably fit inside a 1ft cube, and it is fairly heavy as it includes a substantial electric motor. I have no idea what happened to the rest of the apparatus. It included three interchangeable light sources (a tungsten lamp, a hydrogen discharge tube for the ultraviolet and I think a xenon arc), and the wavelength was selected by means of a quartz double monochromator made by Hilger. I do not know who is technically the owner of this article. I saw and recognised it in a passage in the Physiological Laboratory when I moved back to Cambridge from UCL in 1984 on my appointment as Master of Trinity College.

I am sending copies of this letter to Professor Ian Glynn, head of the Department and to Millikan's widow in California. I quite expect that both of them would agree with me in regarding the collection that you mention as a very suitable home for this historic piece of equipment. I hope that the Working Party would think it acceptable for the collection.

(* originally published in *The Physiological Society Magazine*, **21**, 35)

The Working Party on Historical Equipment, comprising Members of The Society and representatives of the Science Museum, was very interested in acquiring this piece. After Sir Andrew had ascertained that both Professor Glynn and Mrs Millikan were happy for us to acquire the spectrophotometer part, Simon Chaplin of the Science Museum visited Cambridge to examine the piece and take it back to London, where it has been incorporated into The Society's collection.

New membership categories approved at The Society's Annual General Meeting

The AGM of The Physiological Society took place at the University College London Meeting on 5 July. In addition to special resolutions to amend the Memorandum and Articles of Association and Domestic Rules of The Society,* two ordinary resolutions on membership categories were also approved.

The first introduces a new membership category of Associates of The Society to enable everyone with a legitimate professional interest in physiology to apply. This arose from the extension of The Society's educational activities and general outreach to those in society who may be interested in physiology but do not qualify for membership or affiliation since they are not involved in research. This might include school teachers, university teachers whose prime role is in learning and teaching, or simply physiology graduates who would like to maintain contact with the discipline. Associates would not be voting members, so the nature of the membership would not change.

A new group membership category will also be introduced in the autumn for Undergraduates in affiliated departments. To encourage life-long participation in the activities of The Society, pilot projects are now being run to try to find effective ways to establish local undergraduate physiological societies that will form a mechanism for introducing new members and, at least, for establishing contact with future physiology graduates, who we hope will continue as Affiliates if they enter research training, or as Associates if they do not.

The revised membership subscription rates for 2007 are given on p. 45.

*http://www.physoc.org/govdocs

European Young Physiologists' Symposium in Munich

Slightly different from the UK Young Physiologists' Symposia (YPS) known to many Affiliates, the European YPS had an organizing committee consisting of five young scientists from five different European countries. Heike Beck from Germany was the chairman of the organizing committee and, as the local organizer, without doubt was extremely busy with the organization, including bookings and invitations of speakers etc. Birgit Teunisssen (Netherlands), who did an extremely good job in attracting sponsors for the symposium, Katarina Likavcanova (Czech Republic) and Adam Steensberg (Denmark) were heavily involved in reading more than 400 abstracts submitted for the meeting and choosing the best ones for the Oral Communications and the European Young Investigator Award session. And there is myself, happy to have The Physiological Society, who generously sponsored eight Affiliate travel awards and the EYPS party on the Sunday evening, on board. You can imagine that it was not always easy to come to a decision with such a big organizing committee based all over Europe. There were days when we had to write numerous emails and to make many phone calls to get things sorted. But obviously we did overcome all the difficulties.

A big surprise for all of us was the huge interest in the meeting. On 10 December, the official deadline for abstract submission and around 3 months before the meeting, the number of abstracts submitted for the symposium hit 200. We were slightly worried when the deadline for abstract submission was extended, as that extended our deadline as well as we used the same online registration system. Finally, the number of abstracts submitted for the EYPS reached nearly 400 in February. Those abstracts came from all over the world, including Spain, Germany, UK, Russia, USA and even some African countries. I don't know how, but finally we managed to put the meeting together. Until this point the organizers had not met each other, so we were all looking forward to meeting at the symposium.

Top: Professor Pohl (2nd right) and Birgit Teunissen (left) with the EYPS awardees.
Above: Andreas Draguhn (left) with Werner Klingler, winner of the European Young Investigator Award.

The structure of the EYPS differed slightly from that of the UK YPS as we had to include the European Young Investigator Award session in our programme and plan workshops hosted by external companies and specialists. Moreover, with more than 300 posters to be presented, the size of the symposium became extremely large. The organizing committee pre-selected posters for the sponsored poster awards (Biorad and Invitrogen), and these were then assessed by Frans van Nieuwenhoven (Netherlands), Richard Siow (UK) and the organizers. The posters were of outstanding quality and the presenters did an excellent job of 'selling' their posters to the jury. But unfortunately only three awards were available, so a tough decision had to be made. We decided to award Eiko de Jong (Groningen, The Netherlands), Adriana Stan (Dusseldorf, Germany) and Hayo Castrop (Regensburg, Germany) for their excellent poster presentations.

For the morning sessions we invited young and outstanding speakers to present their work – Esther Ludgens (Maastricht, The Netherlands) and Dieter Lambrechts (Leuven, Belgium) gave excellent and exciting talks which were much appreciated by the audience. The morning sessions were chaired by Richard Siow and Frans van Nieuwenhoven who also decided the award for the best Oral Communication (Isabelle Frey from Munich, Germany). Professor Draguhn (University of Heidelberg) joined Birgit and myself to assess the Oral Presentations for the European Young Investigator Award in the afternoon. Although we came to a clear decision about the winner of that award (Werner Klinlger from Ulm, Germany), all the speakers proved to be highly competitive on an international level.

It should be noted that there was an impressive audience at all the talks (on average more than 100 people). Also the three workshops had a very good turn out as they were of practical relevance for many of the participants (qPCR by Biorad, RNA Interference by Invitrogen and Stem Cell Research by Professor Goetz, Munich, Germany).

The 'Frauenkirche' in Munich

Left, from front: Dieter Lambrechts, Jörg Niehüser-Saran, Birgit Teunissen and Esther Ludgens.
Right from front: Frans van Nieuwenhoven, Katarina Likavcanova, Richard Siow, Adam Steensberg and Heike Beck.

After a long day of listening to scientific talks and getting involved in discussion, it was not only the organizing committee but also most of the participants who were looking forward to the EYPS party at the Institute of Physiology in the evening. The party was a fantastic opportunity for all of us to make new friends or just to chill out. Sitting together with the other members of the organizing team that night we felt not only relieved that everything had gone smoothly but also a bit proud about the success of the symposium. Certainly, looking back there are a few things we all would do better next time, but we are more than happy to leave this rather hard and demanding job to others and are keen to share our experience with those organizing the next EYPS.

Finally, I want to thank everybody who helped us to make this symposium such a great success –particularly Professor Pohl for having the idea of a symposium designated to young investigators on a European level, Giovanni Mann for supporting my idea of getting The Physiological Society involved and the Deutsche Physiologische Gesellschaft, FEPS, The Physiological Society, Biorad, Invitrogen and Roche.

Jörg Niehüser-Saran
King's College London, UK

(photos by David Rowlands and Jörg Niehüser-Saran)

Where next? Physiologists of the future

Career advice for final year undergraduates

Although it seems like a life time now, it wasn't that long ago that I woke up in a cold sweat thinking 'one year left … what on earth am I going to do when I've finished?' That was just before the beginning of my final year as an undergraduate.

Being an organised person, ignoring the situation and hoping it would go away wasn't an option so I began randomly applying for PGCEs and PhDs – I really didn't know what I could do with my degree and skills, but I had to do something.

Knowing then what I know now would have made me realise that, firstly, most final year undergraduates do have that sudden realisation (or panic attack) that the 'real world' is looming in the not so distant future and, secondly, there's a wealth of information and support out there relating to career development, it's just knowing where to look. But actually that in itself is a problem, where should you look?

The careers office at my university was good but as a scientist I felt it didn't quite cater to my needs – I wanted to know what a PhD really entailed and, more importantly, what I could do with it if I got one. And a post-doc … what's that? And okay I went on to do a PhD but what are the options as a scientist if you don't opt for further postgraduate study? So we're back to that question again, where should you look?

The simple answer is 'the learned society'.

My first formal introduction to the concept of 'learned societies' was during my first post-doc when my best friend 'volunteered' me to write *A day in the life* for *The Biochemist*. I wouldn't consider myself a biochemist, far from it (anything with the word chemistry in it sends a chill down my spine), but an eager and ever-willing post-doc I was.

Approximately 3 months after submitting my article I was sent five glossy copies of *The Biochemist* all containing a rather cheesy picture of me in a glowing white lab coat, pipette in hand – and now I wonder why there's a stereotypical image of scientists! After reading my article to remind myself what I was supposed to do on a daily basis I flicked through the rest of the magazine and I was amazed to find so much interesting information. There was a very relevant article, *Focus on careers*, written by the Education Projects Manager, another on job hunting (including tips for applying for jobs online or by email), lots of newsy items and, of course, the science.

I should probably point out that I joined a learned society during my PhD; however, nobody ever explained the real value of joining beyond free meeting attendance!

When I moved to the States for my second post-doc I decided to join a relevant membership organisation. This time I made use of all resources: meeting attendance, journal access, newsletters, networking opportunities, free attendance of a technical skills workshop, career development resources and much more. Well worth the $70 subscription.

Now, as the Education and Membership Manager at The Physiological Society I am in the perfect position to help support the careers of young physiologists but before I explain how I (we) do that I should perhaps explain what The Physiological Society is.

The Physiological Society was founded in 1876 as a gentlemen's dining club providing scientists a forum to discuss their research. Although we still host dinners during our meetings they are now enjoyed by all scientists (women were introduced to The Society in 1914) from over 50 countries worldwide. The Society's key aims are to promote the advancement of physiology and to facilitate communication between scientists and other interested parties. For information on Society activities please visit www.physoc.org

As a membership organisation we currently offer two membership types: Ordinary membership for those who hold an appointment in physiology or other related sciences at an appropriate (postdoctoral) level in a recognised institute, and Affiliate membership for graduate students or newly qualified postdoctoral researchers.

Affiliate membership offers a number of benefits including: free meeting attendance and programmes, eligibility to apply for travel grants of up to £400 or The Young Physiologists' Bursary Scheme, free or discounted attendance of all Society organised/sponsored workshops, quarterly editions of *Physiology News*, access to our Special Interest Groups, monthly e-newsletter, careers advice and networking opportunities.

Table Resources currently offered by The Physiological Society and those undergraduates would like

Current resources	Suggested resources
• The Young Physiologists' Bursary Scheme (grant to attend meetings) • Discounted Meeting attendance • Vacation Studentships (VS) - up to £1,200 to support you whilst working in a lab over the summer holidays • Young Physiologists' Symposium (YPS) (attendance only) • Opportunity to write for *PhysiologyNews* • Technical skills workshops • Online access to *Physiology News* • Careers conferences/advice • Links with schools • Undergraduate prize for physiology • Excellent networking opportunities (with physiologists at all stages of their career)	• Free attendance at Society Meetings • Published list of Members who are interested in supporting VS • Eligibility to run YPS • Writing skills workshop • Communication skills workshop • Hard copy of *Physiology News* with an undergraduate section • Careers guidance and workshops • Online forums • Travel grants • Funding for PhDs • E-newsletter • Access to Special Interest Groups • Mailing lists • Funding for seminar schemes • Option to remain associated to The Society if not eligible for Affiliate or Ordinary membership

A rough guide to setting up your own Undergraduate Physiological Society

One, do your research. Try and identify a Member of The Physiological Society within your department/faculty, they will hopefully be able to offer you some support and guidance. If you approach the right person, i.e. head of department (if you still have one)/programme manager, you may be able to use your negotiation skills to get some financial support. Find out what links are already in place with The Physiological Society, i.e. do we support your departmental seminar schemes, award vacation studentships and undergraduate prizes? If possible get a list of everyone who studies physiology (and remember physiology runs through many biological sciences/medical courses).

Two, arrange a meeting. Invite everyone on your list to meet, if you were able secure financial support I'd suggest buying snacks/drinks – food is always a great way of drawing in the crowds. It may be worth attaching a copy of the above article to your invitation as an overview of why you're interested in setting up a society.

Three, the meeting. Use this opportunity to sell the benefits of starting a society. It's also a great time to find out what undergraduates at your university really need in the way of career development (I'd love to hear what they come up with). You're going to need some support to run your society so I would suggest recruiting a few willing volunteers.

Four, running your society. How you divide up the running of your society is really up to you. Sit down with your willing volunteers and write a list of activities you would like to organise and then divvy them up between you, you will however need someone to keep the momentum going and make final decisions so I was advise electing a Chairperson. You'll also need a treasurer to collect subscriptions – the subscriptions you collect can be used to support the running of your society. However, if you decide that you would like all of your members to receive hard copies of *Physiology News*, The Physiological Society will invoice you for the number of copies sent. A database of member email address should be set up and it is important to keep this updated and to ensure that The Physiological Society has the latest version at all times.

And finally … give me a call (if you haven't done this already). I can arrange for various resources to be sent to you, set you up to receive our e-newsletter (and *Physiology News* if requested) and advise you on how to organise your activities.

The Physiological Society through individual undergraduate societies can help support the career development of many young physiologists and we are very much looking forward to hearing from you.

In order to encourage life-long participation in the activities of The Society we are looking to re-introduce a membership category for undergraduates. We are currently piloting this scheme in a couple of universities to try to find effective ways to establish local undergraduate physiological societies.

Back in April I received an invitation from Hannah Budd and Vishaal Sood inviting me to speak to the Undergraduate Physiological Society at the University of Glasgow. Hannah and Vishaal had taken the lead on setting up their society and had successfully managed to recruit approximately 40 members all of whom had an interest in physiology. So they had 40 members, £5 from each of them, enthusiasm and motivation, one social event under their belts but no real idea what to do next. The purpose of my visit was to talk about The Society, benefits of current membership categories, resources we currently have on offer for undergraduates and how they could develop their own society. It was also a great opportunity for me to find out what the undergraduates wanted from The Physiological Society.

Ever the scientist, I've put together a little comparison table (see previous page) showing resources we currently offer and resources undergraduates would like.

As you can see the two lists are fairly comparable but the Membership Services Committee is currently discussing which resources we can develop. I should point out that The Society looks to support the careers of as many young physiologists as possible and we would not be able to do this if we chose to fund a PhD.

So, where next …

We have and are developing more of the resources you need and are keen to hear from any undergraduates with an interest in joining The Society. Rather than offering individual membership we're looking for keen volunteers to start up undergraduate societies within their own institutions. (a great addition to your cv!) For guidance on how to do this please read A rough guide to setting up your own Undergraduate Physiological Society.

You may also be interested to hear that The Society is looking to pilot an Associate membership category for those with a professional interest in physiology who don't qualify for Affiliate or Ordinary membership. We are currently developing this membership category and further details will be posted on the website shortly. The one very obvious benefit of Associate membership is that it allows you to stay in touch with physiology and physiologists and will provide you with access to resources to help support your career development.

If you have any questions or suggestions regarding Undergraduate membership, Associate membership or indeed Affiliate or Ordinary membership please get in touch. dbrown@physoc.org

Donna Brown

2005 finances

The financial statements were approved by the Trustees on 3 May 2006. Due to Charity Commisssion reporting requirements (SORP05), the statements have been presented in a slightly different format from previous years. The emphasis is now on activity reporting such as publishing, meetings and education. The main changes are an expanded Trustees Report, which shows the main objectives for each activity, and looks at performance and future plans. There is also a detailed financial review. The actual numbers have been restated to show direct costs of each activity. To complete the SORP requirements, the 2006 financial statements will also apportion overhead costs to each activity; this will enable the readers to see the 'true cost' of the activities.

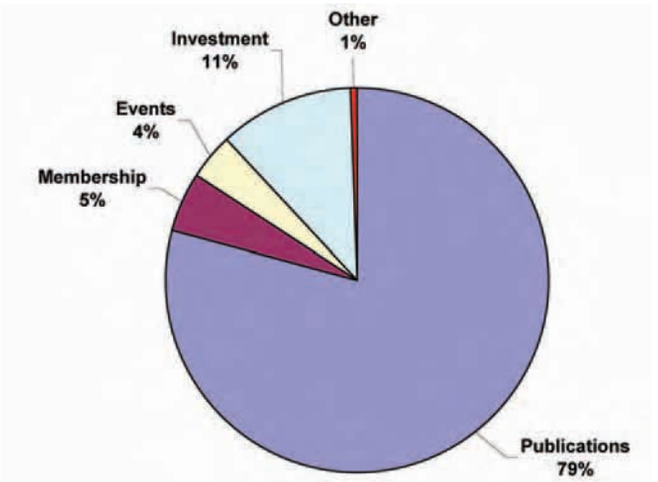
Summary accounts are shown in the 2005 Annual Report and the full financial statements can be found on The Society's web site in the Member area (Member documentation):

http://www.physoc.org/downloadfiles/2005FinancialStatements.pdf

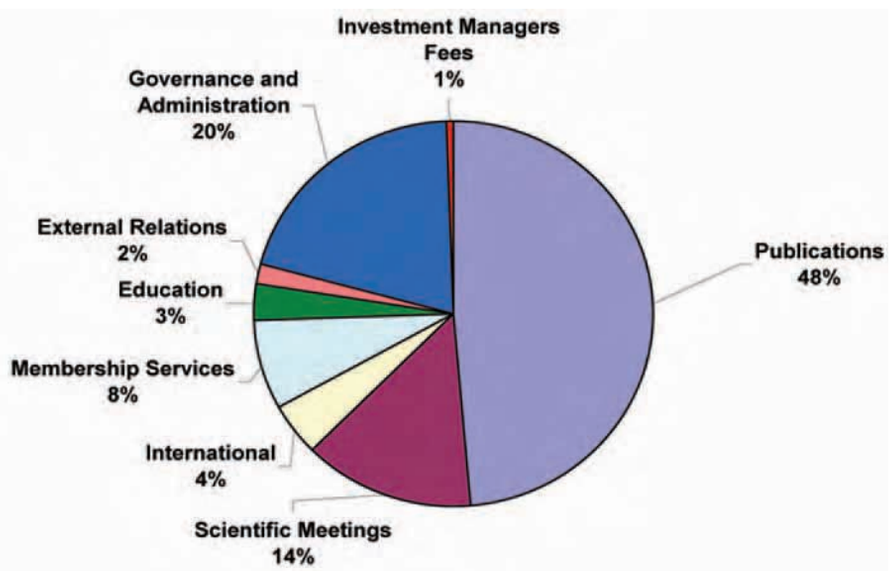
Please contact me with any questions; these accounts were presented to the membership at the Annual General Meeting on Wednesday, 5 July at University College London.

Casey Early
Finance Manager

Society Treasurer Graham McGeown (top) and Finance Managert Casey Early



Pie charts showing income (above) and expenditure (below)



Highlights
- Total income £3.3m, up from £3.2m in 2004
- Strong performance on investments
- Society net assets at historically high level
- New SORP reporting including expanded 'financial review'

Financial performance
- Total income† has increased by £200k. Healthy increase in journal (3%) and Members' subscriptions (7%) and investment income (8%)
- Net surplus from journals† constant at £1m
- Other charitable expenditure largely within budget (incorporating the recharged income)
- Result (before investment gains) was a **surplus of £296k** (2004: deficit of £51k)
- Net movement in funds of £1,719k (2004: £532k)

Financial position
- Total Society funds stand at £10.4m (2004: £8.7m), an increase of 20%
- Majority of this increase due to investment performance; investments valued at £7.3m LGIM Tracker Funds and £2.4m property
- Bank cash has increased to £0.9m, but total cash has decreased (£0.2m into tracker funds)

Plans for 2006 and beyond
- Review of investments and reserves policies
- Complete SORP requirements

† Excluding exceptional items

Gossip from the Parliamentary and Scientific Committee

The Parliamentary and Scientific Committee meets about once a month whilst Parliament is in session and I try to attend all sessions that may be of interest to our membership. Feedback from Members indicates that my subsequent articles are of interest, so I hope to publish my notes, based on my personal understanding of these meetings, on a regular basis.

Science in court – expert witnesses in the dock (22 May 2006)

This was a very thought provoking meeting for any physiologists who might find themselves summoned as expert witnesses. The presentations were from Baroness Helena Kennedy QC, James Badenoch QC (The Expert Witness Institute), and Professor Robert Forrest (The Forensic Science Society). The main points were as follows.

Kennedy said that expert witnesses are expected to help courts make decisions beyond reasonable doubt, as one facet of multi-layered evidence. However, some trials have notoriously erred by placing too much reliance on expert witnesses, resulting in high profile miscarriages of justice, particularly in alleged child abuse or murder cases. The GMC has become so concerned about this that they are now prepared to strike off doctors deemed to be neglectful in giving evidence, quite a change as previously they viewed the expert witness arena as being outside their control. Helena Kennedy chaired an enquiry looking into how expert witnesses might be more effectively assessed and used by the courts. She made the point that judges need to hold properly managed sessions to discuss and assess evidence from sometimes conflicting expert witnesses. Judges should consider whether evidence presented has been properly peer reviewed, and whether the witnesses are qualified and of good standing in their professional communities to guard against quacks. Checks should also be made that the potential witness is expert in the exact area under discussion, for example Roy Meadows was encouraged to express opinions about the probability of child deaths occurring under certain circumstances when he was not a statistician. The USA provides a potentially useful model in that their judges are provided with procedures and guidance on deciding whether evidence is pertinent and a witness appropriately qualified. I said in the subsequent discussion that this is something the wider scientific community could assist with, rather than leaving non-scientifically trained judges to try to assess complicated, and occasionally dubious, scientific evidence unsupported. Kennedy also made the very interesting point that, in her view, medics can be particularly vulnerable to making errors as expert witnesses as they are used to working as diagnosticians, and so can tend to express their personal medical beliefs rather than knowing how to present scientific evidence. Diagnostic method is not the same as scientific judgment.

Kennedy's long experience of the legal system has made her a firm believer in the adversarial system as being the best way of securing justice. However, potential expert witnesses should be aware that the adversarial system tends to try to push witnesses into expressing certainties even where these are not scientifically valid. Prosecutors don't like to admit doubt, any doubt is a gift to the defence. Expert witnesses need to keep reminding themselves that they represent the scientific and medical communities and are therefore essentially neutral witnesses for the court, no matter which side has called them to give evidence. It is not their role to be judge and jury, and there is an important difference between how they would normally express a professional opinion at work and acting as an expert witness trying to present scientific evidence. Courts are not the place to fly kites. Witnesses need to beware if they appear in court to describe a specific part of the case, such as their role in the initial treatment of an injury, of being pushed into acting as a more general expert witness. It is better to refuse to be drawn.

Badenoch then reflected on his experiences in the civil courts, a slightly different standpoint to Kennedy's criminal cases. He said that he had encountered many dubious 'experts', for example some insurance companies are notorious for maintaining lists of 'tame' expert witnesses. He was concerned that the role of expert witnesses is currently under too much of a spotlight in the Press, and is subject to much ill-informed media comment sometimes vilifying experts. He would also be concerned if the GMC became too keen to strike medics off as this would potentially deter witnesses from coming forward. The combination of these factors seemed to be leading to the unfortunate situation of public confidence in expert witnesses being diminished and experts becoming more and more afraid to give evidence. This needs to be addressed as judges can't do their jobs without expert witnesses. Good progress has been made in expert witness practice in the civil courts, the Rules of Civil Procedures already give very detailed advice for witnesses. Kennedy is trying to get a similar code adopted in the criminal courts, but this is not straight forward as so much more is at stake in criminal cases.

Forrest rounded up the session by reminding everyone that the legal system has been wrestling with the problem of the effective use of scientific evidence for a long time, citing the trial of Dr William Palmer in 1856. A large number of suspicious deaths had clustered around Palmer's family, friends and medical practice, strychnine and other poisoning was suspected, but test results were conflicting and there were suspicions

that samples had been tampered with. The great and the good of the scientific community were summoned as witnesses, and the court struggled to evaluate the masses of circumstantial evidence with forensic evidence that was sparse and controversial. 150 years later nothing much has changed. Some areas have systems of recognised experts, for example public health analysts, but this would be difficult to extend to all scientific fields. Kennedy expressed reservations about assembling lists of potential witnesses – people keen to put themselves forward for these can be the maverick characters that it is best to avoid.

All the presenters made the point that medics, judges and lawyers need more fundamental scientific training to cope with all this. Judges and law students need more training in the assessment of scientific evidence, and more science graduates should be encouraged to enter the legal and medical professions. Expert witnesses might also benefit from some legal training to cope with the highly pressurised court environment. However it is very important that training does not become coaching in the presentation of specific cases. In the subsequent discussion I, and the representatives of several other learned societies, raised the issue of the apparent increasing exclusion of fundamental scientific training in medical courses. In response to this, Forrest strongly made the point that medics need a good foundation in all the 'ologies' before they start to study medicine. Apparently the USA could again provide a good model for this, as it is the norm for people there to start to study medicine as postgraduates. The various Parliamentarians present expressed strong support for these views.

Human reproductive technologies (19 June 2006)

This session centred around the role of the Human Fertilisation and Embryology Authority (HFEA). The presenters were Professor the Lord Robert Winston and Professor Peter Braude of KCL, both of whom addressed regulatory issues of the HFEA.

Winston woke everyone up and sparked off a lively debate by asking questions about some fundamental inconsistencies in the organisation's regulatory role. Is it justifiable to select one branch of medical practice for such regulation? The case is often made that the HFEA is essential to ensure public confidence that gametes and embryos are treated appropriately. But what about paediatricians – don't they stand even more chance of damaging babies and children than IVF doctors? Yet the public does not cry out for their equivalent regulation. It is difficult to get approval for research on embryos, yet society allows abortion. Another issue is how clinical practice is actually regulated. Over half of multiple pregnancies in the UK are generated by IVF. Multiple pregnancies often produce more complications than single baby pregnancies, resulting in a burden on the NHS. The NHS is also not keen to provide IVF, so provision has been swept into private practice for those who can afford it. Once in the private sector, it is more difficult to effectively regulate and there is suspicion that patients are being exploited by some sectors of the industry through overcharging, that some clinics manipulate data for the HFEA league tables of pregnancy rates, and that women in the developing world are being exploited for their eggs. In egg donation, it is not allowed to pay the donors but egg sharing arrangements are OK. Loss of anonymity for gamete donors now means that women who shared their eggs could end up being traced in 18 years time by a child. This could be especially difficult for women who shared their eggs but did not become pregnant through their own IVF treatments. For researchers, Winston noted that HFEA approval resulted in doubling up of aspects of the overall approval process, for example in the area of ethical reviews. Winston asked if HFEA is considered to be a model for the world, then why has only Canada followed suit? HFEA might even be considered to be stifling some areas of research, for example in the area of embryonic stem cells comparatively few papers are published in the UK. Even the USA with its overt anti embryonic stem cell research political climate produces more. HFEA is supposed to promote public trust in science, but the relevant social science surveys have not been done. The opposite may be true for all we know.

Braude then reminded everyone that the HFEA was set up to protect parents and children by monitoring the efficacy and safety of new technologies, to allay public concerns about possible 'Frankenstein science' and to protect scientists by providing them with an approval umbrella for their work. The HFEA has taken a lot of flak on behalf of individual scientists. However, our long experience of regulation in this area now means that the time is ripe to look at what does not need regulating. He also pointed out inconsistencies in the role required of HFEA. For example, the welfare of child provision (the idea of checking out the potential parents to see if they are fit to be parents) is unique to IVF. It is not a requirement for other fertility treatments. The length of allowable frozen storage is also too restrictive in precluding long-term storage for research purposes. The only sanction for misdemeanours is to remove treatment licenses with consequent chaos for patients in the middle of treatments. Intermediate sanctions need to be created. Progress towards the creation of new stem cell therapies is being inhibited by current regulations. Embryos cannot be kept *in vitro* for more than 14 days. Embryos with disease processes identified by pre-implantation diagnosis often can't be used for subsequent research so scientists end up relying on cloning instead. The current ban on all forms of reproductive cloning will affect patients seeking to eliminate diseases transmitted by mitochondria in their offspring, where potential treatments include inserting their nucleus into a donated egg free from mitochondrial disease. He also highlighted the impact of private practice on research, potential good researchers being diverted into lucrative IVF practice.

Ian Gibson MP asked how do we define an embryo and its relationship to a human being? Braude responded by saying that society needs to move

beyond the tyranny of the embryo, natural reproductive processes are very wasteful of gametes and embryos. The debate over when life begins is centuries old, in previous times life was not automatically considered to start at conception. Some religions try to focus on the question of when the 'soul' enters the fertilised egg. But how can this deal with the 'souls' of twins – in a lab it is possible to turn twins back into one individual. There is a huge diversity of religious views on embryos, making it impossible to regulate research on this basis. Technology also moves on so fast that any regulatory body needs to be able to handle legislation flexibly and to maintain the confidence of the public, who are getting more nervous through media scare stories about designer babies.

Liz Bell

From 'ologies' to 'omics': issues for our long-term survival

Ian McGrath

For this year's joint meeting of Heads of Physiology and Pharmacology I was invited to give a talk entitled *From ologies to omics* with no further remit. The internet helpfully provided 'physiomics' which, no doubt, we have already (or should) feature in this magazine (see www.physiome.org) but also provided far too many other examples with this suffix, usually including c-omics, indicating that I had been spoofed.

The real remit concerned the pressures that have acted on the ologies to shape our current position and how we should respond. Essentially, the effects of several big demographic and other factors have come together in the last ten years to challenge us. These are: the Robbins expansion of universities in the 1960s; the research-driven academic agenda; the life curve and consolidation of the worldwide pharmaceutical industry; changes in teaching and learning for health professions and, of course, the rise of -omics, with the implication that physiology is not part of this zeitgeist. My general drift is that many such factors are common to physiology and pharmacology so that this particular alliance can be useful in moving forward.

The Robbins expansion and the research driven academic agenda

The Robbins expansion created new universities and expanded existing ones in the 1960s giving a great boost to the -ologies but, at the same time, it set a demographic time bomb. The rapid expansion from the mid 60s to mid 70s placed a spike on the age profile followed by a latent period of low recruitment. The relatively ample staffing then presented a soft target for further expansion of student numbers in the 90s. This was, of course, exacerbated by the popularity of human biology with students and led to the highest student:staff ratios ever seen.

Unfortunately, this coincided with the start of the research-driven academic agenda, not inherently a bad thing, but an unfortunate time to be coping with very high numbers of students. This undoubtedly created an atmosphere in which, in some institutions, the -ologies were perceived to be on the teaching rather than the research side of the scales.

The development of -omics (databases of whatever) has also been an important part of this new research agenda. This has resulted in incredible databases crying out for integrative scientists to translate the numbers back into function.

The prioritisation of translational research had a further effect. The divisions between academic disciplines were considered to be superfluous alongside the growing unity of biology. This led to amalgamations of departments (relatively easy to handle) or (more problematically for the -ologies) the creation of departments within universities focused on biological or biomedical topics such as 'cardiovascular science' or 'neuroscience' topics, i.e. that look more like research institutes than academic departments. Since universities continue to teach students, more or less along disciplinary lines, this means that teachers for a single course are drawn, increasingly, from different units, divisions, etc. I believe that this has dangers for sustainability of these scientific disciplines. While academic staff have been trained in the -ologies the danger is minimal. But what happens once they all retire? Is this a Luddite argument? I thought so once, being a bit of a hybrid myself. But now I wonder.

The impact of the pharmaceutical industry

The fat years for -ologies following the Robbins expansion coincided with the rise of the pharmaceutical industry based, in no small part, on the -ologies' graduates streaming out of universities and on collaborations with university laboratories. However, in the 90s, as the industry consolidated and turned to high throughput technologies, the opportunities for collaboration waned, particularly in integrative science, removing some fuel from the -ologies. At this point many of the staff who were skilled in integrative techniques left industry, a move that their managements subsequently regretted, leading to them joining forces with the learned societies to revitalise the *in vivo* skill base. This was exacerbated by another societal factor, the distaste for animal experimentation, which led universities to soft pedal away from using animals in university teaching.

The importance of links to medical training

The -ologies also owe much of their existence in universities to the training of health professionals. Changes in this sector present considerable threats. Although it is not often mentioned as a big factor, in my view the disengagement of the -ologies from medicine started when it became

financially irrational for medically trained personnel to take up careers in university pre-clinical science departments. In the post-war generation of eminent -ologists, a good proportion were medically trained but this is now almost unknown. This is coupled with the apparently unstoppable trend towards the removal of pre-clinical science training in favour of scenario-based 'professional' training.

Together these factors produce a more distant relationship between the -ologies and medicine that is to the detriment of knowledge-based medicine and is corrosive to the maintenance of the -ologies. A subtext here is that the -ologists often do contribute as substantially as in the past to professional training, by enthusiastically participating in the new educational formats, but this occurs below the radar of those who have the power to create departments of -ology or recruit new staff. They will wake up in about 5 years time, as the last of the Robbins recruits retire, to find that there are no longer any -ologists around who have an interest in medical training. Those younger staff who remain will have spent their entire careers so far concentrating on the career-enhancing qualities of their research, on teaching -ology to scientists and existing in departments whose title and composition is related to some fashion or other in the 1990s.

(Oh yes, there is a personal element here but I think we can generalise, i.e. what on earth can 'Division of Neuroscience and Biomedical Systems' mean?). If academics grow up in environments dominated by topic-orientation, will they have an interest in discipline-based training? I think not and I believe that this is destructive to the sustainability of scientific capability. I have spent my career so far working with colleagues in a number of clinical disciplines and I believe that the key point is that clinical disciplines are consumers of science whereas pre-clinical disciplines, like other basic science disciplines, are producers of science. If we forget this we will end up with mediocrity.

Questions for the future

So where do we go from here? I have a few survival questions.

- **where will the next generation of -ologists come from?**
  - what core skill set do they need?
  - what environment will keep this updated and developing?
  - what is the key stage for students to identify with an -ology while retaining breadth and flexibility?
- **do staff identify with students of an -ology? Or are they all neuro- or cardiovascular scientists, etc.**
  - who are the role models for the students? To turn an old question round – can we identify research with teaching?
- **-ology or -ologies? *In individual institutions,* can pharm and phys survive apart? *Should* they be separate? Does commonality strengthen them? Can we find ways to strengthen the distinct identities while operating together in order to fend off the academically corrosive phenomenon of 'cardiovascular departments' etc.**

On the national and international level it seems obvious that certain issues are best sorted out at the level of the Biosciences Federation and others by learned societies for individual -ologies. However, the degree of commonality between the -ologies for integrative mammalian biology is very considerable and should lead to more joint initiatives and strategic alliances. The obvious one to start with would be waking up the medical establishment to the consequences of the loss of science from the medical curriculum. Apparently judges are already starting to think that medically trained expert witnesses have inadequate scientific training to be reliable.

The phys/pharm alliance has already proved its potential in the alliance with the pharmaceutical industry on *in vivo* skills. Perhaps we should extend this to a broader front across the spread of intellectual and technical skills required for translational research, the current buzzword with great potential for misinterpretation. The key is to maintain the distinctive capabilities of the disciplines and keep them visible in order to keep them sustainable. Let's fend off the topic-named departments before it's too late.

It will be disappointing if this has not been at least a little provocative. Please send any contributions to this debate to lrimmer@physoc.org for publication in *Physiology News*.

Ian McGrath
Chairman of the Executive Committee

Council members 2006–2007

At the Annual General Meeting of The Physiological Society on Wednesday 5 July at University College London, the following were confirmed as members of Council for 2006–2007:

Present Council members who were re-elected

J C McGrath (Chairman), C H Orchard (Vice-Chairman), J G McGeown (Treasurer), D A Eisner (International Secretary), J Ashmore, D R Corfield, P L Greenhaff, S K Hall, J Hanrahan, P T Harrison, A King, S L Lightman, C Schwiening, S V Smirnov, D Sugden, A Tepikin, K D Thornbury and T Tiffert.

New members of Council

P Kumar (Meetings Secretary)
D J A Wyllie
V Gladwell

Other members of Council

O H Petersen (President)
W A Large (Editor-in-Chief, *The Journal of Physiology*)

Jeremy Ward

Honorary Treasurer 2001–2005

As Jeremy Ward and I have adjacent offices in New Hunt's House at King's College London, I forgot that he had actually retired as Honorary Treasurer of The Physiological Society at the AGM in Bristol 2005.

Jeremy, in liaison with Dafydd Walters, steered The Society through quite difficult times, and we were all appreciative of their efforts. Jeremy introduced the concept of cost centres for The Society's different activities, e.g. Meetings, Membership Services, Education and External Relations.

As stated by our current Honorary Treasurer Graham McGeown (Annual Report 2005), 'Jeremy's planning and foresight have provided a good foundation on which to build for the future.' I would personally like to thank Jeremy for this initiative. These cost centres are now established procedure and have greatly assisted The Society's need to prepare the financial statements in accordance with the updated *Statement of Recommended Practice* (*SORP05*).

Jeremy Ward at the Benevolent Fund desk at the UCL Physiological Society Meeting.

I genuinely value Jeremy's advice and friendship and, as evidenced by his continued involvement with the Benevolent Fund, Jeremy remains a life-long supporter of The Physiological Society. Finally, it is a pleasure to welcome Jeremy as my new Head of Department of Physiology at King's.

Giovanni Mann

Governance documents

Extensive revisions to The Society's governance documents were approved at the Annual General Meeting on 5 July. The revised documents are available to read on The Society's web site at http://www.physoc.org/govdocs.

The governance documents have been extensively revised to remove inconsistencies and updated in line with the 2005 strategic review of The Society's activities.

The principal changes concern the rights of the various classes of membership.

Honorary Members have been given the same rights as Ordinary Members, including that of voting at General Meetings of The Society. Corporate Members will now be known as Corporate Partners and Affiliate Members as Affiliates. Both Corporate Partners and Affiliates will be able to attend, but not vote at, General Meetings of The Society.

Payment arrangements and the handling of arrears have also been clarified.

Members with any queries about the governance documents may contact Simon Kellas, The Society's Committee Secretary and Office Administrator, at:

skellas@physoc.org (email) or
020 7269 5725 (telephone).

Membership subscriptions

The Annual General Meeting of The Society, held on 5 July at the UCL Meeting, agreed the following membership subscription rates for 2007.

For membership of The Society and entitlement to Notices, Meeting Programmes, *Physiology News* and electronic access to *The Journal of Physiology* and *Experimental Physiology:*

Ordinary Members	£90 (Direct Debit discount £10)
Retired Members	Free

Members of The Society may subscribe to:
A hard copy of *The Journal of Physiology* by an additional sum:

Ordinary Members	£120 (Overseas Members £120)

Or to a hard copy of *Experimental Physiology*

Ordinary Members	£75 (Overseas Members £75)

For Affiliate membership of The Society and entitlement to Notices, Meeting Programmes and *Physiology News:*

Affiliate (online only)	£20 (Direct Debit discount £5)

If paper copies of Notices and Programmes are required, there will be an additional charge to cover postage costs of:
£5 (UK & RoI)
£20 (Europe)
£25 (rest of the world)

BIOSCIENCES FEDERATION

How does one get the money to support a really big project?

Programme grants are difficult to get and many research scientists think that their chance of a project grant submission being successful will be diminished if the amount sought is much out of the ordinary. Funders deny that this is the case, but are not really believed. So the active researcher wanting to develop a largish team and research programme resorts to writing a portfolio of grant applications. In a sense the major project is 'salami sliced' into smaller projects that fit better with the system.

However, these tactics are not helpful if one seeks to develop a really big project. If this had been the tactic for mapping the human genome, I wonder how much would have been achieved today. And, of course, there are other big projects to be undertaken across the biosciences.

Currently, the Karolinska Institute is leading a major attempt to raise antibodies to all human proteins. The main sponsors of this work are the Wellcome Trust and the Wallenberg Foundation, although industry is also making an important contribution to the overall cost. This arrangement, whereby major funders come together uniquely for a particular project, is a very interesting approach to finding support for a big project. Indeed, in some cases it may be the only way to obtain large sums of money.

Hitherto these arrangements have been rather *ad hoc*: there has been no platform for making introductions. The new Eurobiofund (a dreadful name because it is not a fund at all!) has the potential to change the landscape and will certainly provide the necessary platform to introduce exciting large scale science to consortia of funders. The Eurobiofund is essentially a forum for scientists to interest public and private funders in large scale projects. The first forum will be in Helsinki in December and is supported by the European Commission. In January, *Nature* (**439**, 244) stated that the Eurobiofund 'may end up being just a small step towards the ideal, but it is the biggest single step that we have seen for some time. European scientists should give it their full support'. The call for expressions of interest closes on 4 September – but there will be another one next year. No matter what area of the biosciences you are in, if you have a grand idea and can muster persuasive arguments in its support, you might find the Eurobiofund to be of interest.

Closer to home, the Biosciences Federation (BSF) is beginning to think about how it can make a distinctive and effective contribution to discussions about the Research Assessment Exercise. Clearly there will be another RAE and equally clearly metrics will play an important role in the outcome. The key question concerns the metrics used and how they are interpreted. There is a possibility that different metrics will be used for different areas. For example the metrics for the Humanities do need to be different from the metrics for the Biosciences. However, one can also argue that different metrics could be applied usefully to different biosciences – for example, is it sensible to compare numbers of spin out companies in ecology with the numbers arising in biochemical areas? 'Certainly not', many would say but all the biosciences will have to cope with a single array of metrics. A strength of some of the metrics is that they arise from the peer review process. This obviously applies to grants and refereed publications but it also applies elsewhere – for example to funds obtained from venture capitalists or seed funds. However, this is not true for some important activities that should be included in the analyses. For example, assessment of quality is much more problematic when one considers outreach activities. I would certainly welcome individual views on how to tackle this question.

This is an 'interesting' time for enquiries that will impact upon the research landscape. The BSF has already responded to a Parliamentary enquiry about Research Council Institutes and we are currently developing our views about the coalescence of MRC funds with the research funds of the Department of Health. The real difficulty in all of this is to understand the detail – and where there is no detail, to predict what it might eventually be. Consider the merging of MRC and NHS research money. At one level it seems a sensible idea to have a single fund of public money for research in this area. However the idea immediately seems less attractive to many if a consequence of change is altered accountability.

All of our responses to enquiries require effort and research. Currently there is too much for our small team to tackle. However thanks to increased support from some Member Organisations (including The Physiological Society) we are now able to strengthen our team. I hope to introduce the new members to you in the next issue of *Physiology News*.

Richard Dyer
Chief Executive, Biosciences Federation

(http://www.bsf.ac.uk)

Call for Nominations for the Biosciences Federation Science Communication Award 2006

The Biosciences Federation Science Communication Award recognises research-active bioscientists from UK universities and institutes who make an outstanding and consistent contribution to communicating science to the public.

The Award has a first prize of £1,000 and a runner-up prize of £250, which will be awarded at a Members' Meeting of the Biosciences Federation in November/December.

Nominations will be evaluated by an Award Panel comprising two representatives from the Award sponsors, Pfizer, two from the Biosciences Federation Council, and an external representative eminent in the field of science communication.

Nomination of research-active bioscientists from UK universities or institutes must be made by an individual from a Biosciences Federation Member or Associate Member Organisation by submission of a completed Nomination Form.

The deadline for receipt of nominations is 14 September 2006.

For more information and nomination forms see
http://www.bsf.ac.uk/awards/sci_comm2006.htm

One of the delights of the English language, especially for a native speaker, is its obscure by-ways: those curiosities that appear to have no rationale whatsoever, but just are. An example is bizarre collective nouns. I am not talking just the common-or-garden ones, like a pride of lions, but ones that are wilfully obscure and daft; a parliament of owls, for instance, or a conspiracy of ravens – or even an ostentation of peacocks.

The last of these gave me an idea, which came to me, as these things sometimes do, in the midst of a rather tedious University committee meeting. The exams season having just finished (at least in British universities) you will probably not be surprised to hear this was an EXAMS committee.

Anyway, as the Exams Officer tried to explain to us how it was entirely in accordance with accepted departmental practise for two academics to have marked a report separately at 64 and 66%, and then have agreed a mark (but without actually having met) at 68% rather than the more immediately obvious 65%, I thought:

What would the 'right' collective noun be for a group of university scientists?

A few spring to mind: how about:

A **disputation** of physiologists

An **antiquity** of anatomists

A **curmudgeon** of biochemists (alternative: 'a reduction')
(NB 'curmudgeon' may also be used as a collective noun for anatomists, or physiologists over the age if 45 specialising in medical teaching)

An **intransigence** of pharmacologists

A **distribution** of statisticians

A **condescension** of neuroscientists (or of clinicians)

An **introversion** of molecular biologists.

Of course, apart from these common-or-garden discipline-based groups, there are all the exotic new specialisms needing collective nouns too; for instance:

A **ligation** of genetic engineers

An **extrapolation** of mathematical (systems) biologists (also of biophysicists)

A **contradiction** of experimental psychologists

An **inflation** of stem cell biologists.

And in any discipline, when at a conference, you can always spot:

An **inebriation** of conference attendees.

Next, in fields which are not scientific, but cause scientists much pain when talking to their families/neighbours/students, my favourite has to be:

An **obfuscation** of nutritionists/alternativists/homeopaths (although a **dilution** of homeopaths is also possible)

However, in the specific context of exams meetings, with which I started, we could not leave without:

An **accommodation** (5 star if you want to keep them happy) of external examiners

An **aggravation** of administrators (alternatives: 'confusion', 'profusion').

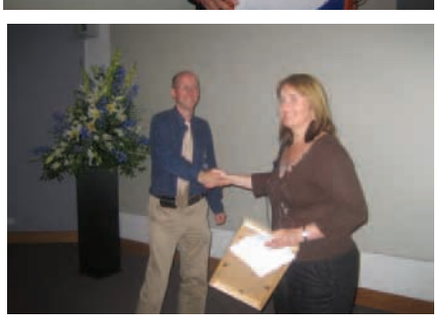
And finally, of course, given that exams meetings in June take place in high conference season:

An **absence** of Professors.

See you next time.

Mark Cain

Plenary and Prize Lecturers at the UCL Meeting



From the top:
David Attwell (The Physiological Society Public Lecture); Neville H McClenaghan (The Sharpey-Schafer Lecture), right, with new Society President Ole Petersen; Thomas J Jentsch (Hodgkin-Huxley-Katz Prize Lecture), right, with Giovanni Mann; Susan Wray (Joan Mott Prize Lecture); and Helen Kennedy (Wellcome Prize Lecture) with Corné Kros.

(*photos by Prem Kumar and Austin Elliott*)

David L Yudilevich

1930–2006

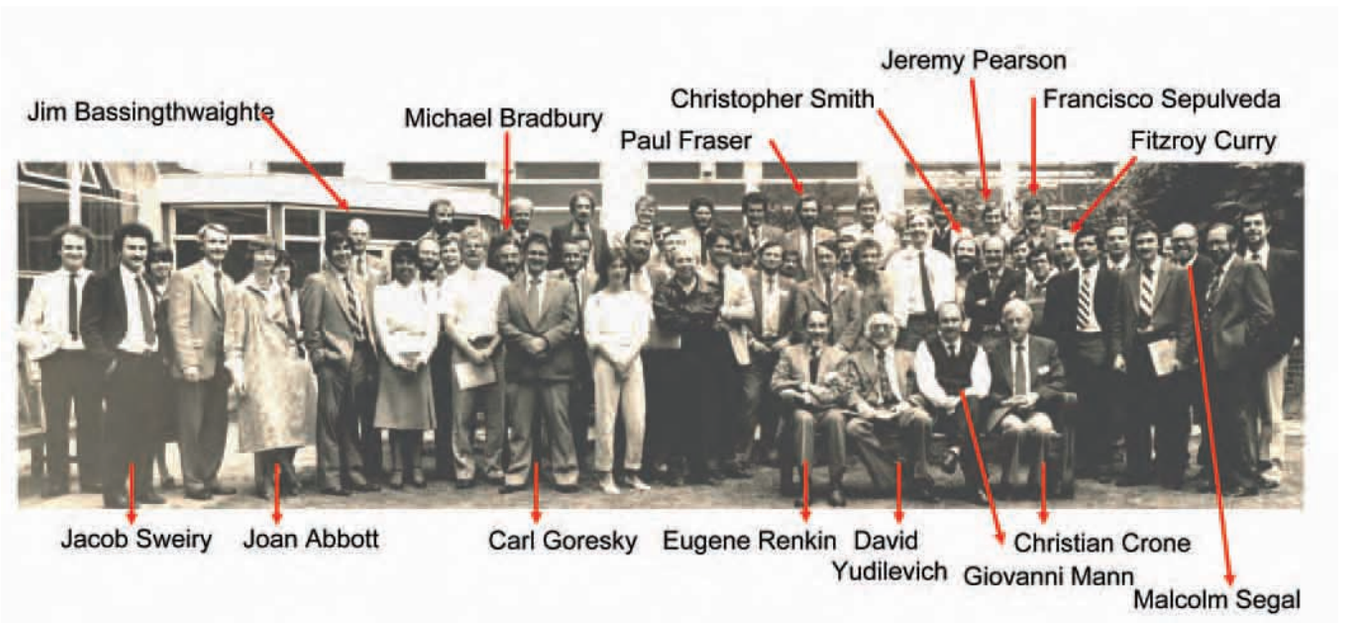
David L Yudilevich, my mentor and colleague, passed away in London on Sunday 28 May 2006 in the presence of his family and close friends. David's children, Jessica and Ivan, were at his bedside, and he was moved by his grand-daughter, Susanna, reading to him. His funeral was held in Golder's Green and was attended by close family friends and academic colleagues from the UK and Chile.

Above: David scanning the horizon in the Andes in Chile.
Below: David hosting an International Symposium, *Carrier-mediated transport from blood to tissues*, held at Queen Elizabeth College in 1984.

David was born in Santiago, Chile on 15 June 1930 and received his MD in 1957 from the Universidad de Chile. After three and half years postdoc in the USA, David returned to the Medical School in Santiago until, on 11 September 1973, the Chilean radio announced that a military coup was taking place. An unsigned letter from Hugh Davson enabled the family to sail from Valparaiso to Britain to begin collaborative research with Laurence Smaje at University College London, with the support of Doug Wilkie, the Jodrell Professor and Head of Physiology.

In 1974 David was appointed as Professor and Head of the Department of Physiology at Queen Elizabeth College, University of London. As Head of Department from 1974–1985, David always encouraged research-led teaching initiatives and appointed Simon Howell to a Readership in Physiology and Christopher Smith and Giovanni Mann to Lectureships in Physiology. Under his leadership, the Department of Physiology at Queen Elizabeth College prospered and hosted meetings of The Physiological Society. Following the merger of Queen Elizabeth and Chelsea Colleges with King's College London in 1985, David stepped down as Head of Department and Peter Baker, FRS became Head of the merged Department of Physiology.

David was passionate about research and during his early career made seminal contributions to the field of capillary permeability, studying microvascular permeability in the isolated perfused gastric mucosa, heart and brain using the multiple indicator dilution technique. He was a respected and close friend of many colleagues in Chile (Francisco Sepulveda, Rosa Deves, Luis Sobreiva, Mauricio Boric, Felipe Barros, Elisa Marusic, Claus Behn, Alejandro Goic and others), USA (John Pappenheimer, Eugene Renkin,



David crossing a suspension bridge in Chile

Jim Bassingthwaighte, Carl Goresky, Walter Duran, Halvor Christensen and many others), Denmark (Christian Crone), France (Andre Syrota), Spain (Salvador Peran, José Viña), Israel (Ioav Cabanchik) and UK (Michael Bradbury, Laurence Smaje, Richard Boyd, David Eisner, Clive Ellory, Richard Naftalin, Peter Baker, Peter and Linda McNaughton, Jeremy Pearson, Christopher Smith, Ole Petersen, Richard Olver, Charles Michel, Geoffrey Burnstock, Geraldine Clough, Paul Fraser, Roberto Navarrete, Gerta Vrbová, Olga Hudlicka, Peter Gahan, Stephen Hirsch and many others). Hugh Davson had invited David to the UK after the coup in Chile, and upon arrival with his family David immediately began investigating the permeability of fenestrated capillaries in the salivary gland together with Laurence Smaje and Giovanni Mann in the Department of Physiology at University College London.

At Queen Elizabeth College, David extended the indicator dilution technique to study carrier-mediated transport of nutrients (amino acids, glucose, vitamins, and calcium) across the maternal and fetal interfaces of the isolated perfused guinea-pig placenta (Bryan Eaton, Jacob Sweiry, Caroline Wheeler-Jones), blood-brain barrier (David Barry), salivary epithelium (Giovanni Mann, Carlos Bustamante, Stuart Wilson) and lastly umbilical vein endothelial cells from normotensive and gestational diabetic pregnancies (Luis Sobrevia, Mauro Parra, Giovanni Mann).

David was an invited speaker/organiser of numerous international conferences, and I recall some memorable ones. David hosted an international meeting on *Carrier-mediated transport of solutes from blood to tissue*, which led to the publication of a book in 1985 edited by D L Yudilevich and G E Mann. The photograph, taken at Queen Elizabeth College, captures the international profile of this meeting! The second memorable occasion was an international meeting held in Lanjaron, Spain, which again resulted in the publication of a book in 1989 entitled *New methods in the study of transport across the cell membrane*, edited by D L Yudilevich, R Deves, S Peran and Z I Cabantchik.

David was committed to strengthening research links between Chile and Britain, culminating in his appointment as Honorary President of the Joint Meeting of The Physiological Society and Sociedad Chilena de Ciencas Fisiologicas in Pucon, Chile in November 1999.

David remained research active throughout his academic career and well into retirement. He published more than 100 articles in peer-reviewed international journals, and during the last 10 years of his retirement enthusiastically researched the travels of Darwin and Alexander von Humboldt in Chile and South America. His unabated quest for knowledge and enjoyment of science (both bench-based and historical) is evidenced by the series of books he published in retirement on Darwin (*Darwin en Chile 1832-1835: Viaje de un naturaliste alrededor del mundo*) (published in 1996 & 1997[1]) and *Chiloe por Charles Darwin* (published in 1998) and Humboldt (*Mi Viaje por el Camino de Inca 1801-1802* (published in 2004[2]). In addition, David organised numerous stimulating symposia on Darwin and the Beagle and Humboldt's travels at venues in Chile, France, Germany, Spain and the UK. During his last visit to King's College London in May 2006, David was intending to deliver an invited keynote lecture at a symposium organised by the Cervantes Institute in Tel Aviv, Israel.[3]

In retirement, David's contribution to physiology was further acknowledged by awards of an Emeritus Professorship of Physiology at King's College London, Professor Titular in the Faculty of Medicine in the Universidad de Chile and Honorary Membership of Sociedad Chilena de Ciencas Fisiologicas.

David Yudilevich was a unique, lively and driven individual, always seeking to explore new horizons alone and with his close friends and colleagues. I remember with affection our travels by car through Chile and there are just too many entertaining stories about David's travels to scientific meetings.

His 76th birthday would have been on 15 June 2006, and I just knew that he could never slow down. Colleagues in Santiago gathered for a special memorial dinner to celebrate David's life on 15 June 2006. Perhaps David, standing in the Andes in Chile, with his characteristic colourful travelling bag(s), highlights his wanderlust and appreciation of science, nature, life and, above all, his family and children Jessica and Ivan.

Giovanni E Mann

[1] http://www.universitaria.cl/consulta.pl?q=pub&c=14&id=327

[2] http://www.humboldt200.cl/inca.html

[3] http://telaviv.cervantes.es/Portada_50_1.htm

Trust and Deceit

A tale of survival in Slovakia and Hungary, 1939-1945

By Gerta Vrbová
2006, Vallentine Mitchell.
181pp. £14.50
ISBN 0 85303 630 6

Gerta Vrbová is Professor Emeritus in developmental biology at University College, London. A renowned physiologist and member of The Physiological Society for over 40 years, she has recently unlocked dramatic memories of her early life.

In this book she revisits the events in 1939 that uprooted her as a 12 year old from a close and loving, comfortably off Jewish family in Slovakia. She recalls, with surprising clarity, her flight with her mother from her home town of Trnava and the years spent living under assumed identities in Hungary before capture by the Gestapo in Bratislava at the end of 1944. Gerta had recently learned of the atrocities being carried out at Auschwitz via a chance meeting with her childhood friend and future husband Rudi Vrba who was one of the very few to have escaped from the camp. Indeed, she had helped to distribute his report on the situation there that was sent to various high authorities in Europe, who did nothing. The knowledge of the fate that would almost certainly follow deportation to Auschwitz spurred Gerta to take the first of a series of enormous risks, which culminated at the end of the Second World War in 1945, in her finding herself back in Slovakia as an 18 year old with no surviving close family, no formal secondary education but who miraculously, and against all the odds, was still alive.

This is a tale of enormous risk-taking, assumed identities, physical hardship, luck, cunning and, above all, pure guts combined with an extraordinary ability to know instinctively who to trust and who must be deceived. Some of these experiences, as Gerta remarks wryly at the end of her account, were to stand her in good stead for her career as a successful scientist in later years.

Most of us brought up in the UK, with all its faults, can have no concept of what this type of life must have been like. If you are one of these people, I suggest you read Gerta Vrbová's book and find out. It is a chastening story.

Thelma Lovick

Until 30 September, 2006 readers of *Physiology News* may obtain copies of *Trust and Deceit* at the reduced price of £13, including postage and packing. To order your copy contact the publishers, Vallentine Mitchell at:

Suite 314, Premier House, 112-114 Station Road, Edgware, Middx HA8 7BJ
Tel: +44 (0)20 8952 9526
Fax: +44 (0)20 8952 9242
Email: info@vmbooks.com
Web site: http://www.vmbooksuk.com

Space physiology

By Jay C Buckey
2006, Oxford University Press. 284pp. £35.99
ISBN 0 19513 725 5

This book is an excellent reference point for scientists and students interested in the effects of inactivity on the human body.

The author manages to present a detailed and up to date review of the most 'hot topics' in space physiology: calcium and its loss, muscle wasting and weakness, cardiovascular deconditioning, changes in body composition, psychological status and well being, neurovestibular function and motion sickness, the effects of radiation exposure, physiological demands of extra vehicular activities, gender differences in physiological responses, the medical risks involved in spaceflight and the medical care requirements.

The book also reviews the various methods, whether physical or pharmacological, used as counter-measures for the prevention of deterioration, or for post-flight rehabilitation, of the major physiological systems in actual as well as in simulated spaceflight.

In presenting this information to the reader, Dr Buckey went into considerable depth in explaining the mechanisms of the physiological adaptations to spaceflight, spanning from the molecular to the organismic level, citing both animal and human studies performed from the dawning of manned spaceflight to nowadays. Undoubtedly, this is the most comprehensive handbook on space physiology presently available.

Marco Narici

Michael Rennie adds:
In his preface Dr Buckey lays out his aim: to enable space crews to live and work effectively in space and to provide guidance for the wide community of scientists, physicians and engineers who support space crews. He further says that his objective is to provide a practical handbook and reference to enable flight surgeons, astronauts and support teams to make informed decisions about medical care and physiological maintenance. Himself a Spacelab astronaut and a doctor, if anyone could write such a handbook he should be able to.

How well has he succeeded? The book contains a summary of much of the current information concerning a wide spectrum of physiological, pathophysiological and even psychosocial knowledge gained from research over the past 50 years, and especially the last 15. To that extent the book will be valuable to anyone wishing to become involved in research on how the body adapts to immobilization, microgravity and space flight and would certainly be an excellent text book for students studying the physiology of the human body under extreme conditions. Many of the chapters are effectively self-contained with sufficient background information to make their content

understandable to most medical students or senior undergraduates in the life sciences. Each chapter ends with recommendations based on current knowledge which I suppose should be the sections most likely to fulfil Dr Buckey's primary aims. The problem is that for many of the topics the recommendations are rather woolly. In the areas I know most about maintaining muscle and bone mass and nutrition, the recommendations seem to have little about them which is specific to space flight and indeed, so far as I am aware, there are no interventions which have been shown to have a substantial effect in preventing loss of muscle and bone and it is even difficult to get astronauts to eat a balanced diet in space. The recommendations concerning gender and crew selection could probably have been written by an agony aunt for an upmarket woman's magazine.

Nevertheless, the book is comprehensive and so far as I could tell, up to date and well referenced. It does however sometimes read more like a list than a review and I missed the presence of any vignettes concerning the experiences of astronauts which would have illuminated the text. However, I found much in the book that was new to me and it should be a useful aid in teaching and learning physiology.

Michael Rennie

Adrenaline and the inner world

An introduction to scientific integrative medicine
By David S Goldstein
2006, The Johns Hopkins University Press. 312pp.
£16.50 (paperback), £43.50 (hardback)
ISBN 0-8018-8289-3

Everyone thinks they know about the autonomic nervous system. It's one of the first things you learn about in physiology. It seems relatively simple once you've written down the basic road map of connections and transmitters. And anyway it's all classical physiology, the stuff of Nobel prizes 50 and 70 years ago, but old hat now. David Goldstein's excellent book gives the lie to all that. First and foremost, it's an excellent review of what the autonomic nervous system is and what it does. It turns out that the simple concept of opposing sympathetic and parasympathetic systems is more of a hindrance than a help in visualising how our internal environment is regulated. Much better is to understand the different patterns of activation of various components of the system in response to different circumstances. Goldstein expertly and engagingly reviews what these components are and how they work. In doing this, he also deftly introduces the other theme of the book, the evolutionary, systems-based integrative approach which is so necessary for interpreting physiological contexts and for understanding how detailed physiological knowledge relates to medicine. Subsequent chapters emphasise this with descriptions of disorders of the autonomic nervous system (the dysautonomias) and their treatments.

The final chapter explains why, after some decades of extreme reductionism, the future of applied science must be integrative. This book pulls off a difficult trick: it takes a subject which you think you know about, yet manages to leave you with significant enhancements of both specific knowledge and general approach. Highly recommended (whatever your specific field) for students and teachers alike.

John A Lee

Late news

UCL 2006

Final registration figures for The Society's Main Meeting at UCL in July topped 1,000. Over 400 people attended David Attwell's Public Lecture on Brain/Power, and some 430 participants enjoyed the outdoor (and rain-free) BBQ extravaganza at Regent's College. The Society's events team hope that all those who attended enjoyed both the scientific and social programme.

Main Meeting 2008

The Society is delighted to announce that its Main Meeting in 2008 will be hosted by the Department of Physiology, Development & Neuroscience at the University of Cambridge, UK.

Centre of Excellence

The Society has awarded a Centre of Excellence grant to Sergei V Fedorovich of the Institute of Biophysics and Cell Engineering at the National Belarus Academy of Sciences. For further information on the Centres of Excellence Scheme please visit http://www.physoc.org/international.

Science Media Centre

A Seminar on *Making the case for animal research in the media* will take place at the Science Media Centre on Tuesday, 14 November in a central London venue (to be confirmed) from 1600 to 1800. The event will be followed by a wine reception. For further information, or to register, please email smctemp@ri.ac.uk.

Open Meeting

An Open Meeting on *Acetaldehyde-related pathology bridging the transdisciplinary divide,* organised by the Novartis Foundation, The Royal Society and The Physiological Society, will take place on Friday, 8 September in the Franklin Wilkins Building, King's College London, 150 Stamford Street, Waterloo, London SE1. All welcome, but pre-registration is essential at http://www.rsm.ac.uk or by email to events@rsm.ac.uk or telephone Ms Bina Arpino at the RSM 020 7290 3946.

Notices for the winter 2006 issue of *Physiology News* should reach the Publications Office by 21 September. Please send contributions to lrimmer@physoc.org

BRITISH PHARMACOLOGICAL SOCIETY

4th James Black Conference

University of Hertfordshire, De Havilland Campus
11–13 September 2006
The challenges of drug discovery and development.
http://www.bps.ac.uk

AUTUMN SCHOOL IN COGNITIVE NEUROSCIENCE

Oxford
25–28 September 2006
http://www.cogneuro.ox.ac.uk/autsch

LIVERPOOL MEDICAL RESEARCH COUNCIL GROUP

Pancreatitis and calcium signalling

Liverpool Medical Institution, UK
22–26 January 2007
A British Society of Gastroenterology (BSG) Research Workshop to review progress in understanding the pathogenesis of pancreatitis, to subject this understanding to constructive scrutiny with input from research workers outwide gastroenterology, to enhance interchange of ideas and collaborations, to engage and encourage younger researchers in the field and promote biomedical research within the BSG.

MOLECULAR TECHNIQUES FOR LIFE SCIENCES WORKSHOPS

PCR Theory and Practice

22–26 January 2007
A five day course to introduce participants to this core technique covering the basics to quantitative Real-time PCR. Cost: £870 (Standard), £740 (CPD Accredited).

For further information and application form visit our web site:
www.caledonian.ac.uk/mtls
or contact: Mrs J Pierotti MTLS Administrator, Biological and Biomedical Sciences, Glasgow Caledonian University, Cowcaddens Road, Glasgow G4 0BA, Scotland UK
Tel:: +44 (0)141 331 3243
Fax: +44 (0)141 331 3208
Email: mtls@gcal.ac.uk

IUPS

Kyoto, Japan (27 July–1 August 2009)
UK (July 2013)
http://www.iups.org

LIFE SCIENCES 2007

Glasgow, Scotland
8–12 July 2007

The Physiological Society has joined forces with the Biochemical Society and the British Pharmacological Society to organise a scientifically broad and exciting programme that includes:

240 speakers
10 high profile plenary lectures
Over 60 symposia
Workshops
A lively trade exhibition
Joint poster sessions

Sign up for Life Sciences 2007 email alerts at:
http://www.LifeSciences2007.org
for all the latest programme information

For general enquiries please contact
info2007@lifesci.org

SOCIETY MEETINGS

Ribeirão Preto, Brazil
27–30 August 2006
Joint International Meeting with the Brazilian Physiological Society and Young Physiologists' Symposium.

Heidelberg, Germany
13 September 2006
Focused Meeting
Control and modification of excitation-contraction coupling in healthy and diseased muscle.

Charles University, Prague
21–23 September 2006
International Workshop
Lung function in health and disease.

Bristol, UK
4–5 December 2006
Focused Meeting *New developments in stress physiology: from gene to man*.

Edinburgh, Scotland
12–13 February 2007
Focused Meeting *Perinatal physiology: from uterus to brain*.

Belfast, N Ireland
4–5 April 2007
Focused Meeting *Ion channels and the microcirculation*.

Glasgow, Scotland
8–12 July 2007
Joint Meeting of The Physiological Society, Biochemical Society and British Pharmacological Society (see details, left).

Bratislava, Slovakia
10–14 September 2007
Joint Meeting of The Physiological Society, the Slovakian Physiological Society and FEPS.

Manchester, UK
October 2007 (to be confirmed)
Focused Meeting *Cardiac electrophysiology*.

Bristol, UK
17–18 December 2007
Focused Meeting *Renal cortex: physiological basis of glomerular and tubular diseases*.

For more information visit The Society's web site at

http://www.physoc.org

Portugal Focused Meeting
20 April 2006

Clockwise from top left: The pool at the hotel conference centre; Symposium dinner (from left) Henry Danahay (Novartis, Horsham), David Sheppard (Bristol), John Hanrahan (Montreal) and Bill Colledge (Cambridge); Alan Verkman (San Francisco) giving the keynote lecture; Peying Fong (Baltimore) and Anil Mehta (Dundee) doing the 'cilia' dance; Shmuel Muallem (Dallas) and Hugo DeJonge (Rotterdam) in deep conversation; a representative of the Mayor of Lagoa welcoming participants to the Algarve; Margarida Amaral (Lisbon) and Mike Gray (Newcastle) awarding the poster prize to (left) Zhe Xu (Bristol) and Andre Schmidt (Lisbon). The poster was a joint presentation between the Bristol group (David Sheppard) and the Lisbon group (Margarida Amaral); The organising team (*photos by Martin J Hug*).

More photographs from the Portugal Meeting appear on the inside front cover.