Front cover: A video-print of a *ctena intestinalis* four cell stage embryo, held with a suction electrode and about to be microinjected with biotin. The procedure was performed by students on the Plymouth Cell Physiology Course (see pg 33) with the assistance of David Becker and Peter Mobbs. Courtesy of Jon Robbins.
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These guidelines are intended to assist authors in writing their contributions and to reduce the subsequent editing process. The Magazine Editorial Group is trying 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 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 denouement or conclusion.

Length of articles
This will be determined by the subject matter and agreed between the contributor and the commissioning editor. Articles will vary in length from 200 words to a maximum of 800 words.

Submission of articles
Authors should submit text in the form of a disk accompanied by a printout wherever possible. Use of disks reduces the risk of introduction of errors during re-typing. It is helpful to give brief details of the computer, operating system and software package(s) used (DOS formatted Wordperfect 5.1 files preferred, but not essential).

Deadlines for submission
See Notable Dates (inside covers of 1996 edition of the Grey Book) or contact the Editorial & Production Office. Late submissions will not be accepted or publication will be deferred to a later issue.

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

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

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

Suggestions for articles
These should be made (in writing, by phone, or in person at Scientific Meetings) either to the Editor, to the Editorial Assistant or to the relevant member of the Magazine Editorial Group (see left).

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Chris Peers ............................................................. Science News & Views
David Davies ............................................................ Teaching & Technology
Tilli Tansley .............................................................. Traces of the Past
Valerie Cox .............................................................. Young Physiologists
John Chad ............................................................... Special Features
Frances Ashcroft ........................................................ Policies & Politics
When the Physiological Society was last in Sheffield in April 1991, the Department of Biomedical Science had recently been created by merging the older Departments of Anatomy and Physiology. Although part of a general drive for greater financial efficiency, this merger also recognised the convergence of the study of form and function. I must thank my predecessor in the post of Chairman of Biomedical Science, Professor Tony Angel, for successfully managing the integration of two distinct academic Departments and leaving a Department well positioned to exploit the new opportunities in biology.

At the same time, the remaining biology departments of the University were also combined into two larger units, the Departments of Molecular Biology & Biotechnology, and Animal & Plant Sciences. Together, we form the School of Biology where we occupy adjacent buildings. Increasingly, we are working closely together to adopt an integrated, multi-disciplinary approach to the study of biological problems, and in the recent Research Assessment Exercise this Department, for the first time, joined with the other Departments in the School to make a return as a single Unit of Assessment for Biology.

Revolutions in biological thinking

The past 10 to 15 years have witnessed major changes in biology, both in experimental approaches and in our understanding of biological processes. The rapid development of molecular genetics has laid bare many of the nuts and bolts that make up complex organisms, and the Genome Project will undoubtedly soon reveal the nature and organisation of much of the human genome - perhaps the culmination of a reductionist phase of biology that began with the great anatomists and physiologists of the 16th and 17th centuries. Nevertheless, just as knowing the list of components used to construct a car engine does not tell us how the engine works, so a list of genes that comprise the human genome will not tell us how the human body functions. So, I now believe that we are poised on the edge of a very exciting phase in biology, a synthetic phase in which we shall attempt to understand how the various components that make up an animal interact to produce the whole. Here, another revolution in biological thinking of the past 10 years has something to offer. It is extraordinary, and totally unexpected, that the control mechanisms by which various gene products are interrelated have often been dramatically and highly conserved throughout evolution, so that genes, their products and the regulatory systems that operate in organisms such as the fruit fly or the nematode worm also operate in higher animals including humans. It is remarkable, for example, that a single gene (Pax-6), the deletion of which leads to a failure of eye development in mice and humans, causes eye development when expressed in such unlikely sites as the wing or leg of a fruit fly; or, that a gene involved in patterning the embryos of flies (dpp) is closely related to genes that are able to induce bone formation in mammals, so that the Drosophila DPP protein itself is able to induce bone formation from appropriate stem cells in mice and rats. This conservation of regulatory functions now allows us to make full use of a wide range of experimental model systems in a way that has direct pertinence to human biology.

Integrating traditional approaches with molecular genetics

We, in the Department of Biomedical Science, are now in a strong position to integrate the more traditional approaches of Physiology and Anatomy with these new developments in genetics. It is therefore with great pleasure that I welcome the Physiological Society to Sheffield to hold its January meeting in 1997, hosted by the Department of Biomedical Science, at this very exciting time for biology, for Physiology and for our Department.
Cell Biology - The Department of Biomedical Science is divided into 3 major areas of research interest, Cell Biology, Neuroscience and Gastrointestinal Physiology. Within the Cell Biology group my own research focuses on the use of teratocarcinoma cell lines, isolated from testicular tumours, as tools to investigate the regulation of cell differentiation during early human embryogenesis. Testicular cancer is one of the most common cancers of young men, and our research also has implications for tumour biology. The cells with which we work, apart from resembling early human embryonic stem cells, are able to differentiate into neurones in culture. In collaboration with Mark Dunne, Gavin Reynolds and Carl Pearson, we are using these to investigate the biology of embryonic neurones, as well as for modelling aspects of human neurodegenerative disease.

Neuroscience - Released from the Chairmanship of the Department, Tony Angel has been able to devote more time to his research into anaesthesia. In collaboration with the Departments of Pharmacology, Anaesthesia and Control Engineering, he has set up a new Centre for Research into Anaesthetic Mechanisms (CRAM), with a goal of integrating various interdisciplinary approaches to the study of anaesthesia. A new laboratory to house this Centre is being refurbished within the Department. Meanwhile Ken Clark continues to develop his techniques for studying the motor control of gait and locomotion, and was recently rewarded with a grant from Proctor and Gamble to adapt his analytical techniques for assessing the efficacy of drugs that affect movement. Other neuroscientists within the Department, notably Gavin Reynolds and Carl Pearson, are focused upon understanding the mechanisms that underlie neurodegenerative and psychiatric disease, particularly Alzheimer’s disease, AIDS, schizophrenia and Huntington disease.

Gastrointestinal Science - Gastroenterology has a long history in Sheffield and our current research efforts divide into several strands: David Grundy investigates the neural regulation of gastrointestinal function, whilst Peter and Jackie Hardcastle focus on the regulation of transport in the intestinal epithelia, particularly in relation to the defects associated with cystic fibrosis. Whereas the initial clinical symptoms of this disease are usually associated with the respiratory tract, defects are also found in other epithelial systems throughout the body. In collaboration with Chris Taylor in the Children’s hospital, the Hardcastles are using transgenic mouse models to examine the mechanisms underlying the pathogenesis of cystic fibrosis. Roy Levin is also interested in the regulation of transport by the gastrointestinal epithelium, but especially in dysfunction associated with malnutrition, a condition that is a major cause of death throughout much of the world. From a different perspective, Dave Rumsey continues his long standing interest in diet and its effects upon gastrointestinal function.

Electrophysiology is one of our strengths and in an exciting new development we are establishing a Laboratory of Membrane Function, bringing together Mark Dunne and Stan White, who both run groups investigating membrane function using electrophysiological and other techniques. Mark Dunne recently found that the congenital condition, hyperinsulinaemic hypoglycaemia of infants (PHHI), involves a defect in a potassium channel that functions in the regulation of insulin secretion (see Science News & Views, this issue) Stan White is investigating the regulation of secretion across the kidney tubule epithelia and the differentiation of cells within that system. The new Laboratory of Membrane Function will provide a focus for further developments and recruitment of new staff to focus on signal transduction mechanisms. Other members of the Department with interests in membrane function and epithelial transport, particularly in relation to the gastrointestinal tract, include Peter and Jackie Hardcastle, and Roy Levin. They, together with newly appointed lecturers Jonathan Kibble and Louise Robeson, will interact closely with the new Laboratory.

Developmental Genetics in Sheffield - While Developmental Genetics may seem a far cry from the traditional interests of
Physiologists, we believe that our new program in this area, being established jointly with the Department of Molecular Biology & Biotechnology, will provide many new experimental approaches to our existing Physiology programs and allow us to establish an interdisciplinary research grouping uniquely positioned to exploit the recent advances in molecular genetics and to relate the structure and function of newly recognised gene products to their role in the whole animal. For example, the new program will include the establishment of a transgenic mouse unit within our animal facility, helping many of our existing research groups to take advantage of transgenic techniques for answering traditional questions in physiology. We have been fortunate in recruiting Philip Ingham from the ICRF to the new Chair in Developmental Genetics, and seven or eight new posts are to be established as part of this new unit, with interests ranging from Drosophila to Zebra Fish and the laboratory mouse. The teaching Symposium, organised by Stan White as part of the January meeting, is designed to help introduce many of the new molecular genetic techniques to physiologists.

Teaching in Sheffield

The Department teaches science undergraduate students in three honours schools of Physiology, Anatomy & Cell Biology and Neuroscience, and also takes a lead role in the more broadly based degree courses of Biomedical Science and Biological Science, in which students are able to select modules from all the pre-clinical sciences, or the full range of biology subjects to meet their own specific needs. The Biomedical Science course, now in its fourth year, is proving extremely popular and accounts for about half of our total science student intake. The continuing rise in student numbers is leading us to reassess the way in which we teach our traditional subjects and is giving us an opportunity to develop courses in which we are able to integrate much more closely the study of structure and function. We have recently established a CAL facility to help in this respect.

Our post-graduate students continue to play an important part in the research of the Department, which is now part of the newly established Graduate School. All post-graduate students are now required to participate in an individually tailored training program, which includes a series of courses organised by the Department in collaboration with the Graduate school. These courses are designed to broaden a research student’s experience and to teach a range of generic skills that are likely to be essential in their subsequent career.

We continue to play a significant role in teaching pre-clinical medical and related students, and our new Medical Curriculum, in which basic science and clinical sciences are more closely integrated, has been well received. As a result of an agreement between the University and the new ASEAN Medical School in Ipoh, Malaysia, beginning in 1997, we will be receiving an additional 120 medical students from Malaysia every year to undertake pre-clinical studies, so that our medical student class will rise to about 320 students per year. The new teaching block being built to accommodate the newly increased class is giving us an opportunity to re-organise both pre-clinical and science teaching in a more efficient way. We will also be appointing about 11 new staff members over the next 3 years, providing another opportunity for enhancing development of the Department.

Conclusion

I hope that, in this brief outline, I have been able to give you an idea of the many exciting developments taking place involving the Department of Biomedical Science. As highlighted in the recent Government Foresight Exercise, multi-disciplinary approaches to the study of biological problems are becoming increasingly important. I believe that with the integration of Anatomy and Physiology within one Department, and our close collaboration with the other Departments within the School of Biology, will provide a strong basis in Sheffield for both teaching and research in the new environment that Universities find themselves in the UK. My colleagues and I in the Department of Biomedical Science hope that you enjoy your visit to Sheffield, and welcome the chance to show you how Physiology is thriving here.

Peter Andrews
Arthur Jackson Professor of Biomedical Science
Chairman of Department
The Committee met in Leeds on 10 September, its first meeting since the Society’s AGM. This year there has been a substantial change in the composition of the Committee. Kwabena Appenteng, Richard Boyd, Janice Marshall, Noel McHale, John Widdicombe, David Miller, Laurence Smaje and Richard Vaughan-Jones have all left and Frances Ashcroft, Maynard Case, Clive Ellory, Brian Harvey, and Alan North have become members. This leaves the Committee somewhat smaller than last year, and the workload for each member somewhat larger.

Scientific and Charitable Expenditure of the Society

The main business of the September meeting is to start the process of decision making about the scientific and charitable expenditure of the Society during the following financial year. Some of the work of the Society is now devolved to its Subcommittees, the composition of which is given in the Grey Book. Bids for expenditure were therefore made by those chairing Subcommittees as well as by the Officers of the Society. The Committee had the task, after (sometimes heated!) debate, of giving its assessment of these bids by ranking them. The decision-making process continues at the Treasurer’s Advisory Subcommittee and at the November Committee Meeting. Inspection of the Society Accounts in the Annual report of the Society will show that the Society spends in all some £600,000 on its scientific and charitable purposes each year, while membership subscriptions contribute about £120,000 only. Thus income from the *Journal of Physiology* and from investments is crucial to the functioning of the Society.

UK National Committee

Over the past year or so, a number of learned societies in the biological sciences have been debating the possibility of collaborating in advancing the interests of cellular, molecular and physiological life sciences in a number of areas. These areas include Government and other public policy, the formal education of scientists, public understanding of science, general media relations affecting learned societies, and matters affecting career development of scientists. There has been widespread support for the formation of a UK National Committee, and it was agreed that the Physiological Society would become a member of this grouping, with the Committee Secretary acting as the Society’s representative.

In addition, the Committee considered the financial report for the first half of the financial year, approved membership subscription changes already indicated to the AGM of the Society, and agreed revised charges for offprints. The memberships of editorial boards and subcommittees were agreed. The process of making nominations for Honorary Membership of the Society was begun. Scrutineers of abstracts were appointed for the coming year, and a number of grants to Special Interest Groups Designated Sessions were approved. A working party was formed to plan celebrations for the 1000th Scientific meeting of the Society, which neatly falls in December 1999 at the University of Birmingham. The annual meeting with Cambridge University Press, who print and distribute the Society Journals, was considered, as were the Minutes of meetings of a number of Subcommittees. Notably, the Treasurer was able to report that a contract had been signed with Oxford University Press for the publication of a *Companion to the Body* and that the Society would become cosponsor with the Biochemical and the Genetical Society of a new journal, *Genes and Function*, to be published by Blackwells and Portland Press. This journal would publish physiological work on transgenic animals.

After very considerable discussion, which reflected differences of taste and opinion that are likely to run through the whole of the Society, it was agreed to continue the practice of reading Minutes of the Scientific Meetings at Society Dinners and of having after dinner speeches. But it was now with the stipulation that brevity would be a requirement of speechmakers.

If you have any items that you feel the Committee should discuss, please contact the Committee Secretary, Peter Stanfield.

Christina Docchar

£5.8 billion

The Committee of Vice Chancellors and Principals has estimated that by 2005/06 UK universities will face a funding gap of approximately £5.8 billion. The article argues that filling that gap with increases in student fees will not be easy.

THES 1246 20 September 1996

Source: SPIN
Recent months have seen several changes to the staff in the Department of Physiology in Bristol. The sad and untimely death of Reg Chapman at the end of 1995 has already been reported in the Magazine and this, together with the election of Roger Thomas to the Chair in Physiology at the University of Cambridge and the appointment of Jonathan Ashmore to the Bernard Katz Chair of Biophysics at UCL, meant there would be several vacant posts in the Department for this coming academic year. These have now been filled and we are delighted to have Roland Jones, Corne Kros and Julian Paton joining our ranks.

Immediately prior to this appointment, Roland has been a Wellcome Trust Senior Research Fellow in the University Department of Pharmacology in Oxford. He has been appointed to a readership and he will form a focal point for cellular neuroscience research in the Department. Corne Kros is currently a Royal Society University Research Fellow in the School of Biological Sciences at the University of Sussex. He is interested in the sensory transduction mechanism of the cochlea and his work will complement that of Matthew Holley and Paul Kolston (existing members of the Department), and Nigel Cooper (see below), so creating a strong group in hearing research. Julian Paton has already been a member of the Department for two years, as a British Heart Foundation lecturer, but he has now been awarded a proleptic lectureship. He and his group will be continuing their work on the central control of the cardiovascular and respiratory systems.

There is a movement too amongst those holding fellowships of various sorts within the Department. Christof Schwiening (Wellcome Trust) left during the summer to take up a lectureship in Physiology at Cambridge. Michael Evans (Wellcome Trust) has accepted a lectureship in the Department of Communication and Neuroscience at the University of Keele, and Peter Skorupski (BBSRC) will be moving to Queen Mary and Westfield College in the New Year to take up a lectureship in Biology. We wish them well in their new posts. In their stead we are pleased to welcome Nigel Cooper as a new Royal Society University Research Fellow.

Fiona (Evelyn) Duncan became Secretary of the Department of Physiology in April 1996. Fiona’s first job, very appropriately, was a “Complaints Clerk” with International Photofinishers in Cambridge. From there to the Scientific Periodicals Library as an Editorial Assistant, and later to the Bursar’s, then the Senior Tutor’s, offices in Newham and Robinson Colleges respectively. She became known to many of us when, in 1990, she became Administrative Officer (II) for Student Affairs at the Clinical School, when she was involved with things like organising admissions, 2nd MB exemptions, and the clinical student timetable. She was promoted in 1992 to the job of Administrative Officer (I) in charge of Resources at the Clinical School.

Suzanne (Lee) Dickson became a University Lecturer in Physiology in August 1996. Suzanne read Pharmacology (her third year subjects were Physiology, Pharmacology and Pharmacological Physiology) at the University of Edinburgh. She became a graduate student at the Babraham Institute where she was supervised by Gareth Leng for her work on neural control of growth hormone secretion. She gained her PhD in July 1993. Between January 1993 and September 1994, she remained at Babraham as a Higher Scientific Officer working on the central site and mechanism of action of growth hormone-releasing peptide, GHRP-6, funded by a grant from Merck Research Laboratories. She was appointed to a Lectureship in Anatomy and Human Biology at King’s College, London in October 1994. Suzanne is the principal investigator on a 3-year MRC Project Grant held jointly with Professor Gareth Leng in Edinbugh.
Christof Schwiening was appointed to a University Lectureship in Physiology from August 1996. He read Physiology at the University of Bristol and then went on to work on a PhD on intracellular pH regulation in locust neurones under the supervision of Roger Thomas. He spent the year 1990-91 in the Department of Cellular and Molecular Physiology at Yale University working with Walter Boron on a NIH-funded Fellowship where he gained experience with fluorescent pH and calcium indicators as well as isolated mammalian cells. He then returned to Bristol - initially as a Research Assistant employed on a MRC grant and then, since 1994, as the holder of a Wellcome Trust Research Career Development Fellowship. In his current work, he is attempting to move away from the intracellular environment and instead is concentrating on trans-membrane ion fluxes, using a technique which involves enclosing single cells in micro-droplets under oil. Christof is married and has two daughters.

Dino (Antonio) Giussani was born in La Paz, Bolivia - but is a British citizen. He was appointed to a University lectureship in Physiology from October 1996. According to his curriculum vitae, Dino’s education did not begin until he started at the University of London (Royal Holloway and Bedford New College) reading Physiology and Zoology in which he obtained a First Class Honours degree in 1989. He then went to University College London (Department of Obstetrics and Gynaecology), and obtained his PhD in August 1992 for a thesis entitled ‘The role of the carotid chemoreceptors in the control of the fetal cardiovascular system during acute hypoxaemia’. He remained at University College until October 1993 during which time he also worked at the Universidad de Chile, Santiago, Chile on cardiovascular and endocrine responses to acute hypoxaemia in the llama fetus. He then moved to the Laboratory for Pregnancy and Newborn Research, College of Veterinary Medicine, Cornell University, Ithaca, New York - the Director of which is Peter Nathanielsz, formerly a Lecturer in our Department. Dino will be based there until September 1996, and has been working in a number of areas of perinatal and fetal physiology. He is fluent in Spanish and English, and has been honoured for his football.

Alan Findlay

NEWS FROM DEPARTMENT OF BIOSCIENCES, UNIVERSITY OF HERTFORDSHIRE

Following recent interviews Dr Wendy Purcell was appointed Head of Division of Physiology, Pharmacology and Toxicology with Dr John Wilkinson as Deputy.

Dr Wendy Purcell was recently awarded a Media Fellowship with the BBC and selected as The Wellcome Trust Media Fellow. She will spend some 6-8 weeks working with the BBC World Service Science Unit in order to facilitate the public understanding of science. Science and technology media fellowships are intended to create a greater awareness and understanding of the workings of the media among practising scientists and engineers. The first hand experience of the conditions and constraints of working journalists makes fellows better equipped to communicate their science to the general public, their students and their colleagues.

Wendy Purcell

HUGH BOSTOCK APPOINTMENT TO A PERSONAL CHAIR UNIVERSITY COLLEGE LONDON

Hugh Bostock, of the Sobell Department of Neurophysiology at the Institute of Neurology in London (currently affiliated with University College London) has recently been made a Professor of Neurophysiology in the University of London. Hugh, who graduated from Oxford with a BA in Chemistry and with an Msc in Physiology from UCL, will be well known to many members of the Society. He may have first come to their notice via his elegant computer demonstrations at Society Meetings of his measurements with Tom Sears of action currents in demyelinated dorsal root axons, in which he had refined earlier experiments of Rasminsky and Sears so as to demonstrate continuous conduction in the internodes of these axons. He has continued to research in this area ever since. His studies from experiments in vivo, in vitro and in man, in both normal and pathological conditions have made him an authority on the distribution and function of sodium and potassium channels in myelinated nerve. Recent measurements in man using measurements of “threshold electrotonus” (reviving ideas from the times of Lorente De Nô) have excited clinicians as providing new hypotheses into the aetiology of motor neuron disease, as well as possible means of monitoring the condition.

Peter Kirkwood
The Leeds Meeting

The recent Leeds Meeting was full of interest and debate not only within the Cardiovascular/Respiratory Session but also in both the Respiratory Session and Autonomic Session and symposium. In our Designated Session there were 16 Oral Communications, 10 Poster Communications, two Demonstrations and one Demonstrated Communication. The latter was much appreciated despite the small technical problem of a burst perfusion line! I was also impressed by the demonstrations of circulatory adjustment to orthostatic stress and carotid baroreceptor stimulation in humans. In addition, I personally thought that the inclusion of a one minute verbal presentation with a single slide during the approval session for Posters and Demonstrations was a worthwhile improvement. I would appreciate hearing your opinions on this subject.

Future Dates for your Diary

I would like to bring your attention to the symposium at the Sheffield Meeting which is entitled: “Respiratory and Cardiovascular Adaptation to Chronic Hypoxia” to be staged on 6 January 1997 with the Scientific Meeting to follow from 7-8 January. This symposium will aim to cover both scientific and clinical aspects and looks to be most interesting.

The next Designated Session will be held at Trinity College Dublin (24-26 March 1997); the deadline for submission of abstracts is 12 December 1996. I have invited Professor David Adams from the University of Queensland to give a Designated Lecture. His field of expertise concerns the role of intracardiac ganglia in control of the heart (exact title to be announced shortly).

Finally, if you are intending to go to the First International Society for Autonomic Neuroscience in Cairns, Australia next September please inform Joel Bornstein of your intentions; he has asked for this information and his email is: joel@plexus.physiol.unimelb.edu.au.

I would like to finish by inviting you to contribute ideas for future speakers and themes for a symposium. Please contact me if you have any suggestions - now is your chance!

Julian Paton
DEVELOPMENT AND PLASTICITY

With the approval of the convenor of the former Developmental Neurophysiology Special Interest Group and the Committee, this Group has been re-invented as the Development and Plasticity Group. Following the ‘Mechanisms of Synaptic Plasticity’ symposium organised by Richard Ribchester and David Price at the Edinburgh Meeting it became clear, from the attendance and discussion, that ‘development and plasticity’ is a major field of interest for many Members of the Society. The revised Group will provide a forum for presenting work on plasticity and development at the neuromuscular junction and development and plasticity of the visual system and the hippocampus. The Group will have a Designated Session at the Dublin Meeting (24 - 26 March 1997). The new convenor will be:

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Physiology Unit, MOMED
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HEART AND CARDIAC MUSCLE

The recent Heart and Cardiac Muscle Designated Session at Leeds was well attended. At this meeting, authors of Posters were asked to give a five minute talk with up to two slides, before the Poster was voted on. This went very well, and I encourage colleagues to support this new format.

The next Designated Session of the Group will be in Dublin 24-26 March 1997.

After three years in the position, I have decided that my tenure as organiser of the Heart and Cardiac Muscle Special Interest Group should end. I have looked around the membership for a young and energetic replacement. After some discussions I approached Dr Stephen O’Neill (Liverpool) and Dr Simon Harrison (Leeds) and both have said they are keen to take up the position. So I would like to propose to the membership that these two people take on the role as joint organisers of the Group.

If anybody has any alternative suggestions please contact either myself or Chris Fry (email: chris.fry@ucl.ac.uk). If there are no objections I propose that their tenure begin on 1 January 1997.

Barry Hirst

C Y Jung (Buffalo, NY)
Proteins that interact with the glucose transporter: implications for function

R M Krupka (London, Ontario)
Channelling free energy into work in biological processes

In addition to the invited lectures, this symposium will include Oral Communications on the topic of “Glucose Transport”. There will be a symposium dinner in the evening, with a limited number of places, and the cost will be approximately £26.00.

During the Scientific Meeting, Professor Heini Murer (Zurich) will present the Epithelia & Membrane Transport Designated Lecture, entitled “Molecular mechanisms of proximal tubule reabsorption of phosphate”.

The Group will hold a short business meeting in Sheffield. The agenda for this meeting will include confirmation of Dr Peter Brown (Manchester) as the new convenor for the Group.

Barry Hirst

Meetings Secretary’s Office

EPITHELIA & MEMBRANE TRANSPORT

The Sheffield Meeting will be preceded by a symposium in honour of Professor Wilfred Widdas, an active and regular contributor to the Group’s Sessions, organised by Richard Naftalin:

Glucose Transport: a functional approach

W F Widdas
The red cell glucose transporter - a functional approach

A Carruthers (Worcester, Massachusetts)
The kinetics of human erythrocyte sugar transport

W D Stein (Jerusalem)
Kinetics of the multidrug transporter (P-glycoproteins) and its reversal

G D Holman (Bath)
Relating the structure of the glucose transporter to function

R Devés (Chile)
System y+L: the broad-scope and cation modulated amino acid transporter
**HUMAN PHYSIOLOGY**

The next Designated Session of the Human Physiology Group will take place at the Sheffield Meeting, to be held on 7-8 January 1997. This Session will feature a Designated Lecture by Professor Eric Hultman of Stockholm who will review the metabolic basis of fatigue. The annual business meeting of the Group will be held at some point during the Meeting. Details of the time and the agenda will be circulated when the Meeting programme is known.

The second Designated Session of the year will be held at the Cambridge Meeting in December, and will feature a symposium to be organised by Tony Sargeant.

In addition to these two Designated Sessions, the Human Physiology Group has been invited to participate in the meeting of the Irish Section of the Nutrition Society. This meeting will take place in Dublin on 16-18 June 1997, immediately preceding the 8th European Congress on Obesity which will also take place in Dublin. The meeting will feature a symposium on nutritional aspects of exercise, and there will be opportunities for the presentation of oral and poster communications. Discussions are also under way for a joint meeting with the Scandinavian Society for Physiology to be held in Oslo in October 1997, and further details will follow very shortly. In addition to this rather hectic programme there will certainly be a number of papers of interest to human physiologists at the Physiological Society Meeting at Trinity College Dublin (24-26 March), even though it was not possible to hold a Designated Session of the Group.

**Molecular Physiology**

One of the great difficulties in introducing a new technique into an established discipline is language. Molecular biology has evolved its own "jargon" that eases communication between like-minded scientists but which makes it incomprehensible to anyone outside the subject. As a result, it has proved difficult to realise the enormous value that molecular biology can offer to the study of physiology. It provides potential to the study of the structure-function relationships for proteins and the dynamics of gene expression. By way of reverse, physiologists are needed to unravel the ever increasing sophistication of transgenic and gene knock-out animals.

In an effort to bridge the communication gap, we will hold a one day teaching symposium at the Sheffield Meeting of The Physiological Society. This has been co-organised by Dr Stanley White at Sheffield University and Janet Allen at University of Glasgow. It will take place on Thursday 9 January 1997. A line-up of superb communicators have accepted the challenge and agreed to contribute to the symposium which has been provocatively labelled: "Jargon-Free Molecular Biology for Physiologists".

Topics and speakers include:

- **C A R Boyd (Oxford)** - Molecular Physiology - why it matters for physiologists
- **D Hornby (Sheffield)** - How to clone your gene of interest
- **K Page (London)** - RT-PCR in tissues and cells
- **G Gould (Glasgow)** - How to express your gene of interest
- **M Leyland (Leicester)** - Mutagenesis
- **A C Dolphin (London)** - Uses of antisense technology
- **R Dimaline (Liverpool)** - Quantitation of messenger RNA
- **W Brammar (Leicester)** - Regulation of gene expression
- **W Colledge (Cambridge)** - Transgenic approaches to physiology

**Trinity College Dublin** A workshop on laboratory methods in Human Physiology is planned for Easter 1997. This will take the same form as the earlier workshop which covered aspects of blood sampling and analysis. The proposed workshop will cover cardiovascular and respiratory measurements. Further details will follow shortly.

Roz Maughan

Janet Allen
NEUROENDOCRINOLOGY

There have been two successful meetings of the Special Interest Group for Neuroendocrinology this year. The first at University College London included a symposium on the non-reproductive effects of gonadal steroids, chaired by Professor Julia Buckingham. This was followed by a Poster session in the afternoon, a Designated Session with 11 Communications and the G W Harris lecture on the neuroendocrine control of growth given by Professor I C Robinson. Professor E E Baulieu opened the symposium with a review of the neurosteroids. Dr G Gillies then discussed her studies on steroids and neural development and was followed by Dr R Stanhope who presented some clinical aspects of steroids and growth hormone release. After the break the topics were the effect of ovarian steroids on the hypothalamic-pituitary-adrenal axis and on the neurohypophysial system, the speakers being Professor G P Chrousos, Dr J Morris and Dr M L Forsling. The Communications and Poster presentations covered a wide variety of topics, many of them related to the theme of the symposium.

There was another Designated Session at the Meeting in Edinburgh in July. Many of the Special Interest Group attended the oral presentations and there was much discussion following each paper and during the Poster Session. The sessions also highlighted the wide ranging interests of the Group. However, it was a long day with the final poster being approved at around 18.25.

More meetings are being planned including a joint meeting next year with the Special Interest Group for Renal Physiology which will deal with recent developments in the neuroendocrine control of fluid balance. We are always in need of suggestions for exciting workshops and symposia and sending them in ev ery easier now: e-mail them to m.forsling@umds.ac.uk.

Mary Forsling

PhD tutors are underpaid and undertrained

A report by the Association of University Teachers, the National Union of Students and the National Postgraduate Committee reveals that PhD students are poorly paid and untrained for their teaching duties. The article discusses what steps can be taken to remedy this problem.

Guardian 10 September 1996 p.9

Source: SPIN

RENAL PHYSIOLOGY

A meeting of the Renal Special Interest Group was held at the Leeds Meeting of the Society. A broad range of topics within renal physiology was covered in nine Oral Communications and four Posters. At the Poster approval session a one minute presentation for each Poster facilitated discussion and seemed to work well.

In view of the ISN meeting in May and the IUPS Conference at St Petersburg in June/July 1997 the next formal meeting of the Group will be held at the St Thomas’ Meeting of the Society, 7-8 November 1997.

Physiological Society recommendations are that Special Interest Group convenors should be rotated every three years or so and it is now time for me to hand over to a successor. The normal procedure is to elect a new convenor at a business meeting of the Group. It would be helpful if anyone within the Renal Special Interest Group who would like to take on this role would write to me in the first instance.

Dave Potts

RESPIRATORY PHYSIOLOGY

The Leeds Meeting

They say you can tell a Yorkshireman - but you can’t tell him much. Well, any Yorkshireman that inadvertently ventured into Lecture Theatre 2 of the Roger Stevens Building at Leeds University on Wednesday 11 September would have been told quite a lot about the control of breathing during what was one of the most lively meetings of our Group for some time. Another 9am start guaranteed an extra night for many in what must have been some of the most bizarre accommodation ever offered to Phys Soc delegates. It was certainly a common topic for the week - suffice to say that to be ruled by your own bladder is bad enough, but to be held hostage by someone else’s is quite something else! If I may paraphrase Professor Milledge’s quote on sleeping in the Henry Price Building but many wish they could”.

16 Oral Communications and one Designated Lecture were given including presentations from colleagues in Germany (Dr Pierrefiche), USA (Professor Mitchell), France (Dr Benchetrit)
and Japan (Professor Honda) and once again these demonstrated the breadth of interests within our Group. The first Pfizer round in our Special Interest Group also took place and I was certainly pleased not to have been in the position of having to make a choice between the entrants who were all excellent. In the end the selection committee chose Rachel Landauer for her talk on the reversible and age-dependent effects of chronic hypoxaemia upon peripheral chemoreceptor sensitivity. Congratulations also go to Simon Gladwell who was the prize winner from the Cardiovascular/Respiratory Control Pfizer round. I shall make further bids to have more Pfizer rounds in the future, so watch for details.

A highlight of the day was the Designated Lecture given by Professor Gordon Mitchell of the University of Wisconsin, Madison USA entitled “Modulation and Plasticity in Respiratory Control”. In exemplary fashion, Professor Mitchell described the significant adaptive potential that exists in respiratory control and it appears that you certainly can teach an old goat new tricks. Gordon’s comparative neuroscience background made for an absorbing lecture which ended with a slide showing that LTP could be abolished at a $P_{CO_2}$ of 80mmHg. Not sure how much I’d want to remember if I let my pH fall so low!

The Session began with the London PET group’s experiments into the motor control of speech. Dr Murphy’s first slide had the words “BUY BOBBY A POPPY” written in so large a format that whenever I shut my eyes I can still see them in all their 256 point magnificence. Dr Murphy also explained that in the pre-circulated abstract booklet his figure had been accidentally misprinted by leaving out all the grey scales from his averaged PET scans but that these had now been put back in. And I thought the aim of science was to remove the grey areas!

The willingness of undergraduates to partake in somewhat-heroic respiratory experiments, as typified by communications given by Dr Corfield and ‘soon-to-be Dr’ Pedersen, is to be commended but I think we had a first with a recurring discussion on the relative intelligence of these undergraduates when compared to ducks. Not quite as obvious as one might initially think and at time-out I think the undergraduates had it by a head by virtue of knowing to stop breathing if someone(thing) else was looking after their bloodgases for them. JG Tansley mumbled something about his subjects at Oxford not being as stupid as ducks but intriguingly offered no direct evidence.

**The Sheffield Meeting**

Just enough space left to remind everyone of the Symposium on “Respiratory and Cardiovascular Adaptation to Chronic Hypoxia” at Sheffield University on Monday 6 January 1997. More details elsewhere. It promises to be a great day intellectually and socially and I hope to see you all there. PS for the Londoners - bring a jumper!

**Notice of Future Meeting**

Trinity College Dublin: 24 - 26 March 1997. Abstracts please for the Designated Respiratory Session at this Meeting. Submission dates 2-12 December 1996. There are few places in the UK with a stronger tradition of respiratory physiology than Dublin so please try to get an abstract in.

Prem Kunar

**SENSORIMOTOR CONTROL**

Next year looks like being an interesting and busy year for the Group. The first of three Sessions planned for 1997 will take place at the Trinity College Dublin Meeting in March. I am delighted that Dr Daniel Wolpert has accepted an invitation to give a Designated Lecture to the Sensorimotor Control Group at this Meeting. Daniel has recently established a research group at the Sobell Department of Neurophysiology, Institute of Neurology, after working for three years at the MIT in Boston. Daniel’s interests are in the neural computations involved in motor control which he is investigating using a novel experimental approach in which computer controlled apparatus is used to create “virtual environments”. In Dublin, Daniel will talk about recent work on internal models of sensorimotor integration and visuomotor learning in a lecture entitled: “Internal models in human motor control: a computational and psychophysical perspective”. I hope as many of us as possible will cross the water to make this a lively Session (deadline for abstracts; 12 December).

In the second half of the year there will be two further Sessions of the Group. In September we meet in Bristol where there will also be a Motor Control Symposium organised by Dr Richard Apps. In November we meet in London at St Thomas’ at what is likely to be the last Physiological Society Meeting to be held at the Sherrington School of Physiology. Several special events are being planned for this Meeting including the Sherrington Lecture which will be given by Professor Anthony Taylor.
Turning to more mundane matters, can I take this opportunity to remind you that it is important, when filling in abstract submission forms, to complete the box indicating the Special Interest Group Session at which you wish to present your Communication. If you forget to complete this box there is a risk that your Communication will be programmed in a General Session. This has, unfortunately, happened at recent Meetings.

Finally, now that we have a Society magazine, expensive surface mailings to members of Special Interest Groups have become more difficult to justify. In order to maintain the possibility of disseminating information to the Group in between publication of the Magazine I intend to experiment with "email shots". If you have recently started using e-mail or if your address now differs from that shown in The Grey Book, I should be grateful if you would let me know (email: j.s.riddell@bio.gla.ac.uk).

Hope to see you in Dublin.

John Riddell

SOMATOSENSORY PHYSIOLOGY

Edinburgh Meeting 2-3 July 1996

The Group convened at the Edinburgh Meeting for a symposium on "Interactions in Spinal Somatosensory Processing Pathways", organised by Sue Fleetwood-Walker, on the Wednesday, followed by a full day of free Oral and Poster Communications. The symposium, held in the grand surroundings of The Royal Society of Edinburgh, made for a good start to the Meeting. Alan Brown reported some very interesting data on collateral connections between spinal neurones giving rise to different ascending tracts, showing that transmission in each ascending pathway is not completely independent of activity in the others. This was followed by a series of talks on amino acid and peptide transmitters in nociception and in the central sequelae of peripheral inflammation. There was a good deal of information on interactions between glutamate and peptide transmitters, particularly the tachykinins, in the spinal cord. There is general agreement that substance P can enhance responses to glutamate, but there remains some controversy as to whether this enhancement is specific to events mediated through NMDA receptors. Methinks there is yet some mileage in this debate. In the middle...
Wiesenfeld-Hallin talked in more detail about the changes in spinal neuropeptides which accompany peripheral inflammation, including factors which may militate against successful analgesic intervention such as increased production of CCK. The day was informative and hugely enjoyable, and thanks must be due to Sue for organising such a splendid day.

The Group’s Session in the Meeting proper saw 14 Oral and 10 Poster Communications. This was a fantastic turn out and I am very grateful to all of those who made presentations. We learnt how stimulation in the PAG appears not to suppress responses of spinal cord cells evoked by thin myelinated axons; marvelled at the richness of the innervation of the Echidna snout; puzzled over how destruction of the VPL nucleus of the human thalamus has different sensory consequences to those of spinothalamic tract section; discovered that the mysterious imidazoline receptors are involved in the central nervous adjustments to peripheral inflammation; and were intrigued by the finding that female rats seem to be less sensitive to painful stimuli in oestrus than in pro-oestrous. These are just some of the findings which stuck in my mind: there were lots of other stimulating papers and the abstracts are worth reading. The level of attendance and the quality of the work presented made me optimistic for the future of somatosensory physiology in the UK.

The Group will convene again at Bristol in September next year. There may be a symposium and we will have another bash at winning a Pfizer prize. I also intend this to be my last meeting as convenor. You have been warned....

Rob Clarke

Medinfar wishes to announce that it has established, with the official sponsorship of the President of the Portuguese Republic, a biannual prize for contributions to mammalian physiological science by an investigator aged under 40 years. The prize of £25,000 (twenty five thousand pounds) will be awarded for the first time in 1997. The recipient will be required to deliver a lecture in the University of Lisbon.

Applications for the prize will be restricted to European nationals (subjects of EU nations and resident in an EU nation at the time of nomination).

National Physiological Societies are requested to make three nominations, Heads of Academic Departments or Research Institutes a single nomination.

The prize will be awarded on the recommendation to Medinfar of an international Jury: Chairman Professor K M Spyer, UCL London; Professor David Eisner, University of Liverpool; Professor Charles Michel, Imperial College, University of London; Professor D W Richter, University of Gottingen, Germany; Secretary Professor Luis Silva-Carvalho, University of Lisbon.

Nominations must be received by February 28th, 1997. Further information and application forms may be obtained from Medinfar.

Medinfar
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REVEALED: A NOVEL K⁺ CHANNEL DISORDER IN INSULIN-SECRETING CELLS

Mark Dunne and Keith Lindley explain how molecular studies of a rare disease helped in understanding the control of insulin secretion and how basic science could lead to novel approaches to therapy.

The study of "nature's experiments" in the form of inherited diseases has proven a time-honoured method of improving our understanding of normal human physiology. Within the last 10 years a number of human diseases have been more fully explained in terms of abnormalities of cell membrane ion channels. Perhaps the best known and most fully described example of changes in membrane ionic conductance being associated with a disease phenotype is cystic fibrosis in which over 500 different mutations of the gene encoding the cystic fibrosis transmembrane regulator protein, a cAMP-regulated chloride conductance, are described. It is becoming increasingly important to recognize that ion channel defects are coupled to altered physiological processes and pathogenesis. Our efforts in this area of physiology are directed towards unraveling a potentially lethal infantile disorder associated with hypersecretion of insulin; persistent hyperinsulinaemic hypoglycaemia of infancy.

The ionic control of insulin release

Since the late 1960s it has been recognized that control of the secretion of insulin from β-cells of the pancreatic islets of Langerhans is related to the cell membrane potential. β-cells are electrically active, and in the presence of stimulatory concentrations of glucose (typically greater than 5.5mM) they will depolarize and generate Ca²⁺-dependent action potentials. This will result in Ca²⁺ influx and the release of insulin through Ca²⁺-regulated exocytotic events; fusion of secretory granules with the plasma membrane and release of their contents (Fig 1). Not until the mid-1980s, through the application of patch-clamp techniques to study isolated β-cell function, were these events further resolved. Our current hypothesis to account for how glucose will cause changes in the cell membrane potential is summarized in Figure 1. In the normal resting β-cell the membrane potential is maintained by the combination of an

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**Fig 1.** Schematic representation of the major ion channels in pancreatic β-cells and their role in stimulus-response coupling. Under basal conditions the ‘resting’ cell membrane potential is maintained by open K⁺ channels. In the presence of stimulatory concentrations of glucose, the intracellular ATP/ADP ratio is elevated, K⁺ channels close and the membrane depolarizes. This leads to the activation of voltage-gated Ca²⁺ channels and an elevation of the cytosolic concentration of Ca²⁺ which triggers exocytosis.
electrogenic Na\textsuperscript{+}-K\textsuperscript{+} ATPase pump and opening of ATP-sensitive potassium (K\textsubscript{ATP}) channels which allow K\textsuperscript{+} to exit the \(\beta\)-cell down its electrochemical gradient. These channels may be considered as an "on-off" switch for secretory events, since changes in their activity essentially governs changes in the cell membrane potential. Thus, in low glucose concentrations, normal \(\beta\)-cells are electrically quiescent, but at high glucose concentrations K\textsubscript{ATP} channel openings are reduced, resulting in a depolarization of the \(\beta\)-cell membrane and the activation of voltage-dependent Ca\textsuperscript{2+} channels. K\textsubscript{ATP} channels are inhibited by intracellular ATP, and their gating governed by changes in the availability of intracellular ADP. K\textsubscript{ATP} channels are therefore metabolically sensitive, and as a result of this, these channels will close as a consequence of glucose metabolism and a concomitant elevation of the intracellular ATP/ADP ratio. The K\textsubscript{ATP} channel has therefore a pivotal role in stimulus-response coupling events. The channel is also of clinical importance as compounds that inhibit these channels will tend to mimic the effects of glucose and act as insulin secretagogues. Indeed, this is the basic mechanism by which sulphonylureas promote insulin release from the pancreas of non-insulin dependent diabetic patients.

Molecular architecture of the \(\beta\)-cell K\textsubscript{ATP} channel

Two major advances in this field over the past 12 months have provided convincing evidence that the hypothetical model outlined above does indeed provide the cornerstone to our understanding the regulation of insulin secretion. First, the molecular architecture of the \(\beta\)-cell K\textsubscript{ATP} channel has been partially resolved, and secondly studies of a rare neonatal disorder have revealed that uncontrolled hypersecretion of insulin occurs in association with the absence of functional K\textsubscript{ATP} channels.

Molecular clues suggest that K\textsubscript{ATP} channels are composed of at least two subunits. One subunit is a member of the family of inward rectifier / ATP-sensitive K\textsuperscript{+} channel pore proteins, K\textsubscript{IR}6.2, also termed BIR ("\(\beta\)-cell inward rectifier"). The other subunit is a larger protein - the high affinity receptor for sulphonylureas (SUR1). SUR1 is composed of 1632 amino acids, and like the cystic fibrosis transmembrane conductance regulator (CFTR) it is a member of a superfamily of ATP binding cassette (ABC) proteins all of which have two nucleotide binding folds, Fig 2. Neither K\textsubscript{IR}6.2 nor SUR1 appear to conduct potassium ions alone, but when co-expressed will generate ion channel currents very similar to the native channel. SUR1 also appears to control the major regulatory and pharmacological properties of the channel complex. The genes that encode SUR1 and K\textsubscript{IR}6.2 are found in humans on the short-arm of chromosome 11, at a locus that is associated with familial forms of so called persistent hyperinsulinaemic hypoglycaemia of infancy (PHHI). We now believe that defects in the SUR1 gene in these patients cause loss of functional K\textsubscript{ATP} channels.

Persistent hyperinsulinaemic hypoglycaemia of infancy

Hypoglycaemia is a common metabolic abnormality seen in childhood, and when this is persistent or recurrent, it is frequently a consequence of hyperinsulinism; PHHI. The pathophysiology of PHHI is incompletely
understood, although a defect in the pancreatic β-cell’s stimulus-response coupling events was first being alluded to in the 1980s. In recent months we have shown this to be a consequence of an absence of functional β-cell ATP-sensitive potassium channels. The condition is thought to be rare in the UK, but the incidence of PHHI in communities with high rates of consanguinity, approaches that of cystic fibrosis, i.e. approximately 1/2,500 live births. PHHI has a variable clinical phenotype, usually presenting within the first few hours/days of birth as severe and maintained hypoglycaemia due to unregulated hypersecretion of insulin. Failure to recognize and treat the hypoglycaemia promptly and adequately carries a substantial risk of severe brain damage because of a lack of alternative fuels to sustain brain metabolism. Medical therapy for the disorder involves increased carbohydrate intake to meet the elevated requirement, and usually one or more drugs which inhibit insulin secretion. One such agent is diazoxide, which was first introduced to treat hyperinsulinism in the 1960s. Diazoxide is a specific agonist of the K_{ATP} channel, and tends to hyperpolarize the β-cell membrane potential and eliminate voltage-dependent Ca^{2+} influx in normal β-cells. However, the responsiveness of children with PHHI to diazoxide is highly variable from extreme sensitivity through to total drug resistance, and patients who do not show adequate responses to diazoxide (alone or in combination with other compounds) usually require a subtotal pancreatectomy to prevent recurrent hypoglycaemia. The variability in sensitivity to diazoxide has until now been unexplained, but is probably related to the absence of K_{ATP} channels.

**Altered ionic control of the β-cell membrane potential**

One consequence of the loss of ATP-sensitive K^{+} channels in neonatal hyperinsulinism will be that PHHI β-cells no longer effectively control their cell membrane potential and this will result in spontaneously electrically active cells. Electrophysiological recordings of isolated cells reveal that they are persistently firing action potentials, and it is this hyperactivity of Ca^{2+} channels, resulting from the K_{ATP} channel defect, that we now believe to account for the unregulated secretion of insulin. Since voltage-gated Ca^{2+} channels in β-cells can be inhibited by nifedipine and verapamil we proposed that these compounds may be of therapeutic value in alleviating the symptoms of hypersecretion, and as a result of our close collaboration with the Great Ormond Street Hospital for Sick Children, London we recently showed that hypersecretion of insulin in a PHHI patient can be successfully treated in vivo with nifedipine.

This type of study reveals how important lessons in biomedical science can be learned from attempting to understand the pathogenesis of rare diseases. From a clinical perspective we have now begun to unravel one of the key subcellular defects associated with insulin-secreting cell pathophysiology. We have shown how K_{ATP} channel defects are causally related to alterations in the control of insulin release from β-cells, and our efforts to date have already alluded to a novel approach in the clinical management of the condition. Finally, in the wider context, these studies have placed more emphasis upon what we understand to be important for the control of insulin secretion under normal conditions; reaffirming the consensus opinion of the role and regulation of ion channels, particularly the K_{ATP} channel, in stimulus-secretion coupling mechanisms.

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**Recommended further reading:**


A ROLE FOR ENDOTHELINS AS NEUROMODULATORS IN THE CENTRAL NERVOUS SYSTEM

Introduction

The discovery of the existence of the vasoconstrictor peptides of the endothelin family in the mid- to late eighties, led to a great deal of excitement over their potential role in cardiovascular homeostasis and their possible therapeutic potential. The isolation, purification and sequencing of the endothelins (ETs) has since allowed the development of both peptide and non-peptide antagonists selective for the endothelin-A (ET-A) and -B (ET-B) receptors, which have also been cloned.

It was clear from early studies that the distribution of ETs and their binding sites are not confined solely to the cardiovascular system. Significant levels of radiolabelled ET binding were discovered in kidney, lung, adrenal gland and intestine. High levels of ET binding were also observed in the central nervous system. This suggested that, in addition to their actions to contract vascular smooth muscle, ETs might have other physiological functions. In particular, the notion that ETs might act as neurotransmitters or neuromodulators in the central nervous system has led to interest over their possible roles in the pathology of neurological disorders such as Alzheimer's disease.

Distribution of ET and ET receptors in the CNS

Localisation of ET immunoreactivity in human brain indicates a widespread, but diffuse, distribution of the peptide in neurones. Highest levels were found in the hypothalamus, with pyramidal neurones in the CA3 region of the hippocampus and neuronal processes in the temporal cortex also showing ET immunoreactivity.

Autoradiographic localisation of [125I]ET-1 binding sites in rat brain indicate high ET receptor concentrations in a number of brain regions, particularly the hippocampus, hypothalamus and the granule layer of the cerebellum. Many cultured neurones also possess binding sites for ETs, in particular primary cultures of cerebellar granule neurones. These cells possess both ET-A and ET-B receptors, relative levels of which alter with time in culture.

Second messenger pathways coupling to ET receptors

The ET receptors are members of the rhodopsin superfamily of G-protein coupled receptors, having seven putative membrane spanning regions with an extracellular NH₂-terminal domain and intracellular COOH-terminal domain. They are believed to couple to phospholipase C resulting in production of IP₃. IP₃ can then act to release Ca²⁺ from intracellular stores. ET receptor activation also causes the opening of receptor operated channels (ROC) in the cell membrane that allow influx of Ca²⁺ from the extracellular medium. This causes depolarisation of the cell which opens voltage sensitive calcium channels (VSCC). Ca²⁺, entering the cells by ROCs and VSCCs can also stimulate release of Ca²⁺ from intracellular stores. A third pathway couples to VSCCs, increasing the probability that they will open in response to depolarisation.
inositol 1,4,5-trisphosphate (IP$_3$) and diacylglycerol. In vascular smooth muscle activation of both ET-A and ET-B receptors results in increased Ca$^{2+}$ influx and release of Ca$^{2+}$ from intracellular stores by a variety of pathways, some of which remain to be characterised (Fig 1). In cells with a neuronal phenotype activation of ET receptors also results in a rise in intracellular Ca$^{2+}$, again due partly to release from intracellular stores and partly to influx of Ca$^{2+}$ from the extracellular medium. In some neuronal cell types however, the release of Ca$^{2+}$ from intracellular stores is entirely dependent on the presence of Ca$^{2+}$ in the extracellular medium and may not be dependent on IP$_3$ production. It may, therefore, be dangerous to assume that the second messenger pathways activated by ETs in central neurones are the same as those activated by ETs in smooth muscle cells.

**Functional effects of ET receptor activation in CNS neurones**

ETs appear to have important roles in modulating the normal function of central neurones. They cause release of vasopressin and substance P from hypothalamic slices and release of a wide range of hormones from both the anterior and posterior lobes of the pituitary. ETs can also cause the release of neurotransmitters from neurones of the central nervous system. The application of ETs to striatal slices or cultured rat cerebellar granule neurones evokes the release of dopamine and aspartate respectively. Thus it has become apparent that ETs have an important role to play in altering neuronal function.

The mechanisms by which ETs alter neuronal

![Fig 2. Effect of ET-1 on Ca$^{2+}$ channel currents in cultured rat cerebellar granule neurones](image)

A. Calcium channel currents recorded from a cell-attached patch on the soma of a granule neurone. Application of ET-1 to the bath causes a reduction in channel opening frequency with no effect on mean open time.

B. Averaged currents from the same cell-attached patch. In the presence of ET-1 the Ca$^{2+}$ current was reduced by more than 90%.

C. ET-1 did not alter the intracellular Ca$^{2+}$ concentration in cells bathed in the same solution used for cell-attached recording. Cells were loaded with fura-2 for fluorescent measurement of intracellular Ca$^{2+}$ levels and traces from 8 different somata are shown. ET-1 was added at the arrow.
function are not fully understood at present. While it is clear that a rise in intracellular Ca^{2+} may underlie many of the effects of ETs, the exact means by which this rise occurs varies between cell types. The dependence of release from intracellular stores on influx of external Ca^{2+} in some cell types, suggests that IP_{3}-dependent release may not be as important as activation of Ca^{2+} conducting pathways in the cell membrane. Since it has been reported that ETs can cause prolongation of L-type Ca^{2+} channel openings in vascular smooth muscle to promote Ca^{2+} influx, it might be expected that they would do the same in central neurones.

However, this is not the case. Fig 2A shows the effect of ET-1 on Ca^{2+} channel currents recorded from a cell-attached patch in cultured rat cerebellar granule neurones. ET-1 has no effect on the duration of channel openings in these cells. The main effect of ET-1 on these channels appears to be a prolongation of the closed duration of the channels, which results in a decreased probability that the channels will open in response to depolarisation. The overall effect is one of inhibition rather than augmentation of Ca^{2+} influx through these channels, as is shown by the current averages in Fig 2B. This effect is mediated by ET-A receptors. It is not due to a rise in intracellular Ca^{2+} directly inhibiting the channels since Ca^{2+} is absent from the extracellular medium. In the absence of extracellular Ca^{2+} a rise in intracellular Ca^{2+} does not occur in these cells (Fig 2C). Neither is the inhibition due to G-proteins directly inhibiting the Ca^{2+} channels, although, a cytosolic second messenger pathway is probably involved. The interaction of ETs with voltage-sensitive Ca^{2+} channels in these cells therefore appears to be very different to that in smooth muscle cells (Fig 3).

In summary, there is increasing evidence which points towards an important role for ETs in modulating the function of neurones in the CNS. However, there may be substantial differences in the signalling pathways utilised and/or the effects of activating these pathways between smooth muscle cells (where ETs were first shown to act), and central neurones.

Further reading


It was with the establishment of Medical Research Council (MRC) in 1920, that the UK developed a structure that enabled physiological research to be actively encouraged and pursued nation-wide. The MRC was originally set-up to implement the National Insurance Act of 1911 which stated that a penny per annum per head of the insured population would be allocated to research. Its principal objective was to “advance knowledge so as to improve physical and mental health and develop the biomedical sciences as such, to maintain a fundamental capacity for research and to support higher education”. To this end, the Council runs two large institutes and a number of other establishments located within university departments, medical schools and hospitals and supports project grants, fellowships, and studentships. In 1978, the MRC budget was £62 million and currently stands at £260 million.

The Thatcherite Era

However, during the Thatcherite era of the late 70’s and 80’s, the source and structure of research funding began to change. The government urged scientists to forge greater links with industry (particularly the pharmaceutical and chemical industries) and the charitable sector. This was probably an attempt to focus research efforts into the development of technology which could eventually be translated into increased economic wealth.

Figures from the Association of Medical Research Charities (AMRC) show that industry now funds well over 50% of all health-related research with the charitable sector (combined income of £360 million in 1994/95) out-funding the MRC. Whilst this shift has benefited certain aspects of research, it is becoming increasingly obvious that the private sector is being asked to compensate for the reduction in government expenditure in research and development, which has fallen by £1 billion a year over the last decade, and set to fall by a further £400 million in the next 4 years. Furthermore, university funding has continued to decline annually and this year saw a 5% overall cut in grants amounting to ~£150 million. These latter cuts will particularly burden the charitable sector who are under ever increasing pressure to fund university and hospital infrastructural grants to support the provision of major equipment, maintenance of buildings and essential support staff. It is also somewhat alarming to note that 40% of all staff in universities are now on short term contracts funded largely from outside sources compared to only 20% 10 years ago.

The Wellcome Trust has unquestionably cushioned biomedical research against some of the worst cuts, funding over 3000 people (including many support staff) in research and investing a substantial amount in the refurbishment of laboratories, particularly in universities. This huge financial commitment has only been possible through investment of money raised from the sales of its shares in Wellcome plc, which gave the Trust an income of £340 million in 1995. I believe this money, along with substantial funds from charities like Imperial Cancer Research (£48 million) and the British Heart Foundation (£31 million), has proved essential in maintaining our momentum and competitiveness in medical-related research abroad. However, obtaining funds from the charitable sector will become increasingly more competitive, in a climate where the MRC turns “alpha-rated” projects and the pharmaceutical industries are now significantly reducing...
spending on research and development. Furthermore, the extra money that the government made available after the 1993 White Paper on Science and Technology, has been skimmed off existing research council budgets and shifted to joint ventures with industry.

The National Lottery - a “double whammy” for medical research

Biomedical research in the UK is likely to suffer in more ways than one from the National Lottery. In the first four months of this year, charities say they have lost approximately £70 million, and it will be virtually impossible for them to recoup this money from the lottery due to strict criteria imposed by the National Lottery Charities Board (NLCB). However, it is hard at this stage to determine exactly what the long term effect will be, since the Lottery has only been in existence for just under two years. There is however, a general feeling that the Lottery will continue to siphon off donations from those charities who have little legacy funding and who therefore rely heavily on public donations. The hardest hit appears to be the cancer charities; one in particular lost a great deal of money when it was forced to abolish its scratchcard game because of falling demand after the Lottery was introduced. Despite this, the total annual research budget of the AMRC is still rising, although one should bare in mind that the average cost of a project grant has nearly doubled in the last five years.

After complaints by the research charities who were excluded from the first round of grants awarded by the NLCB, it was announced that grants in 1996/1997 will concentrate on health, disability and care. Thus, charities were optimistic of receiving a sizeable amount of the £150 million the NLCB will be responsible for distributing annually. However, it was recently conceded by Timothy Hornsby, chief executive of the NLCB, that medical research would face fundamental barriers in securing support, not least because the Board’s primary aim is to “make an impact on the lives of people suffering poverty, disadvantage and discrimination”. This will mean that applications will have to target people in these groups. It seems ironic that such a policy will discriminate against a large fraction of medical research which seeks to understand the fundamentals of physiology and to develop medical technology. Such research may take years to have an impact clinically, and yet nonetheless, offers vital hope to eventually curing certain types of life-threatening or disabling diseases. If one does however, manage to succeed in meeting the initial criteria, then the application must first be peer reviewed by the appropriate charity, receive an alpha rating, but even then only one application per charity will be accepted by the NLCB. Thus, whilst the majority of the public wants medical research to be supported by the Lottery, legislation will largely prohibit applications unless it primarily targets small sections of the community and is from an organization who has not yet attracted substantial funding.

Lucie Clapp
The Rayne Institute
St Thomas’ Hospital

T

The Wellcome Trust Prize

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A POSITIVE SCIENTIFIC EXPERIENCE IN WOODS HOLE, MA, USA.

This year I was fortunate enough to be invited, with Antony Galione, to the Marine Biological Laboratory (MBL) to teach the Ca\(^ {2+}\) and Signalling Section of the Summer Physiology Course at the Marine Biological Laboratory in Woods Hole, Massachusetts in the USA. Two summers ago I had been to the MBL as a student on the Neural Systems and Behaviour Course. Both courses were such positive experiences I wanted to bring the MBL and the summer courses to the attention of young physiologists in Britain.

The MBL is an independent non-profit making research and educational institution and was founded in 1888, so in American terms it has a rich tradition. Since 1888 it has been a “mecca” for scientists in the summer largely because it provides an excellent opportunity to use the diverse marine organisms from the rich waters of Cape Cod as models for understanding fundamental aspects of biology. The summer courses are a major part of life at the MBL although a smaller scientific community exists there all the year round. A number of the long summer courses are of interest to physiologists:

- Embryology: Cell differentiation and gene expression in early development
- Neural systems and Behaviour Neurobiology
- Physiology: Cellular and Molecular Cell Biology

In addition there are a number of short courses including imaging techniques, computational neuroscience, vision research and rapid electrochemical measurements.

The longer courses tend to last from 6-8 weeks. Physiology lasts for 6 weeks and then a proportion of the students have the opportunity to stay and do some post-course research on some aspect that they have found particularly interesting. Six weeks seems a long time but because of the pace of the Course time goes very quickly; the course is intense in true American style but no less enjoyable for that. As both a student and a faculty member I found it a very refreshing approach and thoroughly enjoyed the openness and enthusiasm that epitomises science at the MBL. In addition to long days spent in the lab (15 hours is not unusual) there is plenty of opportunity to learn from a wide diversity of seminars and talks that are also going on at the MBL. The science taught on the Courses uses marine organisms as much as possible and the Physiology Course tee-shirt is testimony to this. Tee shirts are a tradition of all the courses at the MBL and are usually thought up and designed in a couple of hours before the deadline of getting them to the printers!

Student section

Students are selected on very different bases, often depending upon the course. In Physiology the students tend to be relatively young graduate students (eg in their second or third year - in the States this means that following their lab rotations they have decided on a lab in which to do their Ph.D) although several were nearing or had just completed their Ph.D. In addition the courses are excellent value for students who have not specialised in a physiological science before and on this years course there were 2 mechanical engineers and 1 aeronautical engineer. None of them knew how to use a Gilson pipettman at the start of the course and so all enjoyed a very steep learning curve! However knowledge is not that important; the course is there to teach and one thing that the students had in common was their enthusiasm most often coupled with intelligence, creativity and the ability to work hard. This makes the teaching both easy and challenging!

Learning a wide variety of techniques

The subject base of the Physiology course is really cell biology in the broadest sense. Students learn a wide variety of techniques such as protein and nucleic acid purification, cell and organelle fractionation and become expert in their use of advanced light microscopy (including a number of different confocal microscopes) to study the actions of these proteins in vivo. A large feature of the course is the understanding of the cell cycle, something I found as a neurophysiologist quite enlightening! In the Ca\(^ {2+}\) and Cell Signalling section this year the students used fluorescence video microscopy on sea urchin eggs to study...
The 1996 Physiology Course T-Shirt

FRONT

BACK

Protocol for the MBL Physiology Course

1. Dounce homogenise brains in sea water (Woods Hole, MA)
2. Every morning, incubate in an alternating light dark cycle in Lillie Auditorium for 60 min ± 2 hours ... nap frequently
3. Macroject 10 X Caffeine
4. Add glucose - PASTRIES AND COOKIES
5. Spin at high speed to remove cytoskeletal and membrane components
6. Add Big Daddy Moose (Big Daddy Moose)
7. Add SWOPE ATP regenerating system 3 times daily (the morning application may be skipped)
8. Triturate in Xs ice cold beer, kindly provided by Captain Kidd
9. At 3am transfer into 55C water bath at Stony Beach
10. Allow 1 picosecond sleep

Ca²⁺ signalling events at fertilisation as well as membrane events by actually recording from the eggs (eggs are surprisingly excitable cells). To complement the physiology they also used sea urchin egg homogenates to look more closely in vitro at mechanisms of Ca²⁺ mobilisation. All this and time for mini-projects in 9 days!

As a scientific experience the courses at the MBL are second to none. If you feel that you have the drive and enthusiasm to participate it will provide you not only with new techniques and knowledge but also with contacts and friends in the US. As far as funding goes, if you are accepted on a course then a number of grants are made available to you to pay the tuition fees; it is then up to you to find money to pay for the flight and the accommodation (which is quite frugal but cheap). I was fortunate enough to obtain a generous grant from the Dale and Rushton Fund in 1994 which went part way towards the cost. It is indeed a privilege to study at the MBL and presents a great opportunity. If your appetite has been whetted by this small introduction you can find out more by browsing the MBL web page or by writing directly for a Prospectus. Closing dates for applications are in March.

http://www.mbl.edu

The Marine Biological Laboratory
7 MBL Street
Woods Hole
MA 02543-1015

Ruth Einson
Dept of Pharmacology
University of Oxford
Dear Editor,

I am working on an annotated edition of the poems of the late Professor Sir William Empson, for publication in the Penguin English Poets series, and would be most grateful if any of your readers can enlighten me with points of reference or clarification in respect of two cruces that leave me quite baffled.

The first, which seems to refer to an experiment in transfusion (or perhaps perfusion?), features in one of Empson's best-known poems 'Missing Dates':

They bled an old dog dry yet
the exchange rills
Of young dog blood gave
but a mouth's desires

That couplet appears to refer to an experiment in which an old dog was given a transfusion with the blood of a young dog, but that the process unhappily revived the old dog's (sexual? carnal?) appetite for no more than a month. Indeed, it is perhaps meaningless, though I may be incorrect in my layman's understanding that a blood transfusion either works within half an hour or so or else it doesn't work at all? (Of course, it is also quite possible that I am misconstruing the verses.) However, Empson in his own note to the poem stated, 'It is true about the old dog, or at least I saw it reported somewhere'. The poem was published in 1937, and I believe he must certainly have read such a report (he may misremember it but he wouldn't make it up), in a newspaper or more probably in a scientific journal of the time. (He had been acquainted with J B S Haldane since 1929, and took a lively interest in all the sciences.)

The other crux features in a poem called 'Invitation to Juno' (as the title implies, it is a wooing poem and concerns the mating, twinning or correlating of unlikely partners), which was first published in the Cambridge Review in May 1928:

Courage. Weren't strips of
heart culture seen
Of late mating two periodicities?
I would greatly appreciate any information or suggestion about these cruces.

John Haffenden
Professor of English Literature
University of Sheffield
Sheffield
S10 2TD

Dear Editor

Following the symposium held last year in Edinburgh to mark the 150th anniversary of the first identification of the disease leukaemia by John Hughes Bennett (1812-1875), I am being encouraged to write the biography of Bennett.

Initial research has revealed how little has been written on Bennett's life and his considerable achievements as a leading Edinburgh physician, physiologist and teacher of the last century and, indeed, how much of what did appear was based more on conjecture than fact. Bennett's reputation in France and the USA was equally high and he was one of the very few British authors of the period whose work was translated into Japanese.

I have made reasonable progress on tracing his family history, although latterly this has been somewhat hindered by the fact that Bennett left four daughters and his only son, a physician, died a bachelor. I have also been able to study some of Bennett's papers, and a number of physiologists who recall working to the John Hughes Bennett Laboratory established in 1901 for experimental physiology have kindly shared their memories with me. I wonder if any readers have particular information on Bennett and his work, or any Bennett memorabilia, or copies of textbooks written by him. If so, I would be delighted to hear from them.

Gordon Piller
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A DECISION IN THE LIFE OF......

Andrew Nicoll has decided to leave research and academia and go into school teaching. In this article he outlines what he thinks is good about British science, but why he made the decision to leave it.

I am a fixed term lecturer in physiology at Bristol University and have decided to leave my post in January to become a school teacher. In this article I would like to explain the reason behind my decision but at the same time to consider what I think are the good points about British science. In a recent article in The Physiological Society Magazine (No. 23, Summer 1996) Andy Randall described his experiences of returning to UK science. I do not share all of his often unfavourable comparisons between British and American science. In my view Britain is, in many ways, a rather good country in which to do research and the problems we currently face are also being experienced in other countries. For me it has sadly been the obstacles which have outweighed the benefits of science in the UK.

UK versus USA

- The general scientific environment. The atmosphere in the average British science department seems to me to be co-operative, democratic and social. Although I personally had good experiences in the American laboratory in which I worked, it is not difficult to find unhealthy competition between postdoctoral research assistants within scientific groups in the States. I have yet to come across one academic department in an American university with a common room!

- Funding. Funding is tight, but the amount of money per head of research worker in the USA is not orders of magnitude greater than here and is presently declining. The UK produces more scientific papers per unit funding than any other country, and the Wellcome Trust is the biggest medical charity in the world (larger than the US Howard Hughes). I worked in an Ivy League university neuroscience department as a postdoctoral assistant, where the roof leaked every time it rained and the department did not posses any specialist electronics technicians or a mechanical workshop.

- Career conditions. It is true that most senior American academics are better paid than their British counterparts, but in my experience at the junior end of the scale, things are not necessarily better on the other side of the Atlantic. At the postdoctoral/junior academic level, the salary to cost of living ratio is not particularly favourable in many parts of the USA: and you can forget getting a credit card or buying a house as a foreigner in America! In the UK, we have more five/tien year fellowship schemes than in the USA and more is done here to encourage junior researchers to obtain their own grants. At the senior end, of the Ivy League universities only Brown and Harvard pay tenured staff a full salary, and “professors” in most of those institutions have to find large chunks of their salaries from external grant income. At some universities, up to eighty percent of an individual academic’s salary is derived from external funding.

Areas of concern

Having said all of the above, there are obviously difficulties here in Britain, especially the current low success rate in obtaining project grants. With the exception of the organisation of teaching (see below), many of our problems are also found in the USA:

- Structural imbalances. As in the USA, only a minority of grant applications are funded in the UK, and this is only partly a result of lack of funds owing to this country’s large social security and defence bills. The Research Assessment Exercise has increased grant “demand” too. Every lecturer in our...
eighty plus universities now wants to be armed with project grants and a platoon of postdoctoral workers; every Head wants his/her department to be equipped with programme grants and armed with a battalion of research fellows. Hence there has never been a better time to find a postdoctoral appointment, either here or in the States. However, the structural consequences of this are obvious: too many scientists being supported by insufficient grant money and being trained for jobs which will not be there later on in a career. I think I am correct in saying that only one in seven postdoctoral workers in biomedical sciences in Britain will eventually take up a lectureship, a similar number to that in the USA. A system in which everyone has a laboratory with five postdoctoral workers for every PhD student is clearly unstable and represents, without more secure long term prospects, a misuse of the temporary staff concerned.

Short termism. One of the hallmarks of British science was always our willingness to undertake good quality work even if it does not produce instant rewards. This potential is being undermined by two trends: the first is the need to produce quick publications whether or not the problem is solved, and the second is the notion that a project cannot be properly conceived unless it is testing a hypothesis. The potential negative effects on research of this approach have been overlooked in my opinion. Obviously, anyone can frame a grant application in terms of a hypothesis if they so wished, but by its very nature, science is open ended and many areas of study are not suitable to be hypothesis driven. In my own field (cortical circuitry), I cannot “test” the “function” of, say, strong superficial layer inhibition but I can say with certainty that we will not understand the brain unless we record from its cells! I also detect an even worse trait among reviewers of papers and grants: bandwagonism. Unless you are using molecular biology, laser photostimulation, infrared microscopy and triple whole cell patch recording (or whatever else is fashionable), then you must be asking the wrong question!

Teaching. As we all know, the staff/student ratio is declining in British universities, approaching that in US and Australian universities. We cannot go on teaching students in the way we have done so up to now (regrettably). It is no longer justifiable to give individual student tutorials or have twenty academics spending hours agonising over degree classifications, especially when the average graduate is going to get a job as an accountant or stock broker. There must also, in future, be academics who concentrate on research and those who concentrate on teaching, but this will only be achieved when teaching lecturers are not regarded as second class citizens. The Americans woke up to these facts many years ago: contact time for academics in my present department average 130 hours a year plus a hefty load of administration. My former supervisor in America felt hard done by with comparatively light administrative duties and only fifty student contact hours.

An offer I could not refuse

I completed my D.Phil in 1992, went to work in the USA for a year and I will have been in Bristol three years by the time I leave. Since being here, I have been awarded two out of the three project grants for which I have applied and I have also undertaken what I hope has been regarded as a fair share of teaching and administration in the department. I have decided to finish two years before the end of my contract because I do not feel I can compete long term in the present research market and do not feel that any of my teaching efforts will
ultimately benefit my career. There seem to be too many good people in their late thirties struggling to find permanent appointments and in present circumstances, I do not foresee the much expected large number of vacancies becoming available when the "bulge" of academics appointed in the 1960s begins to retire. Under the present academic regime, the current fashion of making so-called proleptic lectureship appointments, while understandable, is rather short sighted and potentially damaging to academic departments. A most stressful part of a lectureship is the constant sense of under achievement, whether that be from sweating over the outcome of (probably ultimately unsuccessful) grant applications or sitting in pointless committee meetings re-inventing the wheel with "exciting" teaching ventures. In short, there seems to be so little reward for the effort one has to put into the job. My new post teaching biology involves three hundred contact hours per year, few extracurricular activities and offers a significantly greater salary, a permanent contract and "real" Summer holidays. My new school is largely boarding, and as they are giving me a house to live in as well, it was an offer I could not refuse.

Obviously, I would have preferred to stay in higher education (HE), but post-16 education in the UK is changing and I hope my move into school teaching will not necessarily be a one-way jump. With universities offering access courses and schools going into college level certificate teaching, I think the boundaries between school and university teaching responsibilities are becoming blurred. What is more or less certain is that whoever wins the next election, the state funded higher education sector will not get significantly more money. This means that, unlike the salaries of MPs, academics will not get a 30% pay rise to bring them back to 1970s levels. Hence, improvement in conditions in HE will have to be brought about by changes the structure of research and teaching in the UK. I therefore leave HE with mixed feelings. Teaching the Tiffanys and Jamies of this world will be, as they say, a challenge, but the aims and execution of the job are clearly defined and therefore I hope the results will ultimately be more rewarding.

Andrew Nicoll
Department of Physiology
University of Bristol

Researchers try crystal ball gazing to predict future

A team of futurologists put together by British Telecom has tried to predict when artificial hearts, livers, and kidneys will come into clinical use. It estimates that there will be an artificial pancreas by 1998; artificial blood by the year 2000; and artificial heart by 2010; and the individual’s genome will be part of their medical record by 2015.

BMJ 313 21 September 1996 p.706

Source: SPIN

Research ‘golden egg’

Tim Radford, Science Editor, states that leading scientists have warned the Government that “ignorant and insensitive” plans to manage university research on business lines “would kill a goose that was still laying golden eggs.”

Guardian 10 September 1996 p.9

Source: SPIN
I remember standing near the passenger arrivals exit at San Francisco airport, on August 30th 1982. I had several problems, but the most pressing was very practical: I had two suitcases, each weighing 70 lb (Continental Airlines allowed that much in those days). I needed some US change in order to borrow a trolley, and the nearest foreign exchange booth was miles away, farther than I could carry my bags. I had heard about America, and knew my bags would probably be pinched immediately, or detonated by the bomb squad, if I left them unattended to get the change.

The trouble was, this was the least of my problems.... I had just left a promising medical career and my wife to be, in London, in order to embark on a research plan which was uncertain to say the least, and clearly foolhardy in the opinion of several of the experts I had consulted. With great ingenuity, I managed to solve the immediate problem. Within suitcase carrying distance was a car rental booth. Instead of taking the bus to Berkeley, where I was to start a Master’s degree in Biophysics at the ripe old age of 29, I rented a car. This way I had an easier ride and retained possession of my worldly goods for the outset of my research career; on the other hand, it did cost more. This seemed like an omen; there were clearly going to be numerous obstacles, but I hoped that optimism and initiative would always be able to overcome them.

Required - a technique for imaging neuronal depolarization

It mainly started with Colin Blakemore and Joe Herbert in 1973, who captivated many of my year of medical students at Cambridge with their lectures on the CNS. A year later, during Physiology Part II, John Robson intrigued us with lectures on how the CNS coded information. I felt that I could think of no better career than to research into information processing in the CNS. Later, as a clinical student at UCH, this was realized in concrete form. It seemed to me that there was a gulf in neuroscience between the behavioural sciences and cellular physiology - it was not known how information was moved around the CNS, and in what form. The reason appeared to be that no suitable measurement technique was available; what was needed was a medical imaging device that could image neuronal depolarization (either as action potentials in white matter, or synaptic graded depolarizations) with a time course of milliseconds, and a spatial resolution of a few cubic mm. CT scanners were just coming into clinical use at that time; my idea was to try and develop a device which used similar image reconstruction procedures, but was a thousand times faster and produced images of brain activity.

In my second year at Berkeley, I sat in the library, and attempted to analyze every appropriate technique I could find. Somewhat to my surprise, two techniques did appear to be suitable in principle - Electron Spin Resonance and Electrical Impedance measurement (Holder, 1989); the latter has been the focus of my efforts since, because the technology is more advanced. Of course, Positron Emission Tomography (PET) and now functional Magnetic Resonance Imaging can produce good images of brain function, but this is of metabolic recovery processes such as blood flow or glucose utilization, which occur with a time course of tens of seconds. They do not give any information about the electrical activity over milliseconds, which is presumably the immediate substrate of brain function. The idea was: electrical impedance across neuronal membranes is well known to change during activity, due to the opening of ion channels. It must therefore also change across volumes of tissue during activity when measured with external electrodes. This could, in principle, be reconstructed into tomographic images, as images of impedance can be produced by a method similar to X-ray CT. The unknown factor was whether the impedance changes resulting from depolarization would be large enough to yield scientifically useful images.

How it works

Electrical Impedance Tomography (EIT) works by making multiple measurements from a ring of electrodes placed around the body part of interest. Many such measurements are made rapidly from differing electrode combinations, which are then processed rapidly on a PC to produce a single tomographic “slice” image through the plane of the electrodes. The advantages of EIT are that it is fast, completely safe (as far as is known at present), inexpensive and portable (Holder, 1993). The first commercially available prototype, called the “Sheffield Mark 1”, produced images at up to 24 per second, using an applied current of 5
mA or less at 50 kHz, cost about £15,000, and comprised a box about the size of a video recorder attached to a PC (Fig 1). There has been burgeoning interest in the method: about thirty groups world-wide are now working actively in developing new systems. Almost all are based in medical physics or engineering departments. It has been used to image pulmonary ventilation and perfusion, the heart beating, gastric emptying, and, more recently, lung water, but has not yet found a widespread clinical use. The main problems are a relatively poor spatial resolution of about 15% of the electrode ring diameter (with 16 electrodes), and a wandering baseline.

![Fig 1. The Sheffield Mark 1 EIT system being used to image lung function. Images were collected from either the upper or lower ring of electrodes.](image)

### Developing EIT systems for imaging the brain

On return from Berkeley, I decided to try and combine the development of EIT systems for this purpose with a career in clinical neurophysiology. Following two years as a registrar in Neurology, I moved to the Physiology Department at UCL in 1986, and have remained here since, maintaining various concomitant degrees of clinical activity. I now spend about half my time performing hospital work in Clinical Neurophysiology.

It became rapidly apparent that imaging in the head had particular problems, for which no existing device was suitable. The major difficulty is that the skull presents an obstacle to current flow. I have now built up a group of 6 or so medical physicists, clinicians and engineers, and we have solved most of these problems, at least in saline-filled tank simulations. For example, we can image cranial contents using scalp electrodes, by injecting current through diametrically opposed electrodes. This reduces spatial resolution, but this can be restored by using more electrodes - we now use 64. We now have two newly designed systems, ready for clinical trials in human subjects. From a physiological point of view, I elected, as a first step, to image the relatively large and long-lasting impedance changes which occur in the brain during events such as stroke or epilepsy, due to cell swelling during anoxic depolarization, or accompanying blood flow and temperature changes. We have therefore produced the first EIT images of cerebral ischaemia, spreading depression (Boone et al, 1994, Fig 2), visual and sensory evoked responses (Rao et al, 1996, Fig. 3), and, recently, epilepsy (back cover), all in anaesthetized rats or rabbits with electrodes placed directly on the brain. These are in descending order of difficulty; during stroke, impedance changes by about 50% of the baseline value and this lasts tens of minutes, whilst those during evoked responses of epilepsy are a few per cent over a minute or two. Baseline variability in the images is, by contrast, about 1% over a few minutes.

**How far are we away from the final goal of imaging neuronal depolarization?**

The problem may be reduced to two simple numbers - the size of the impedance change during activity, and the sensitivity of the EIT machine. Our best estimate at present is that there is a gap of about two orders of magnitude. We have measured square wave impedance changes during evoked activity in crab nerve and brain. Whilst a healthy 1% or so in crab nerve, it is about 0.03% in brain during physiologically evoked responses, presumably because a lesser proportion of neurones are discharging and they are less synchronous (Boone, 1995). On the other hand, existing EIT systems have a baseline noise of about 1%. However, this is in existing systems which operate with applied frequencies of hundreds of Hz or more. In single channel prototype square wave impedance systems we have designed, the noise can be reduced to far less - about 0.01%, with averaging. Even if the device works, will it be scientifically useful? I think so: At the least, it could provide similar information to PET scans of brain activity, but be inexpensive and non-invasive and, furthermore, show the order in which different areas are activated. At the best, it could enable
Fig 2. Electrical impedance tomography (EIT) images collected every 15s during cortical spreading depression in the anaesthetised rabbit, using a ring of 16 electrodes placed on the superior surface of the exposed brain. The regions of brain affected by the spreading depression are shown diagrammatically above. Cell swelling during spreading depression causes an impedance increase, which is seen in the EIT images. The onset is correctly seen in the images; later spread is seen to occur with the correct time course, but the physics of the EIT system render it more sensitive to changes at the edge. (Boone K, Lewis AM and Holder DS (1994) Physiol Meas, 15, A189-A198).

mathematical analysis of the envelope waveforms of activity along white matter tracts or grey matter nuclei. With a resolution of a few cubic mm, it obviously could never address the cellular coding of information processing, but I think it could be of vital assistance in pointing to which areas were involved in different tasks, and which were abnormal in different disease states. It is not yet clear whether we will be able to overcome the technical difficulties and produce the “dream” machine. Our current position is that we are confident we can measure impedance changes during evoked activity in the brain, with electrodes placed directly on the brain; whether it will be possible with an imaging system with electrodes placed all over the scalp is still a formidable, but not necessarily intractable, problem.

Is this physiology?

From a personal point of view, this last decade has not been easy. It has not only been that the research is interdisciplinary - it covers clinical medicine, whole animal and cellular physiology, electrical engineering and mathematics. In fact, the bulk of the work over the past three years has been in developing new reconstruction algorithms and hardware, although the emphasis will revert to physiology once the new systems are working. The main difference is that this research is “top down” (i.e. there is a clear application, and the various sciences covered serve as a means to an end), in contrast to the “bottom-up” investigative approach of almost all of my physiological colleagues.

Fig 3. Example of EIT images recorded during binocular photic stimulation. Stimulation was carried out over 2.5 minutes (indicated by the line) at 10 Hz. Images were recorded every 30 seconds. Orientation: Up = anterior, left=right as shown. The principal impedance decrease of 2.5% is over the occipital cortex.
As a result, my efforts seem to sit uncomfortably within any of the traditional disciplines in the life sciences or medical physics. It feels like I have had to divert a lot of energy in establishing a physical base, creating new equipment from scratch, and setting up an interdisciplinary group. On the other hand, the novelty of the ideas appears to have made funding the least of the problems - I have been generously supported by the MRC, first as a training fellow and, latterly, with project grants, and by the Royal Society under its magnificent University Research Fellow scheme, which gave me the medium term security to build up my group. Is it Physiology? My group is presently based in a department of Physiology, which, I believe, is the most appropriate base. With a medical/physiological training, I think that our principal advantage is the ability to define the application, and then refine the engineering design in the light of rigorous experiments in humans or physiological preparations. At present, whilst we are trying to develop the technology, this does not address any fundamental physiological issues, but it certainly requires some rigorous applied physiology in designing and running the experiments, and understanding the results.

Will it all been worth it?

I don’t know yet whether the ultimate goal will be achieved, but it seems very probable that, at least, lesser spin-offs will occur along the way. For example, there is a good chance that our EIT systems could be used as an early warning system for brain injury in neonates or to localize epileptic foci in severe epileptics prior to surgery. We have also made several technical contributions to EIT - for example, a new class of algorithm, and the pioneering of objective procedures for calibrating new multifrequency EIT systems using biological objects in fluid filled tanks. However, deep down, I feel that research should be like cricket: it is the playing, not the winning, that matters. As long as the question is worthwhile, the outcome should be useful, whether positive or negative, provided the work is technically satisfactory. Combination with a clinical career has meant a dilution of the time I have had been able to devote to acquiring the difficult skills for physiological research. On the other hand, the scientific compensations are the opportunity to be stimulated by real life problems in the patients, and the financial security to pursue difficult problems with an uncertain outcome. Would I do it all over again? - definitely, but next time I think I would pack lighter suitcases and take the bus ....

David Holder
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References:


SOFTWARE REVIEW

The Cardiovascular System

Andromeda Interactive, whose UK division is based in Abingdon, have launched a series of computer assisted learning programs supplied on CD rom which run on both Macintosh and PC machines and cover, in some detail, the anatomy, histology and physiology of the cardiovascular system. The investment in this product is considerable, and has involved the consultation of an impressive team of experts in the cardiovascular field. Consequently, the material, in its tangible and visible form, is not cheap in either sense of the word. The product can, at its simplest, run directly from the CD on a stand-alone machine, without eating up valuable hard disk space, or, licence permitting, sit on a network such as Windows NT.

I received three modules to review. The first, entitled Functional Anatomy of the Heart; the second Cellular Mechanisms in Cardiac Physiology, and the third; Cardiac Muscle Action and Blood Flow. The format of all three is based upon a menu-selected set of tutorials which are richly
A captured frame from part of the tutorial on arterial baroreceptors. The original is of course in full colour.

graphical voice annotated sequences which the user can move through and jump around. Seeing the graphics for the first time reminded me of my first exposure to Netter’s artwork in Gray’s Anatomy and Scientific American. The voice-overs, in clear-honed American, can also be viewed or printed as text, although it is best to listen as you watch, especially in the build up diagrams and animations. Some of the less interactive parts the tutorials feel as though they are being delivered via a broadcast-quality video with the user holding a remote control. Each topic can be followed in a logical progression by default, thanks to simple intuitive navigation controls, and it is also possible to set up a prescribed sequence of material, or to jump from topic to topic.

For obvious reasons I concentrated on modules 2 and 3 which cover the more physiological aspects of the cardiovascular system. Module 2 covers the basics of muscle contraction (and this area is useful for teaching the sliding filament concept as applied to skeletal muscle too), autonomic control, and control of blood pressure by nervous and renal mechanisms. As a lecturer and courseware developer in this area I was impressed by the attempt to cut through the confusing issues and yet still put over a coherent explanation of current thinking.

Module 3 deals with the basics of circulatory plumbing, and the relationships of pressure, flow and resistance, moving on to the electrical events in the heart and the cardiac cycle... an ever popular target for computer-animated courseware quickies. Here though, some of the best graphical animations of its type are to be found.

Each module comes with a quiz bank which links back to the taught material. There are also glossary files and reference lists linked to the material, as well as a separate disk of images that can be used for bona fide teaching purposes.

No product like this is going to be perfect. I found my attention repeatedly thrown every time I heard the American-accented voice say “glommy-ruler” in reference to that little capillary ball, and there were some minor hiccups in starting Module 1 on a PC (not a problem on the latest release).

This resource would work well in a library that offers facilities to run multimedia CDs. The material could also be used in guided teaching sessions of up to four people around a machine, or even in the lecture theatre, if the teacher is lucky enough to have the necessary projection resources at his disposal. I was not able to test the product over a network, although it can be used in this way subject to appropriate licence agreement, and a large reserve of disk space!

Free 30 day trial copies are offered by the manufacturer.

Andromeda Interactive Ltd are at 9-15 The Vineyard, Abingdon, Oxfordshire, OX14 3PX,
Tel: 01235 529595, Fax: 01235 559122,
email: medical@andromeda.co.uk, Web pages: http://www.andromeda.co.uk/medical.html

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The Students’ Perspective

Sixteen lucky participants from the UK, Poland, Australia and Germany gathered at the Plymouth Aquarium, home to the Marine Biological Association (MBA), to attend this year’s workshop which was organised by David Ogden from the National Institute for Medical Research, London, and Colin Brownlee, Deputy Director of the MBA in Plymouth. With the historic background of the squid giant axon work by Hodgkin and Huxley in the 1950s, Plymouth is ideally suited for these annual workshops.

Over a period of two weeks the course covered a wide range of currently used cell physiological techniques ranging from voltage clamp to more recent methods such as single cell RT-PCR and flash photolysis using preparations mainly from locally collected marine animals. The students were given the opportunity to work on a variety of experimental set-ups to gain ‘hands on’ experience. For the students to be taught by so many experts in their fields (students were outnumbered by teachers by approximately 2:1) is a rare and invaluable experience. For most of the teachers, the Plymouth Workshop has a firm place in their calendar and they have been coming for several years. The commitment of the teaching staff is the essence of the course and the wide ranging knowledge and experience was very much appreciated by all. Most research institutions cannot match the variety of techniques taught in Plymouth and therefore workshops such as this are important to allow young scientists to appreciate the scope of electrophysiological techniques available. After long hours in the lab, staff and students raised the profit of a local pub which is, conveniently situated between the Aquarium and the accommodation. Not even the weather gave any reason for complaint, apart from the permanent temptation to take the rigs outside. Unfortunately, due to a lack of portable power supplies, this was not possible.

The students would like to thank the organisers, teachers, companies and grant authorities for their support. They hope that many more generations of young researchers will be given the chance to widen their scientific horizons in Plymouth.

A Teacher’s Perspective

The advertisements for this year’s course went out in November 1995 with the characteristic squid-action potential motif, which was originally drawn by Barbara Fulton. The advertisements obviously work, as around 60 applicants apply each year for the sixteen places. This means that in May 1996 a number of people involved with the course had a difficult task assessing the applications and selecting students. This procedure is carried out in a secret location (near the old MI5 building in London) and involves much discussion until a consensus is reached.

Things then go quite for a few months until a few weeks before the course is due to start, when David Ogden gently reminds you of a commitment you made in a weak (relaxed) moment, to teach on the course, again or for the first time. Then a round of frantic phone calls ensue, organising equipment, people, accommodation and food. From a teachers point of view the course is split into two sections: The first “week”, involves arriving at the MBA to an empty room, a pile of boxes and the prospect of building three patch clamp, two single electrode voltage clamp (SEVC), a twin electrode voltage clamp (TEVC), one ion sensitive recording, one dye injection and one dual excitation fluorescent indicator set ups in three days (Details on these and other techniques will be found in the course book, Ogden, 1994). As you might imagine its not just the soldering ions that get hot! However, without fail the set-ups are ready for the first round of student practical workshops, the
Fig 1. Calcium (upper) and inward rectifier (lower) current traces recorded from ciona intestinalis gametes during this year’s workshop. Currents were recorded using single electrode voltage clamp. Calcium currents were evoked by depolarising voltage steps from -80 mV and inward rectifier currents were evoked by hyperpolarising steps from -50 mV.

students having already honed their skills at using microscopes and building electronic circuits.

The second “week” usually involves a fresh set of teachers who take over and run two more workshop rounds. Teaching on the second week means that you do not have to construct the set ups but it does involve packing up at the end. How we get everything back in the right boxes is surely evidence of telepathy! What all teachers on the course have to do, whatever week they are teaching, is go through a crash course on marine biology, as in the tradition of Hodgkin and Huxley we use marine (or at the very least invertebrate) preparations whenever possible. The gametes from ciona intestinalis (sea squirt) are used for SEVC, a ganglion from helix aspersa (garden snail) for TEVC, the patch clamps used dissociated alloteuthis subulata (squid) stellate ganglion cells and raja clabata (skate) cerebella slices. Astacus fluviatilis (crayfish) muscle are used for the ion selective electrode experiments and their swimmeret ganglion for the dye injection experiments. The only preparation that could be called “mammalian” are the PC12 cells which are used for intracellular calcium measurements.

As well as the “permanent” set-ups, a number of demonstrations occur throughout the course, including capacitance measurements of exocytosis and endocytosis, flash photolysis in squid skin and single cell RT-PCR. All the techniques and approaches are supported by lectures given by specialists in the field.

Although teaching on the course can be as much of a test for the teachers as the students, the fact that many teachers come back year after year is due the great satisfaction we get from seeing the students succeed as well as the help and support we are priviliged to from the members of the MBA.

Thanks to all the students, teachers, MBA staff, companies and funding bodies who make this annual event possible. In particular, I am grateful to Peter Appenrodt, Brigitte Held, Alastair Miller and Amanda Smith for their contributions to this article.

For information on next year’s course contact: Dr. D. Ogden, NIMR, The Ridgeway, Mill Hill, London, NW7 1AA.

Jon Robbins
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Reference

Kneeling from left to right: Roddy Williamson, Amanda Smith, Alistair Miller, Tim Cheek, Lucia Sivilotti, Peter Mobbs, John Restins, Peter Appenrodt, John Dempster.

Standing from left to right: Grace Wojcik, Ken McLeod, Virginia Owen, Ken Waun, Eleanor Strain, Michael Paslerlack, Martin Gauthrope, Nick Manison, Peter Wood, Jane Crawford, Boris Barbours, Kate Wardall, Edward Childs, Brigitte Held, Michael Ackley, Paul Goodwin, Geraldine Finnerty, Martin Thomas, Mike Gittschi, Gregor Zapauccia, Maggie Riccio, David Ogden, Thierry Capoud, Jon Robbins, Alasdair Gibb.
Both physiology and molecular biology can gain from applying their technology to the other discipline. For a number of reasons, molecular biology has been slow to make an impact in physiological studies in the UK. Many of the problems stem from the very specialised language that has evolved to assist communication between like-minded molecular biologists but now acts as a barrier.

The first Molecular Physiology Techniques Workshop was held during the first two weeks of September at the University of Glasgow. The intensive two weeks of “hands-on” learning resulted from the hard work and relentless enthusiasm of Richard Boyd. While Committee Secretary of the Physiological Society, he began to explore the possibility of establishing a workshop to teach molecular biology to physiologists in training that was unashamedly based on the successful Plymouth “Microelectrodes” course. The ethos was to create a course where we could teach as much as possible by “hands-on” laboratory practical work, where students would be given a series of lectures mixing “how-to-do” type lectures with talks describing the successful application of molecular biology techniques to physiological science and finally, to provide an environment where the students and teaching staff could interact and form friendships.

An Overwhelming Response

After the first meeting to discuss the feasibility of arranging such a course, the process slowly evolved over the last few years. A financial commitment was made by the Society. The Wellcome Trust were persuaded by Richard Boyd and Peter Stanfield to match the funds provided by the Society. Last summer Richard visited the University of Glasgow to persuade the newly formed Institute of Biomedical and Life Sciences to host the course. Over this last year, the course slowly took shape, guided by a committee comprising Richard Boyd, Peter Stanfield, David Miller, Annette Dolphin and me. While we were all committed to the idea of introducing molecular biology techniques to physiology, I wasn’t prepared for the overwhelming number of applicants in response to the “flier” distributed to members through the Magazine. At the last count, over 110 full applications were received by the Society.

On the 1st September, the 12 participants of the workshop arrived in Glasgow and the weather met everyone’s expectations for the West of Scotland - overcast, cold and very wet. All the participants were young scientists (pre-doctoral or post-doctoral) located in laboratories all over the UK and even St Petersburg. I must admit that I had grave reservations; firstly, that it would be possible to teach molecular biology from scratch to really very sophisticated techniques in the space of two weeks and, secondly, that we could cater for the different levels of background knowledge of the participants and keep everyone occupied and learning. However, the course was a success; even the rain stopped for the entire two weeks and the sun shone most of the time.
A Full Programme

The first week essentially provided a basic cloning type practical run in parallel with measuring fos mRNA by Northern. The second week emphasised more specialised techniques including COS cell and oocyte expression, sequencing and mutagenesis and finally, a two day practical organised by Annette Dolphin on antisense technology and single cell RT-PCR. The days were long; always starting at 9 am and on many evenings a lecture was organised for 6pm. The only free day was Sunday as a computer practical on accessing the databases through the web was organised on the Saturday. Despite the attractions of Glasgow night-life all 12 participants turned up for every session.

The success of the course entirely resulted from the enthusiasm and commitment of everyone who took part; the participants who were fun to teach and interact with, all the people who ran and organised the practical sessions and everyone who made the long journey to Glasgow to lecture. A feature of the success of the course is an “email group” has been formed to encourage everyone to keep in touch and help teach.

The original intention was that the course be run annually, as is the Plymouth course, with initial funding from the Wellcome Trust (who have generously provided partial funding for three years to IMLS at the University of Glasgow) being matched by The Society. The obvious great success of the first course suggests that this expectation is reasonable and that the clearly-apparent need for such training of many younger Physiologists throughout the British Isles will require a continued financial commitment by the Society to this venture, although at a level which the committee feels is appropriate given the many competing financial calls as the St Petersburgh IUPS Congress approaches.

Janet Allen
Institute of Biomedical & Life Sciences
University of Glasgow

Caption Contest

What is Derek Bacon, who was Michael de Burgh Daly’s technician for over 30 years, saying to Tilli Tansey during an oral history interview for the Society archives?

(Photograph by the courtesy of Martin Rosenberg.)

A bottle of wine will be awarded to the person who, in the opinion of the judges, submits the most amusing caption for this photograph.

Entries should reach the following address by 6 January 1997:

Saffron Whitehead (Caption Competition)
Department of Physiology
St George’s Hospital Medical School
Cranmer Terrace
Tooting, London
SW17 0RE
ONLINE RESOURCES

In this issue of the Netwatch column we'll take a look at some of the online resources available that should be of interest to physiologists though much of what follows will also be of general interest.

It seems that these days one cannot escape reading about the Internet and World Wide Web (WWW). It may come as a surprise therefore to hear that many members do not realise the Physiological Society has been running its own WWW server for some time now. Developed in association with Cambridge University Press, Physiology Online contains a wealth of useful information and makes an ideal starting point for the novice WWW physiologist. As well as being able to search the contents of all journals produced by the Physiological Society there is now the facility to view abstracts from recent issues of the Journal of Physiology online. Another of Physiology Online's useful features is a list of all known physiology department WWW sites both in the UK and abroad. Naturally there is an online noticeboard on which you can read the latest news from the Society and there's even a situations vacant page.

Physiology Online can be found at http://physiology.cup.cam.ac.uk/

The fact that you can now read the abstracts of papers in recent issues of the Journal of Physiology is just one indication of the trend towards electronic journals. There are now many peer-reviewed scientific journals that are available in some form on the Internet including high profile journals such as Science (http://www.science.com/) and Nature (http://www.nature.com/). New Scientist is also online (http://www.newscientist.com/) as is Scientific American (http://www.sciam.com/) and the former has a very comprehensive site including a searchable jobs database. There are several good starting points to find other discipline specific online journals. One of the best is the WWW Virtual Library index of academic reviewed journals (http://www.edoc.com/ejournal/academic.html). The range of subjects covered by these journals is quite staggering.

Finally, we move from online journals to online teaching projects and initiatives. Many projects funded by the Teaching and Learning Technology programme (TLTP) have now entered their final stage, the delivery phase. Details of all TLTP funded projects can be found at http://www.icbl.hw.ac.uk/tltp/ and with a wide range of subject areas covered there will almost certainly be projects of interest to most physiologists involved in teaching undergraduates. Much of the software is free to download directly from the TLTP WWW site.

The Computers in Teaching Initiative (CTI) was set up as an ongoing service to the higher education community to encourage and support the use of computers in teaching. There are CTI centers for most academic disciplines though as physiologists the centers of most interest are the CTI Center for Medicine (http://www.ets.bris.ac.uk/cticm/home2.html) and the CTI Center for Biology (http://www.liv.ac.uk/ctibiol.html). Both sites list details of most of the important projects involving all aspects of the use of computers in biomedical education. Both sites also have lists of software teaching packages many of which are free to download. Armed with the combined URLs of the CTI centers and the TLTP projects even the most sceptical Internet user could not fail to find some project of interest, often including free software to download and especially of interest to those physiologists involved in teaching.

As ever we are always interested to hear about any IT initiatives members of the Society are involved in, so please keep those messages coming in. As we reported in the last issue of the Magazine, the Physiological Society has started its own computers in education initiative, the Teaching Resource, so if any member of the Society would like further information of that and any other IT project, please do get in touch. Please address all correspondence to myself at d.a.davies@bham.ac.uk or telephone 0121 414 3255.

David Davies
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From science to psychic snake oil

Christopher Dunkley describes the decline of British state television in broadcasting science programmes. It seems that astrology, aromatherapy, ley lines and the like have replaced "serious" screening.

Financial Times 4 September 1996 p.19

Source: SPIN
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No notice is carried for more than three successive editions. Notices are starred so that readers can see at a glance whether this is the first (one star) or final (three stars) appearance of the notice. Notices for the Spring 1997 edition (to be distributed on 14 February) should reach the Administration Office by 13 January.

European Congress on the ETHICS OF ANIMAL EXPERIMENTATION
17-18 December 1996
Palais des Congrès, Brussels
Members of the animal research community and animal protection community are invited to debate the future regulation of animal experimentation. Organised by the European Biomedical Research Association (EBRA) and the Federation of European Laboratory Animal Science Associations (FELASA). Posters are invited on the following subjects:
- The regulation of Animal Experiments
- Animal Biotechnology
- Replacement Alternatives
- Refinement of Animal Experiments
- The Use of Primates in Experiments
- Public Understanding of Animal Research
- Improved Animal Models
- General


Open Meeting at The Royal Society DISCUSSION MEETING
KNOWLEDGE-BASED VISION: MECHANISMS AND APPLICATIONS
12-13 February 1997
Organised by Dr H B Barlow, Professor R L Gregory & Professor G D Sullivan. Further information from the Science Promotion Section, The Royal Society, 6 Carlton House Terrace, London SW1Y 5AG. Tel: 0171 839 5561 ext 2574/2575, Fax: 0171 930 2170. WWW address: http://britac3.ac.uk/rs/ ***

Open Meeting at The Royal Society DISCUSSION MEETING
WHAT ARE THE PARIETAL AND HIPPOCAMPAL CONTRIBUTIONS TO SPATIAL COGNITION?
19-20 March 1997
Organised by Dr N Burgess and Professor J M O'Keefe. Further information from the Science Promotion Section, The Royal Society, 6 Carlton House Terrace, London SW1Y 5AG. Tel: 0171 839 5561 ext 2574/2575, Fax: 0171 930 2170. WWW address: http://britac3.ac.uk/rs/ *

Designated Sessions at Scientific Meetings
The Society has agreed that part of each Meeting can be set aside in advance for a Designated Session on a special topic. Such sessions will run in parallel with the other sessions of Communications. Suggestions from Members for Designated Sessions at future Meetings can either be made directly to the Special Interest Group organiser or to the Meetings Secretary.

NEUROLOGY FOR NEUROSCIENTISTS
March 24, 25 1997
Magdalen College, Oxford, U.K.
A 2 day conference for young neuroscientists on how clinical neurology can illuminate neural function: imaging of disability and recovery, neuroimmunology and neurooncology. This conference is sponsored by the Federation of European Laboratory Animal Biomedical Research Association (EBRA) and the European Congress on the ETHICS OF ANIMAL EXPERIMENTATION.

European Congress for Molecular Cell Biology
22-25 March 1997
Brighton Conference Centre
This congress organised by "Triangle 3" will cover topics across the full spectrum of contemporary molecular cell biology. The plenary symposia and poster sessions will be complemented by twenty or more concurrent symposia. To receive details of the congress, send an email to ecbo97@immunology.org with the subject of <Update> and nothing in the message itself. You will then receive an automatically generated reply with details. Further information from Triangle House, Broomhill Road, London SW18 4HX. Tel: 0181 875 2400 or Fax: 0181 877 9308. *

CYRO 97
THE APPLICATION OF THE MICROSCOPE IN LIFE SCIENCES
6-9 July 1997, University of York
CYRO 97 is the second of a series of biennial international scientific meetings organised by the Royal Microscopical Society. The conference will cover fundamental cellular processes as well as the disturbance of cells leading to pathological change. Plenary lectures from keynote speakers will describe research at the forefront of science today. Considerable time as been allocated in the programme for poster communications. Registration for CYRO 97 will enable delegates to attend presentations in either conference. Further information from RMS, 37-38 St Clements, Oxford OX4 1AJ. Tel: 01865 248768, Fax: 01865 791237. *

Bedroom Accommodation and Meeting Facilities at The Ciba Foundation
Any graduate in a scientific discipline on a working visit to London, or travelling via London, is welcome to use one of bedrooms for a period of up to two weeks. Charges as from 1 January 1996 are £37 for a single and £47 for a twin room which includes breakfast. Further details from: Sue Venables, The Ciba Foundation, 41 Portland Place, London W1N 4BN, tel (0171) 636 9456.

Visiting Scientists
Foreign visitors of the status of at least postgraduate student, working in laboratories of Members of the Society, may be made "Visiting Scientists" by the Society. The names of such persons, with the dates of their visits and a letter of support, should be sent to the Foreign Secretary, Professor O H Petersen, The Physiological Laboratory, University of Liverpool, PO Box 147, Crown Street, Liverpool L6 9BX.

Reunion at Bristol
In July 1997 the University of Bristol Department of Pharmacology will be hosting the summer meeting of the British Pharmacological Society. This coincides with 21 years of Pharmacology graduates from Bristol. A reunion for former students and staff is being planned and details will be circulated to graduates in advance of the event. Further information is available from Peter Taberner c/o the Department of Pharmacology, School of Medical Sciences, University Walk, Bristol, BS8 1TD. Fax 0117 925 0168. E-mail Peter.V.Taberner@bris.ac.uk.

Further information from the Science Promotion Section, The Royal Society, 6 Carlton House Terrace, London SWY 5AG. Tel: 0171 839 5561; Fax: +32 2 219 32 15. ***
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<td>BENEVOLENT FUND</td>
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<td>To promote new physiological research in the British Isles</td>
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<td>Travel for collaborative research, learning new techniques, practical workshops and training courses: up to £600. Travel to conferences and symposia: up to £300</td>
<td>Applications are considered throughout the year</td>
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<td>To support centres of scientific excellence where high quality physiological research is threatened by lack of resources</td>
<td>Centres of physiological research in Eastern European and Third World countries demonstrating scientific excellence and financial need</td>
<td>Up to £10,000 per annum, for up to three years</td>
<td>Applications are considered at the end of January, March, May, July, September and November</td>
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<td>To allow physiological workers in Eastern European and Third World countries to visit laboratories in the British Isles</td>
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<td>Up to £1,500</td>
<td>Applications must be made by the host in the British Isles, and are considered at the end of January, March, May, July, September and November</td>
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<td>NEW LECTURERS SUPPORT FUND</td>
<td>To help young physiologists to establish independent research programmes</td>
<td>Academic staff in the first year of their first appointment to an established University lectureship in the UK or Eire</td>
<td>Up to £5,000 for consumables, equipment and, in exceptional cases, technical help</td>
<td>Applications are considered at the end of March and September</td>
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<td>POSTGRADUATE SUPPORT FUND</td>
<td>To assist the completion of research projects which have been delayed due to circumstances outside the applicant's control</td>
<td>Graduates (normally PhD students) in departments of Physiology or a cognate science in the British Isles, whose supervisors are Members of the Society</td>
<td>Up to £1,000</td>
<td>Applications should normally be submitted before 31 July, but may be considered at other times</td>
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<td>Young physiologists working in the British Isles who are not yet Members of the Society</td>
<td>Travel grants for collaborative research, learning new techniques, practical workshops and training courses: up to £500</td>
<td>Applications are considered throughout the year</td>
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<td>To enable undergraduates to undertake research projects in the summer vacation</td>
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<td>Up to £500, for maintenance (no support available for consumables or other research expenses)</td>
<td>Applications must be submitted by 31 March</td>
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STUDENT ASSOCIATE PROPOSAL FORM

Surname (In Capitals).................................................................................................................

Forenames (In Capitals)...................................................................................................................

Details of the degree for which you are currently registered:

Degree title........................................................................................................................................

University.........................................................................................................................................

Department........................................................................................................................................

Commenced (date): .................................................. Due to complete (date):.................................

Special Scientific Interest, if any (eg thesis or project title): ............................................................

Current Address

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Please state your permanent/home address, at which we will be able to contact you after completion of your studies.

Tel: .............................................................................................................................................

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At the Sheffield Meeting....

Biomedical Science office staff

Photography by Martin Rosenberg

At the Leeds Meeting....

Professor John Morrison (Left) and Professor Wilfred Jönig admiring the mask used by The Royal Armouries

Interpretation of sword fighting by Samurai Warriors

(Left) Dr David and Mrs Mary Cotterell and (right) Professor Brian and Benita Jewell

Some members of the Neurogastroenterology Group.

(Left to right behind) Dr Malcolm Lidierth, Dr Philip Harrison, Dr Prem Kumar and (in front) Dr Bridget Lamb

Photography by Kathleen Rayfield

Back cover: Electrical impedance tomography (EIT) images collected during artificially induced focal epilepsy in the anaesthetised rabbit, using a ring of 16 electrodes placed on the superior surface of the exposed brain. The electrocorticogram was concomitantly measured from the 16 electrodes, and blood flow was measured at two sites using a Laser-Doppler flowmeter. Impedance changes caused by the epileptic activity may be seen in the EIT images. These were collected every 5 s; only a selection is shown. Courtesy of David Holder.