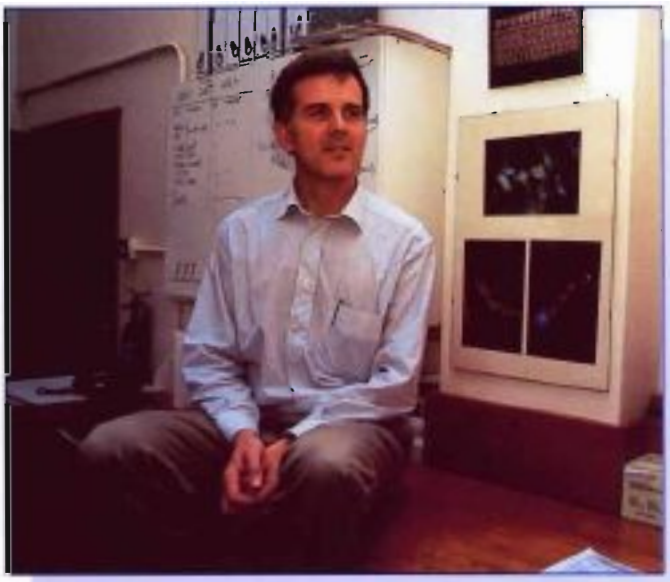
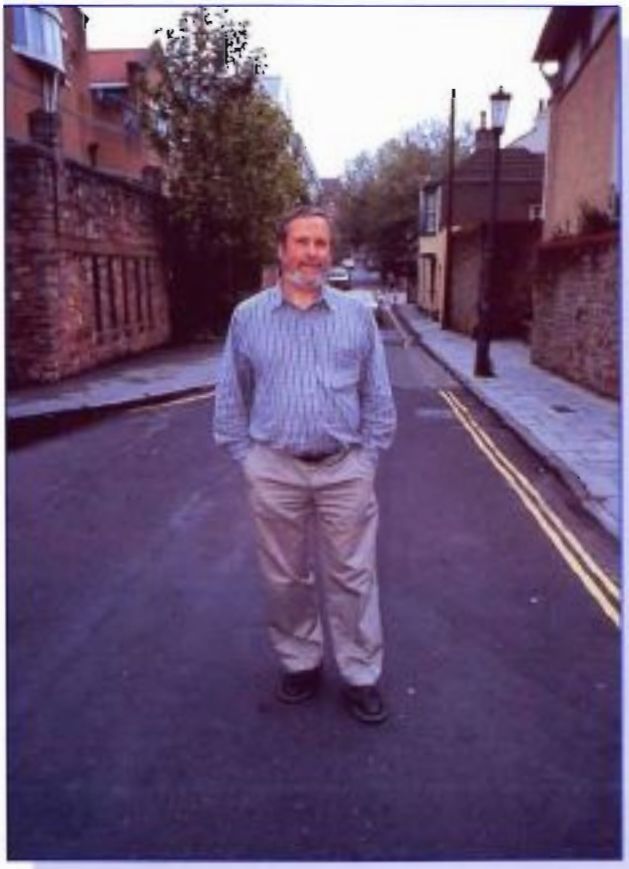
The Physiological Society Magazine

Autumn 1997
No 28

University of Bristol



Dr Matthew Holley



Dr John Luck

Dr Allan Levi (standing left) with his group

Dr David Wooley

Photography by Martin Rosenberg and Saffron Whitehead

Front cover: Scanning electron microscopic view of a single isolated outer hair cell with the apical sterocilia and long cylindrical cell body visible. The cell is about 60 micrometers long. Courtesy of David Furness, Department of Communication & Neuroscience, Keele University.

Contents

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Action Points

- Affiliation Renewal Fees: Payment of fees for the renewal of Affiliation for the academic year 1997-1998 should reach the Administration Office by 30 September.
- Annual General Meeting: The Annual General Meeting will take place during the Bristol Meeting at 5.30 pm on Wednesday 3 September in Theatre One.
- Affiliate Travel Grant Scheme: The next two deadlines for receipt of applications are 30 September and 30 November 1997.
- Cambridge Meeting: Abstracts should be submitted to the Meetings Secretary between 1 September and 11 September 1997.
- Eastern Europe and Third World Support Scheme: The deadline for receipt of grant applications is 30 August 1997.
- Email Addresses: The Society is making increasing use of email addresses. Please can Members inform the Administration Office of new email addresses, or changes to existing ones. Changes can be emailed to admin@physoc.org
- Experimental Physiology: Rapid Communications for the November 1997 issue of Experimental Physiology should reach the Distributing Editor's Office in Newcastle by 1 September 1997. Rapid Communications for the January 1998 issue should reach the DE's Office by 21 October 1997.
- G L Brown Prize Lecture: Departments wishing to host a lecture in 1998 should notify the Committee Secretary by 1 September 1997.
- Grey Book: Members should inform the Administration Office of amendments to their entries, including telephone/fax numbers and email addresses, by 31 August 1997.
- Guy's Meeting: Abstracts should be submitted to the Meetings Secretary between 29 September and 9 October 1997.
- Magazine: Letters and articles for inclusion in the next issue should reach the Editor by 1 September 1997. Advertisements and Notices should reach the Administration Office by 15 September whilst items for the Special Interest Group Forum should reach the Meetings Secretary's Office by 15 September. Items for Committee News should reach the Committee Secretary's Office by 3 October 1997.
- Student Associateship: Members proposing undergraduates in their second year and above for Student Associateship are encouraged to do so at the beginning of the academic year. (An application form can be found towards the back of the Magazine.)
- Student Associate Renewal Fees: Payment of fees for the renewal of Student Associateship for the academic year 1997-1998 should reach the Administration Office by 30 September.
- Suspension of grants: Please note that as from 1 January 1997, until further notice, the following grants will no longer be available - Eastern European and Third World Visitor Fund, MSc Bursaries, New Lecturers Support Scheme, Postgraduate Support Fund.
- UMDS (St Thomas') Meeting: Abstracts should be submitted to the Meetings Secretary between 28 July and 7 August 1997.

Editor

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Web: http: / / physiology. cup. cam . ac . uk

GUIDELINES FOR CONTRIBUTORS

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 dénouement or conclusion.

Length of articles

This will be determined by the subject matter and agreed between the contributor and the commissioning editor. Articles will vary in length from 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

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

Illustrations

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

Author photographs

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

References

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

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).

Artwork & DTP - Denise Redmond, Academic Services, St George's Hospital Medical School, London.

Welcome to Bristol

We are delighted to be welcoming the Society to Bristol for a scientific meeting this September. The last time we hosted a major meeting of the Society was in February 1994, and the head of department at the time, David Armstrong, provided a very full account of the Department which was published in an accompanying issue of the *Magazine* (issue No. 12, Spring 1994). Since then Stephen Lisney has succeeded him as HoD, David having served his 5-year period of office, and there have been other important changes in the academic staff which were reported last Winter's *Magazine* (No. 25). Change continues and by the time of the meeting there will be a new HoD, Stephen Lisney taking on a new job as Chairman of Medical Sciences at Bristol. In this article I will try to bring the picture of the Department up to date.

The Department

We are a medium-sized department with 20 academic staff - 3 professors, 6 readers, 6 senior lecturers, and 4 lecturers and a special lecturer/administrator. We also have 6 independently funded fellows, 21 other post-doctoral researchers and 22 postgraduate students working in the Department. Our research and teaching is very ably and loyally supported by a team of 27 technical staff and 4 secretaries. The annual budget is currently of the order of £3.7M, of which about £1.6M is in the form of research grants. The Department is involved in both the Faculty of Medicine and the Faculty of Science. Its major part is housed in the School of Medical Sciences in University Walk, but there is also a substantial amount of space in the new School of Preclinical Veterinary Sciences, Southwell Street, just a few minutes walk from the School of Medical Sciences.

Research

The Department has a strong record in research in Cell Physiology and Neuroscience, gaining a 5A rating in both the 1992 and 1996 Research Assessment Exercises. This research is well supported by external funding, mainly via project grants from the Wellcome Trust, MRC, BBSRC and the British Heart Foundation, but there are also two Wellcome Trust programme grants. There is other funding from the EC, NIH and the pharmaceutical industry.

Two new research facilities have recently been commissioned: a new electron microscope was installed in the Department in 1996 with the help of funding from the Wellcome Trust, and the Cell Imaging Facility, with confocal microscopes, was opened in 1997. This was a cross-departmental venture by the School of Medical Sciences and the funding came from a joint application to the MRC.

Most research groups centre on one or two tenured staff and virtually all are concerned with excitable tissues, with sufficient predominance of neurophysiology for the MRC to class us as a neuroscience department. However a fair proportion of our research is carried out in collaboration with researchers in other departments in the University and in hospitals in the area. Our work can be grouped into the following main sub-areas.

- ***Mammalian Somatosensory Mechanisms.***

Max Headley's group are studying the actions of excitatory amino acid transmitters in, and the action of anaesthetic and analgesic agents on, spinal sensory processing, while Sally Lawson continues her characterisation of the chemical phenotypes among the subpopulations of dorsal root ganglion cells associated with different types of cutaneous receptors. Stephen Lisney's interests lie in the effects of injury on peripheral nerve fibres, particularly changes occurring in fibres not directly involved in the injury. Bridget Lumb is investigating the role of the hypothalamic /PAG axis in the integration of cardiovascular function and the control of nociception, and Bruce Matthews' work concerns the mechanism of sensory transduction in teeth and the properties of nerves supplying tooth-pulp.

- ***Muscle and Cell Motility***

Donald Lewis is following up the observation that reinnervation of skeletal muscle improves regeneration by stimulating division of satellite cells, and K W Ranatunga has added the use of a laser temperature-jump instrument to his work on contractile activation and the generation of active force (including a component that seems to be independent of Ca^{++}). Tony Ridge is involved in studies of muscle development and of transmitter release and vesicle recycling at the neuromuscular

junction. David Woolley is working on unravelling the mechanism of force generation by flagellar dyneins: he uses a variety of techniques, including those of ultra-rapid cryofixation and release of caged ATP.

- *Membrane and Cell Biophysics*

Robert Meech's interests lie in the properties of ion channels and he is developing molecular biological approaches to the study of channel proteins. Some of his work is carried out in collaboration with Allan Levi and Jules Hancox (see below).

- *CNS Neuronal Circuitry*

Roland Jones is working with in vitro brain-slice preparations and is studying properties of synaptic transmission between various groups of central neurones, while Julian Paton has developed a novel working heart/lung/brainstem preparation in the mouse and is using this to investigate features of the neural circuitry which controls the cardiovascular system and that which generates the respiratory rhythm.

- *Mechanisms of Hearing*

Matthew Holley is at the forefront of raising specific antibody markers to hair cells and there is every sign that these are going to be powerful tools in developmental and regeneration studies on the cochlea. Paul Kolston is using computer modelling of the mechanics of the cochlea as a means of advancing understanding of the physiology of the structure, while Nigel Cooper is using a laser vibrometer to detect the movements of inner ear structures in response to sound, while simultaneously recording activity in the cochlear nerve. Corné Kros is studying the molecular mechanisms used by hair cells to convert sound stimuli into electrical signals.

- *Neural Control of Movement*

David Armstrong and Judy Harris (with Richard Apps and Dilwyn Marple-Horvat) have a large group concerned with the supraspinal control of movement and the organisation of the cerebellum. Brian Bush is exploring the possibility of using EMG recordings from hand muscles while performing repetitive tasks as a means of characterising motor dysfunctions.

- *Cellular Cardiovascular Studies*

Allan Levi's group work on excitation-contraction coupling in cardiac myocytes and the pathophysiology of cardiac hypertrophy. Jules Hancox has succeeded in isolating A-V node cells from the heart and is now studying their biophysical properties. Phil Langton is studying stretch-activated channels in vascular smooth muscle cells and their role in determining vascular tone in blood vessels.

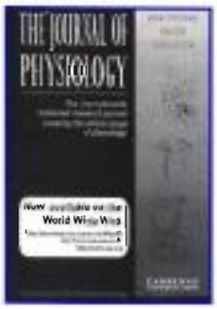
Teaching

The Department is responsible for teaching Physiology, including Histology, to undergraduate students in the Faculties of Medicine and Science: the annual intake of students is 150 to the School of Medicine, 55 to the School of Dentistry, 75 to the School of Veterinary Science, and 20 to the Honours School in Physiology. As well as this, approximately 100 BSc students from other departments take the first year Physiology unit as one of their ancillary subjects, and about 50 take the second year unit. Each year 5 or 6 medical, dental or veterinary students join the final year of the Honours course as intercalating students. Members of staff also contribute to the formal teaching activities of the Graduate School in Biomedical Sciences.

The Scientific Meeting

The meeting promises to be a large and exciting one, and during it we will have the honour and pleasure of hosting two of the Society's prize lectures, the Bayliss-Starling Prize Lecture, to be be given by Professor David Brown, and the Annual Review Prize Lecture, which will be given by Dr. Lily Jan. Eleven special interest groups will have sessions and Professor Peter Dallos will give a designated lecture as part of the Sensory Functions SIG's programme. When you add to this the various symposia that have been organised for before and after the meeting you will appreciate that it is going to be a very busy week. We look forward to welcoming you to Bristol to enjoy both the Science and the city.

Stephen Lisney
Department of Physiology
University of Bristol



Electronic Publishing

Abstracts and Complete Papers for The Journal of Physiology are now available on-line. Access can be made via The Physiological Society Home Page http://physiology.cup.cam.ac.uk/index.html and is currently free. The site is updated as soon as each issue is published. A selection of papers from Experimental Physiology is also available by clicking onto the relevant link on the Home Page.

Membership

Membership Subscriptions for 1998 will remain the same as for 1997. Experimental Physiology Subscriptions will also be printed on the same form which will enable direct debits to be set up for those wishing to subscribe.

It has, however, been agreed to raise the subscription for Affiliates after 5 years to that of Ordinary Members receiving abstracts, Notices, Programmes and Magazines. Such a policy will encourage Affiliates to apply for Ordinary Membership at the appropriate time while avoiding the need for any gap between Affiliation and Full Membership.

Although this year there have been no applications from Teachers of Physiology, it is hoped that the situation will soon change.

Honorary Membership

The Society offers its congratulations to the following Members who were elected as Honorary Members at the Semi Annual General Meeting at Dublin in March.

Professor Ian Glynn

Physiological Laboratory
Cambridge University

Professor Christoph Lüttgau

Department of Cell Physiology
Ruhr University

Professor Denis Noble

University Laboratory of Physiology
Oxford

Professor Erwin Neher

Max-Planck-Institut für
Biophysische Chemie
Göttingen

Professor Bert Sakmann

Max-Planck-Institut für
medizinische Forschung
Heidelberg

Prize Lectures

Newly nominated Prize Lecturers for 1998 are:

The Wellcome Prize	Dr Leon Lagnado	Visual Transduction and Synaptic Transmission in the Retina
The GL Brown Prize	Dr Ian Forsythe	Synaptic Transmission: Lecture Exploring a Mammalian Giant Synapse
Sharpey Schafer Lecture & Prize	Dr Julian Paton	To be confirmed
Annual Review Prize Lecture	Professor Nancy Rothwell	Cytokines as Killers in the Brain
The Joan Mott Prize Lecture	Professor Janice Marshall	The Integrated Response to Hypoxia - from Circulation to Cells

Venues will be confirmed at a later date

Unlike other Society Prize Lectures, the GL Brown Lecture is not given in conjunction with a Scientific Meeting. Instead, the Lecturer and the Committee select a series of Departments in the British Isles from January to March. Heads of Departments wishing to host a lecture should contact the Committee Secretary, Professor Peter Stanfield by 1 September at The Physiological Society, Department of Cell Physiology & Pharmacology, University of Leicester, PO Box 138, Leicester, LE1 9HN. (Email cd22@le.ac.uk).

Molecular Techniques Workshop

This year's Molecular Techniques Workshop has once again proved very popular with many more applications than there are places available on the course. 16 people have now been chosen to attend the course which will run from 1- 12 September 1997 at the University of Glasgow. The course is funded by a generous grant from The Wellcome Trust as well as by The Physiological Society.

Unsuccessful candidates, and those considering applications for 1998 may be interested to know that the Workshop has secured funding for a further year. Details of next year's course will be publicised on the Physiological Society Web Page (http://physiology.cup.cam.ac.uk/index.html), in the Physiological Society Magazine and via Heads of Departments.

Publishing of Scientific Articles

Following sensationalist reporting of a Sheffield Meeting abstract entitled `Changes in brain size in normal pregnancy', the Committee discussed ways of using the media to publicise Science more effectively and to ensure that papers were not written up before they had been formally approved. The Committee and Meetings Secretaries would welcome any suggestions on how to influence the writing up of papers from Scientific Meetings so as to benefit both the authors and the Society.

Strategic Plan

In an attempt to link strategy more closely to the financial expenditure and policy making of the Society, the style and content of the Strategic Plan has now been reconsidered by the Committee. A revised version will be circulated to Members and the Committee Secretary would welcome comments and suggestions before the paper is put to the AGM on 3 September.

St Petersburg - IUPS Conference

The Membership Sub-Committee have reported that 57 Full Members and 63 Affiliates have received grants to the total value of £55,000 under the IUPS Scheme. The number of registrants (including accompanying persons and employees of Blue & White Conferences, Helsinki) exceeded 3,500 and this year's stand was manned by Charlotte Parry and Nina Burdakova. A fuller report will appear in the next issue of The Magazine.

Members are reminded that they should write to The Administration Office as soon as possible to claim any overpaid money or refunds for cancellations that occurred before 30 April 1997.

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

Christina Docchar

PRE-CIRCULATED ABSTRACTS AND THE PROGRAMME OF SCIENTIFIC MEETINGS ARE NOW ON THE WEB

Call up the Society's Web Page on http://physiology.cup.cam.ac.uk and you will see the Abstracts and Programme of the next Scientific Meeting. They are at present put on the Web about two weeks before the paper copies are sent out by post. You can of course print off any number of pages and even the registration form to make a quick reply and be sure about your place at the Society dinner.

The Society has to continually review whether it is using its relatively limited resources as effectively as possible. As part of this re-appraisal I would like to propose a discussion item for the AGM at Bristol that, at some stage next year, only the Programme **and not the Abstracts booklet** would be pre-circulated before a Scientific Meeting.

The main advantages would be the saving of a considerable sum of money (I estimate up to £30,000 in printing and postage costs) which could be used for other items such as grants and improving aspects of Scientific Meetings, and the reduction of the length of time between the final submission date for abstracts and the Meeting itself.

The disadvantage would be that a relatively small number of you do not have access to the Web, but paper copies of the abstracts could be provided if required. Some may also consider that this system will be less convenient than having all the abstracts in a booklet to look at before the Meeting.

I am not trying to steer a particular course but merely open a discussion so that Members can play a role in the development of the Society. I am sure there will be many vociferous arguments at the AGM, and if you are unable to get there I would be pleased to hear your views beforehand so that I can represent them at the AGM.

Coloured Slides at Oral Communications

The instructions on the abstract submission form and in the Programme recommend that speakers show no more than six slides, each containing no more than three curves on a graph or four columns to a table. This is because it is usually difficult to communicate more information effectively to an audience in 10 minutes. In the days when the photocopier, stencil sets and a good typewriter were our only aids, slides also were usually in black-and-white. The advent of computer driven slide-making programs, such as PowerPoint, has changed all that. Speakers are now tempted to highlight aspects of their slides by having them in sometimes hideous colours. Several times at Meetings people have come up to me to complain about the inappropriate use of colour in slides making it difficult to distinguish a line on a graph from other lines or even the background itself. There was one instance when the lines on a graph could be seen only when all the lights had been switched off. This confused both the audience and speaker as the latter tripped over in the dark and the audience didn't know if the Communication had finished. Please consider whether colour really does add anything to the slide, apart from illustrating your outlandish taste in colour matching. Remember that clear contrasts on a computer screen work less well when projected as a slide. Chairpersons will be asked in the future to consider whether too many or too colourful slides detract from the ability of the audience to take in the message of the Communication and this could be reflected in the final voting procedure.

The January 1998 Meeting

A number of the more sharp-eyed of you may have noticed that the location of this Meeting, as advertised in various Meeting Programmes, has changed. Initially placed at Guy's Hospital it was to be a small Designated Meeting associated with the Urological Research Society with a larger general Meeting planned for February. However, circumstances beyond my control, as they say, soon changed matters. The Guy's Meeting had to be changed to the Royal College of Surgeons in London, but the subsequent abandonment of the planned February Meeting meant expanding the January Meeting and moving it back to Guy's. So we are back where we started from with a full Meeting of the Society at Guy's Hospital at the beginning of January - and that is where it will stay. Several Special Interest Groups are represented so I hope it will be a lively Meeting. The life of Meetings Secretary is rarely dull but can have serious effects on one's mean arterial blood pressure sometimes.

Chris Fry
Meetings Secretary

Research in Brief: Imperial puts medical records online

Medical records could soon be fully digitised and include interactive multimedia features thanks to new work from Imperial College, London.

***THES* 1283** *6 June 1997 p.9*

Source: SPIN

BLOOD-BRAIN BARRIER

There will be a Designated Blood-Brain Barrier Session at the UMDS (St Thomas') Meeting 7-8 November, 1997. We would wish to encourage as many members of the Group as possible to present Communications and Posters at the Meeting.

John Greenwood has indicated that he would be happy to hand over the baton as organiser for the BBB Group and David Begley has volunteered to take over as from the UMDS Meeting. Unless of course there are any other nominations for the job. If there are any other nominations for the post could you please inform John Greenwood by Monday 15 September 1997, so that if necessary a ballot can be organised. If you would like to be included on the BBB Special Interest Group mailing list and are not listed as such in The Grey Book could you please let John Greenwood know.

Malcolm Segal m.segal@umds.ac.uk
John Greenwood j.greenwood@ucl.ac.uk
David Begley david.begley@kcl.ac.uk

CARDIOVASCULAR / RESPIRATORY CONTROL

I want to start by saying a big thank you to Professor David Adams for delivering an excellent Designated Lecture entitled "Intrinsic Neural Control of the Heart: Role of Intracardiac Ganglia". His lecture was presented to a large audience at the Dublin Meeting in March. I felt that his lecture was fully appreciated by a broad range of people including both cardiovascular and neuro-physiologists. As for our SIG Session at Dublin, there were 22 Oral and nine Poster Communications which were stimulating, well debated and contributed significantly to the Meeting overall. For your information, following the Session at Bristol this September, the SIG Sessions for 1998 are in Liverpool (April) and Southampton (September). Now on to the up and coming Bristol Meeting to be held 1-5 September 1997.

I have planned a symposium entitled: "Maturation, Modulation & Plasticity in Cardio-Respiratory Control" which will be held on Friday 5 September 1997 in Lecture Theatre One in the Veterinary School, University of Bristol, Southwell Street (five minute walk from the School of Medical Sciences) and follows the scientific programme of the main Physiological Society Meeting at Bristol (2-4 September). This symposium is supported by the British Heart Foundation and The Physiological Society. The design of the proposed symposium is intended to provide information on new discoveries regarding brainstem and spinal cord control mechanisms for both circulation and respiration. There will be nine speakers and three sessions. I am delighted to announce that Gilles Fortin, Carlos Blanco and Sergey Kasparov will contribute to the maturation session, Klaus Ballanyi, Olivier Pierrefiche and David Jordan will talk on modulation and Patrick Gauthier, Tom Sears and Peter Kirkwood will make presentations concerned with plasticity. The social programme is a cocktail reception on the patio at the Clifton Gorge Hotel, overlooking the majestic Clifton Suspension Bridge, followed by dinner in Clifton Village; all are very welcome to attend.

I look forward to seeing you at The Physiological Society Meeting and the SIG symposium in Bristol.

Julian Paton

COMPARATIVE & INVERTEBRATE NEUROSCIENCE

The MBA Meeting, Plymouth

The Comparative and Invertebrate Neuroscience Group held a symposium on "Neuromodulation of Synaptic Function" at the Marine Biological Association, Plymouth. Symposium contributions were given by Paul Katz (Atlanta), Paul Benjamin (Sussex), Leonid Moroz (Urbana and Minsk), John Hildebrand (Tucson), Bob Pitman (St Andrews), Milton Charlton (Toronto) and Jonathan Coles (Bordeaux). Oral Communications and Posters were interspersed with the symposium talks and led to some lively discussions.

The MBA was an excellent host. The Demonstrations and Society reception were held at the MBA with visits to the aquarium and holding tanks to remind us all how much physiology owes to the study of marine and invertebrate species. Comparative physiology was certainly given strong support, with around 150 people attending. We are also very

Plymouth Pavillions where Lectures and Communications were held

grateful for the financial support for the symposium given by The Physiological Society, the British Neuroscience Association and Sheffield Academic Press Ltd, publishers of Invertebrate Neuroscience. We look forward to the next meeting of the Group at Southampton in September 1998 and to another Plymouth Meeting in the not too distant future.

The only dark cloud at the Meeting was that Roddy Williamson, my co-organiser was unfortunately unable to attend, due to a badly trapped nerve in his shoulder. I gather that the patient is now doing well and should have that very same shoulder back to the wheel by the time that this is printed. Thanks very much to Roddy for all his efforts to get the show on the road. It was a great success.

Bill Winlow

EPITHELIA & MEMBRANE TRANSPORT

This is my first opportunity to contribute to the Magazine since taking over from Barry Hirst as Convenor for the Group. My first task is to thank Barry for the great deal of hard work he has put in over the last few years. I hope that I can maintain such a high level of activity within the Group during my tenure.

By allowing myself to be put forward as Convenor it is implicit that I am willing to organise events for the Group. However, I would welcome your suggestions on guest lecturers and possible venues for Sessions and symposia. You can contact me on tel: (0161) 275 5463 email: pbrown@fs1.scg.man.ac.uk. I would personally prefer to hold no more than two Designated Sessions each year (during the university vacation periods). I hope that this will encourage as many people as possible to attend our Communications presented. I have already made one or two decisions regarding where to have Designated Sessions. These will be in Bristol (September 1997), Guy's Hospital (January 1998) and Southampton (September 1998). To redress the apparent southern bias in this programme Manchester will be hosting another Epithelia & Membrane Transport Designated Meeting in March 1999.

A final point is communication within the Group. The Society has now introduced electronic mailing lists for each of the Special Interest Groups. It would therefore be very useful if you could register your email address with Charlotte Parry at the Society's Administration Office, tel: (0171) 631 1458, email: cparry@physoc.org. It would also be helpful if those of you who are not already affiliated to the Epithelia & Membrane Transport Group, but wish to be, could inform the Administration Office.

Peter Brown

G I TRACT

After the Bristol Meeting, the new Convenor for the G I Tract Group will take over:

Dr Paul Andrews
Dept of Physiology
St George's Hospital Medical School
Cranmer Terrace
Tooting
LONDON
SW17 0RE
Tel: (0181) 725 5369
Fax: (0181) 725 2993

Our thanks go to Dr David Grundy, the previous Convenor, for maintaining the Group over the last few years.

Meetings Secretary's Office

HEART AND CARDIAC MUSCLE

Dr Stephen O'Neill has been elected as the new Convenor of the Heart and Cardiac Muscle Group:

Dr Stephen O'Neill
Dept of Veterinary Preclinical Sciences
University of Liverpool
Brownlow Hill
PO Box 147
LIVERPOOL
L69 3BX
Tel: (0151) 794 4231
Fax: (0151) 794 4243
Email: oneill@liverpool.ac.uk

Our thanks go to Dr Godfrey Smith, the previous Convenor, for maintaining the Group over the last few years.

Meetings Secretary's Office

MICROVASCULAR & ENDOTHELIAL PHYSIOLOGY

The next Designated Session for the Microvascular and Endothelial Physiology Special Interest Group will be held at the Cambridge Meeting of the Society from 15-17 December 1997. After discussions with several

members of the Special Interest Group, we are organising a symposium entitled "Atherosclerosis: from molecule to man" for the morning of Monday 15 December. Four keynote symposium lectures will be followed by Oral and Poster Communications, and depending on the number of submitted abstracts, our Designated Session could run from midday on 15 December to midday on 16 December. In addition to general abstracts on microvascular physiology, we particularly welcome abstracts on the role of calcium and ion channels in endothelial and smooth muscle cell signalling. Dr Stewart Sage (tel 01223-333870. email sos10@cus.cam.ac.uk) has kindly agreed to act as our local host for the Designated Session at Cambridge.

A number of Pfizer prizes are awarded each year to postgraduate students presenting Oral Communications in the Designated Sessions of Special Interest Groups. Our Designated Session at Cambridge will be eligible for Pfizer Prizes. Abstract forms and a copy of the rules of the competition and the form to be used when introducing a postgraduate student for consideration for a Pfizer Prize are available from Helen Fitzwilliam (tel/fax 0171 636 5053). Please type Designated Session: "Microvascular and Endothelial Physiology" at the top of your abstract and indicate your preference for an Oral or Poster Communication. The earliest date for receipt of abstracts for the Cambridge Meeting is 1 September and the closing date is 11 September. If you are not a Member of the Society, my colleagues and I could introduce your abstract. Abstracts, accompanied by a completed Submission Form, disk and hard copy should be sent to: Prof Chris Fry, Meetings Secretary, The Physiological Society, Institute of Urology & Nephology, Third Floor, 67 Riding House Street, London W1P 7PN.

You may also be interested in the forthcoming related meetings: (i) European Thrombosis Research Organisation Conference "Endothelium and Adhesion" in Marburg, Germany from 11-13 December 1997 (contact: Prof Klaus Preissner, email: klaus.t.preissner@kerckhoff.med.uni-giessen.de), (ii) Joint Meeting of the German/Benelux Microcirculation Societies (Symposia: "The Effect of Mechanical Forces on Vascular Growth and Function" and "Applications of Cell Physiological Methods in Microcirculatory Research", plus two plenary lectures: "Role of Nitric Oxide and Superoxide Anion in the Control of Vascular Apoptosis" and "Role of Connexins in Vascular Growth and Function") in Mainz, Germany from 23-25 October 1997 (contact: Prof Dr U Pohl, fax: +49 6131 395644) and (iii) British Microcirculation Society in association with the Northern Vascular Biology Group (Symposium: "Neovascularisation and Angiogenesis: Mechanisms and Modulators") in Manchester, UK from 30-31 March 1998.

Finally, many thanks to those who completed and returned the Special Interest Group questionnaire circulated earlier this year. As you may know the Society has decided to replace mailshots to Special Interest Groups with email messages. Thus, the questionnaire was designed to obtain as much relevant information as possible, ie name, address, tel, fax and particularly your email address. In addition, I asked members to provide 5-6 keywords that described their research interests. If you have not yet completed the questionnaire, please could you do so as soon as possible to facilitate the compilation of our database. If you require another copy of the questionnaire, please contact me by email (g.mann@kcl.ac.uk), tel. (0171 333 4450) or fax (0171 333 4008).

Giovanni E. Mann

MUSCLE CONTRACTION

It was good to see a number of you at the Plymouth Meeting of The Physiological Society: I thoroughly enjoyed the proceedings and thought that, although the number of Communications/Demonstrations on "muscle related topics" may have been small, they adequately represented the interests of the Group at the Meeting.

As you may know already, there will be a Designated Session on Muscle Contraction at the Bristol Meeting in September, and I hope that the Session will be well supported with Communications, Posters and/or Demonstrations. Looking further ahead, Designated Sessions are planned for the Meetings at UMDS (St Thomas') (6-8 November 1997, abstract submission period, 23 July - 7 August 1997), at Liverpool (27-29 April 1998) and at Cardiff (December 1998).

Finally, I am still looking for someone to replace myself as the Convenor of the Muscle Contraction Special Interest Group; I would welcome any suggestions from the members; you may contact me by email (k.w.ranatunga@bristol.ac.uk). I look forward to seeing many of you at the Bristol Meeting.

KW Ranatunga

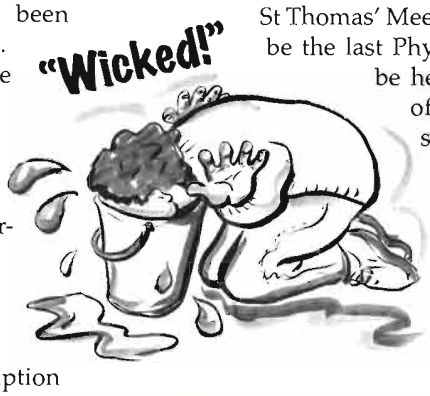
RESPIRATORY PHYSIOLOGY

The Dublin Meeting

To paraphrase: "If you can remember the Dublin Meeting of The Physiological Society, you probably weren't there". For those that can't remember, or perhaps weren't there, we had nine Communications and six Posters in the Respiratory Physiology Session, held on the first morning of the Meeting. A large audience was present throughout, with standing room only at times. Slotting between the Human Physiology and the Cardiovascular/ Respiratory Control Sessions indicated clearly just how blurred the borders between these three Groups really are. As such, most people seemed happy to remain in the same lecture theatre for the whole day which was somewhat ironic as this Meeting probably provided for the best "theatre-hopping" of any, with the three main theatres located immediately adjacent to each other.

Well prepared and presented Communications, mostly given by graduate students (almost certainly not coincidentally), a lively discussion and a never-ending supply of tea, coffee and biscuits all combined to ensure that the "fatigue-index" for the Session, as measured by Roe et al, would have remained close to 1. A range of topics were covered in the Communications, including diaphragmatic function in health and disease, the effect upon CO2 sensitivity of chronic hypoxia and elevated temperature, ventilation and oxygen uptake in exercise and ion channel function in chemo/osmoreceptors whilst the Posters covered topics ranging from the pathophysiology of alveolar type II cells and upper airway muscles to the effect of paddling upon air sac pressure in diving ducks. Just over half the presentations (9/15) described experiments performed at the whole animal or human subject level with the remainder being in vitro studies.

The biggest laugh of the Session - at least for approximately half of the audience - was reserved for Ms Lauren Stewart's description of her subjects as "naive male undergraduates". Her tone, whether accidental or intentional, seemed to imply that a superfluous adjective had been employed in the description. This study examined the effect upon ventilation of water immersion of the face and as well as providing some intriguing data regarding chemoreceptor-independent drives to breathing, will also be remembered for a slide containing the word "Wicked!", used as a description of the feeling experienced as your head is dunked into a bucket of cold water. I'm sure that, at least for anyone under 25 years of age, this description is highly quantitative in a way that no number could possibly be.



For those of you interested in these things (and I know from my conversations at the Dinner that many of you are) we stayed in various guest houses and hotels dotted around the city, some perhaps on the more "iffy" side of the Liffey than others and so it is not possible to provide a definitive bathroom facility update for Dublin. This regular feature will return once we return to student accommodation at future Meetings.

Talking of which, the next meeting of our Group is at UMDS on 7-8 November 1997 where Professor Abe Guz will give a Designated Lecture entitled 'Higher Contol of Breathing - A Neglected Subject'. We then meet again at Liverpool in April 1998 where we have been awarded a round of the Pfizer Prize. All graduate students working in the area of respiratory physiology are strongly recommended to submit a Communication for consideration (see page 171 The Grey Book for details). See you at one of these or perhaps at Bristol where Julian Paton has organised an excellent-looking symposium on "Maturation, Modulation and Plasticity in Cardiorespiratory Control".

Prem Kumar

SENSORIMOTOR CONTROL

There will be plenty to keep us busy this Autumn with two Designated Sessions of the Group and a symposium now arranged.

The next Session of the Group will take place at the Bristol Meeting at the beginning of September. The Programme for this Meeting will have accompanied this Magazine and you will see that Richard Apps has organised a symposium on "Gating of Transmission in Sensorimotor Paths" to be held the day before the main Meeting.

There will also be a Session of the Group at the St Thomas' Meeting in November, which may be the last Physiological Society Meeting to be held at the Sherrington School of Physiology (deadline for submission of Communications, Thursday 7 August). At this Meeting Arthur Prochazka (Edmonton, Canada) will be giving a Designated Lecture to the Group and Tony Taylor will be delivering a Sherrington

Lecture. By the time this Magazine appears you should have received further details of this Meeting, including lecture titles, by email. If you have not received an email with information on the Sensorimotor Control Group then you are not currently registered with the Group and/or have not provided the Society with an email address. If you wish to be added to the email list then contact Charlotte Parry at the Society's Administration Office (tel: (0171) 631 1458, email: cparry@physoc.org).

For 1998 I have asked for Sessions of the Sensorimotor Control Group at the Liverpool Meeting in April and at the Cardiff Meeting in December.

John Riddell

SENSORY FUNCTIONS

Professor Peter Dallos

Bristol Meeting

The Sensory Functions Group will be holding a Designated Session at the Bristol Meeting. The highlight will be a lecture by Professor Peter Dallos, on "Outer hair cells and amplification in the cochlea". Peter Dallos was born in Hungary, but has lived in the USA for more than forty years. He currently holds the titles of John Evans Professor of Neuroscience, Hugh Knowles Professor of Audiology and Professor of Otolaryngology and Biomedical Engineering at Northwestern University. He is a former President of the Association for Research in Otolaryngology (ARO) and has been awarded numerous international prizes and medals. These include the Guggenheim Fellowship, Beltone Award, Amplifon International Prize, Award of Merit from the ARO, Honours of the Association from the American Speech, Language and Hearing Association, von Békésy Medal of the Acoustical Society of America, Sigma Xi Distinguished National Lectureship and the Acta Otolaryngologica International Prize. He is also founding Editor-in-Chief of Auditory Neuroscience and is himself the editor of three books and about 130 research papers.

Cambridge Meeting

A Designated Session on Sensory Functions will also be held at The Physiological Society Meeting at Cambridge, on Monday 15 - Wednesday 17 December 1997. This Meeting will include a one-day Research Symposium entitled "Peripheral and Central Mechanisms of Sensory Coding", on Monday 15 December 1997. The local organisers are David Tolhurst, Hugh Matthews and Ian Winter. The full programme for the symposium, which includes speakers from the USA and from Europe, is as follows:

Johannes Reisert, Physiological Laboratory, University of Cambridge
Odorant responses and adaptation in isolated frog olfactory receptor cells

Anna Menini, University of Genoa
Properties and mechanism of odorant adaptation in isolated olfactory receptor cells

Leon Lagnado, MRC Laboratory of Molecular Biology, Cambridge
Exocytosis at the ribbon synapse of retinal bipolar cells

Simon Laughlin, Department of Zoology, Cambridge
Visual ecology in the time domain

Clay Reid, Department of Neurobiology, Harvard Medical School
Specificity of feedforward connections in the retino-geniculo-cortical pathway

Adam Sillito, Department of Visual Science, Institute of Ophthalmology, London
Context-dependent processing and feedback in primate V1

Wolf Singer, Max-Planck-Institut fuer Hirnforschung, Frankfurt/Main
The role of precise timing and response synchronization in sensory processing

Alan Palmer, MRC Institute of Hearing Research, Nottingham
Segregation of sound sources: are two ears better than one?

Nobuo Suga, Department of Biology, Washington University, St Louis
Egocentric selection by the corticofugal system for processing auditory information

There will be a Pfizer Prize round associated with the Sensory Functions Session for the best Oral presentation made by a postgraduate student. I hope that this, together with the very impressive line up of symposium speakers, will encourage a high level of attendance and a good spread of abstracts, which can be on any aspect of peripheral or central sensory processing. Abstracts should be submitted for the Cambridge Meeting between Monday 1 and Thursday 11 September.

Andy King

Smooth Muscle

Please don't forget the forthcoming Smooth Muscle Sessions. Firstly we shall be pleased to welcome you all here at the UMDS (St Thomas' Hospital) in November. This is going to be a big Meeting with lots of opportunity for interaction - so do come. We shall also be having a business meeting to discuss the future of the Group and in particular replacement convenor/s for Jeremy and Lucilla. Any nominations to Lucilla Poston (l.poston:@umds.ac.uk) please. In January we shall be having a 'below the belt' Designated Meeting with the Urological Society (Guy's Hospital, January 7-9, 1998) at which smooth muscle abstracts on myometrium and urinary tract will be particularly welcome.

Jeremy Ward and Lucilla Poston

SOMATOSENSORY PHYSIOLOGY

I hope a lot of us will be in Bristol for our Session at the late summer Meeting. There are no special events organised but it is always a good place to go. The Group will convene at two successive Meetings this year. I am organising a symposium entitled "Parallel Regulation of Somatosensory Processing with other Physiological Systems" for the St Thomas' Meeting. It will take place on Thursday 6 November, the day before the Meeting proper, within which we will be running a regular SIG Session. I have also put up our SIG to compete for a Pfizer prize at St.Thomas', so you should be rolling out your star post-grads for this event! The abstract submission dates for this Meeting are Monday 28 July - Thursday 7 August. Next year I have arranged for Sessions at the Liverpool Meeting in April and at Cardiff in December.

Somatosensory processing is not something which goes on in isolation from other physiological functions. Indeed, the systems which modify transmission through sensory pathways are usually part of a coordinated, whole body response to a particular set of circumstances. The speakers at the St Thomas' symposium will look at how the somatosensory system is controlled within the framework of other physiological regulatory mechanisms. Co-control has been most extensively studied in the context of defence or alerting responses, in which cardiovascular and sensory systems show adaptive changes which have evolved to enhance the chances of survival in threatening situations. John Coote and Thelma Lovick (Birmingham), Peter Redgrave (Sheffield) and Alex Waters (Bristol) will each deal with various aspects of the physiological basis of defensive behaviour. Alan Randich (Mobile) will continue with the cardiovascular theme by looking at interactions between vagal afferents and nociceptive processing. Other speakers will be Peter Thoren (Stockholm), who will deal with the effects of exercise on sensory and immune systems; Steve McMahon (St Thomas') talking on co-regulation of sensory and autonomic neurones by neurotrophins; and Pat Wall (St Thomas'), who will cover presynaptic gating of parallel inputs to spinal sensory and motor networks. It will be a good day's science, please try to come along.

I look forward to seeing you all in Bristol and London.

Rob Clarke

Meeting at Guy's Hospital London, 7-9 January 1998

This Meeting is being held in association with The Urological Research Society and includes a symposium on the 8-9 January:

"The Physiology and Pathophysiology of the Lower Urinary Tract"

Speakers include:

K-E Andersson	(Lund, Sweden),
A Brading	(Oxford),
M Craggs	(London),
C Fry	(London),
R Levin	(Albany, USA),
J Morrison	(Leeds),
W Schafer	(Aachen, Germany),
W Steers	(Charlottesville, USA)

Oral and Poster Communications are welcomed on all aspects of urological and physiological sciences. Communications should be submitted between Monday 29 September and Thursday 9 October 1997.

Chris Fry
Meetings Secretary

MAGAZINE SURVEY

Dear Readers,

Thank you to all the members of the Physiological Society who completed and returned the Magazine survey we sent out in February. While we received 186 replies this only represents a 7% response rate of the 2,669 numbers of questionnaires dispatched from CUP. So analysis of the survey does not necessarily reflect a consensus view of the Society Membership. I suspect also, that results will be biased towards those members who are particularly interested in the Magazine and so more likely to reply to the survey. Thus 73% of respondents said they read almost all or at least more than half of the Magazine and the comments given at the end of the questionnaire were largely enthusiastic and complimentary. One respondent did complain about the 'gaudy' colour of the questionnaire but according to reliable authority I understand brightest is best if you want anyone to take notice and not simply 'bin it' with the rest of the junk mail. However, I thought it might still be worthwhile to summarize the results.

Most respondents (88%) thought that four issues of the Magazine each year was enough and only 12% wanted to receive more issues. (As Editor I must confess to being relieved at this response). In the next question readers were asked to rate the different sections of the Magazine. The highest rated section was Science News and Views with 64% rating it as 'very interesting' and 31% as 'interesting'. The remainder scored it as 'slightly interesting' or 'not at all interesting'. Some people commented that they would like to see more reviews, others that the topics should be more broadly based. The lowest rated section was Journal Contents with 42% readers scoring it as only slightly or not at all interesting. One respondent commented "Dump the Journal Contents". At the last Magazine Sub-Committee meeting we discussed whether the Journal Contents should be discontinued and now they are available electronically (http://physiology.cup.cam.ac.uk) the decision has been taken to 'dump' them.

The ratings for other sections of the Magazine were comparable. An average of 22% readers rated other sections as very interesting, 40% interesting, 24% slightly interesting and 10% not at all interesting. 91% of readers thought that the length of the articles were 'about right'.

Some of the comments are worth noting. Members working abroad and foreign members found that the Magazine "kept them in touch with Physiology in the UK" although one member felt that there should be "more relevant articles/news/sponsorship programmes for third world physiologists". Several respondents commented that they would like to see more historical material, reminiscences and vignettes and others wanted to encourage more letters from Members and Affiliates. Others asked what had happened to comparative and applied physiology. Popular suggestions for articles were on teaching (including CAL) and training and careers in Physiology. Other ideas included descriptions of classic physiological experiments, cautionary tales in physiology, pros and cons of on-line publication, activities the Committee is pursuing on the political front and new techniques in physiology.

So, if any of these comments or proposals stimulates a small spark of enthusiasm for putting knowledge and thoughts into words, please get in touch. I am always keen to find potential contributors so that the Magazine can represent the activities and interests of all Members and Affiliates.

Finally on behalf of all members of the Magazine Sub-Committee I would like to thank Valerie Cox for all her hard work and contributions to the Magazine Editorial Group over the last three years. She has not only commissioned numerous interesting articles but also took complete responsibility in ensuring that the articles reached the Editorial Office by the deadline dates. Her place on the Sub-Committee (Young Physiologists) has been replaced by Annick Moon, so if any Affiliate or Associate members would like to see some particular subject covered in the Magazine Annick can be reached at Department of Surgery, Medical School, Framilington Place, Newcastle Upon Tyne, NE2 4HH, Fax: 0191 2226988 or email: Annick.Moon@newcastle.ac.uk.

Saffron Whitehead

LOST PROPERTY

A personal organiser was found after the Ceili at the Dublin meeting. The owner can reclaim it by contacting Keith Newton at the London Administration Office on Tel: 0171 631 1457 or Fax: 0171 631 1462 and confirming a few details as proof of ownership.

COLOUR CONTRASTS

Dear Editor,

We write to draw to your attention an interesting addition to the panoply of self-destructive behaviour patterns carried out by scientists. A typical example is provided by the person who has spent months or even years designing, executing and then analyzing experiments. They then spend many hours perfecting their seminar or Physiological Society Communication only to render the whole exercise meaningless with the use of colour slides.

We are sure that colour can be very helpful. (But please remember that about 8% of males have some form of abnormal colour vision). However, as used by many scientists it is a disaster. The most common mistake is to assume that whatever is visible on the computer monitor will also be seen in the lecture theatre. This is rarely the case: unless the room can be completely blacked out (in which case nobody can take notes) and the useful contrast in colour slides will be much less than in black and white. If you do manage to get the room dark enough to show the colour slide adequately, then your talk may be inaudible over the sound of snoring.

Of course, you may really want to hide your data. If so, try a very dark blue background with red lettering and (for the really troublesome slides) pale green lines on the universal blue background.

David Eisner
Stephen O'Neill
Dept of Veterinary Preclinical Sciences
University of Liverpool

HARKING BACK TO PAST GLORIES

Dear Editor,

Physiological Society Magazine

I don't want to create an unhelpful rumpus by writing a "letter to the editor" but can I nonetheless say how disappointed I was to see that 12 out of 27 text pages in the Summer Edition focus on physiological history. What sort of impression of physiology does that give to members? Surely the Magazine must present physiology as an exciting, modern, relevant science, not hark back to past glories. I don't underestimate the difficulties of being Magazine Editor so please be assured my comments are meant to be constructive.

Maynard Case
School of Biological Sciences
University of Manchester

J S ALEXANDROWICZ

Dear Editor,

I would like to say how much I enjoyed the Summer 1997 edition of the Magazine and also the other issues! I spent one week at the Plymouth Laboratory in 1953, learning the methylene blue staining technique from J S Alexandrowicz. What a marvellous person! I hope that in a future issue of the Magazine you might find room for an article on him. I only know part of his story but that is fascinating enough.

W Burke
Emeritus Professor of Physiology
The University of Sydney

THIRD WORLD CONGRESS OF BIOMECHANICS WCB'98

You are cordially invited to the The Third World Congress of Biomechanics, which is authorised by the World Council for Biomechanics (formerly the World Committee for Biomechanics).

Topics covered by the Congress range from Cardiovascular and Respiratory Biomechanics, Spine and Head Biomechanics, Artificial Organs and Implants, Physical Activities and Sports Biomechanics.

For further information and registration forms please contact:

Congress Office
WCB'98 Congress Office
Biomechanics Laboratory
Department of Mechanical Engineering
Faculty of Engineering Science
Osaka University
Toyonaka
Osaka 560
Japan

Fax: +81-6-850-6171, 6182, or 6212
E-mail: office@wcb98.me.es.osaka-u.ac.jp
URL: http://wcb98.me.es.osaka-u.ac.jp/

CLONING IN ON CHANNELS AND DISEASE

Stanley White explains how molecular genetics demonstrates the physiological role of known membrane proteins and "simplifies" a complex renal syndrome.

Over the past five years there has been frenetic progress in the molecular cloning and functional characterisation of plasma membrane channels and transporter proteins from renal epithelial cells. Recent genetic analysis has pointed to the involvement of specific gene mutations in disease processes and has also demonstrated the role of such proteins in normal renal function.

Normal potassium (K^+) handling in the thick ascending limb (TAL) and distal convoluted tubule (DCT)

In the loop of Henle, K^+ is reabsorbed from the ascending limb. Uptake of K^+ occurs across the apical membrane against the electrochemical gradient via an electroneutral tri-porter, which requires one Na^+, one K^+ and two chloride (Cl^-) ions (Fig 1). Loop diuretics inhibit this protein. The driving force for this secondary active transport of K^+ is provided by active Na^+ extrusion across the basolateral membrane via the Na^+-K^+ -ATPase. Some of the K^+ recycles across the apical membrane via K^+ selective channels. This recycling maintains the supply of K^+ to the tri-porter thus sustaining salt reabsorption. In the DCT, Na^+ reabsorption occurs via a cotransporter that requires one Na^+ and one Cl^- ion (Fig 1). This process serves to maintain the luminal hypotonicity generated by the TAL. The cotransporter is not K^+ dependent and is the target of thiazide diuretics. Potassium secretion also occurs in the DCT, primarily via a K^+-Cl^- cotransporter, but there is also evidence that K^+ channels are involved. Diuretics which inhibit salt reabsorption in the TAL or DCT cause an increase in urinary K^+ excretion, since its uptake into the cell is blocked, but secretion continues unopposed.

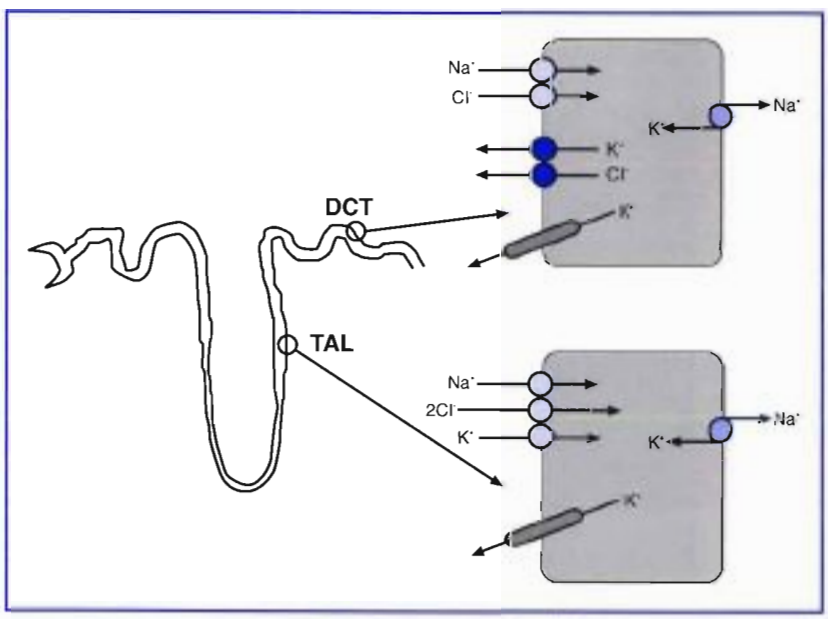


Fig 1. Current simplified models of salt transport in the thick ascending limb and distal convoluted tubule.

Cloning of transporters and channels from the distal nephron

Our knowledge of channels and transporters in the kidney is expanding rapidly. An inwardly rectifying K^+ (IRK) channel family (ROMK) has been cloned from rat and human kidney. These channels have low unitary conductance, high calcium and voltage independent open probability and are activated by micromolar concentrations of ATP and protein kinase A. ROMK1 was the first member of the IRK family to be isolated. It consists of two (M1 and M2) trans-membrane-spanning domains that surround a segment, which is homologous to the well-characterised H5, pore domain of voltage-gated ion channels (Fig 2). In my laboratory, we have shown that ROMK protein is located at the apical membrane of distal nephron cells (Fig 3) including TAL, DCT and principal cells of the cortical collecting duct. The location of ROMK protein is consistent with the idea that this family of proteins is involved in the secretion of K^+.

Both the thiazide-sensitive Na^+-Cl^- cotransporter (TSC) and the loop diuretic sensitive Na^+ - K^+ - 2 Cl^- cotransporter (NKCC2) have also been cloned from mammalian kidney. Despite differing ionic selectivity and sensitivities to diuretics, these proteins share about 60% homology at the amino acid level. The encoded proteins comprise 1002 (TSC) and 1095 (NKCC2) amino acids and both posses 12 potential transmembrane spanning domains (Fig 4). TSC is expressed in outer and mid cortex, while NKCC2 is expressed predominantly in outer medulla and at lower levels in cortex and inner medulla.

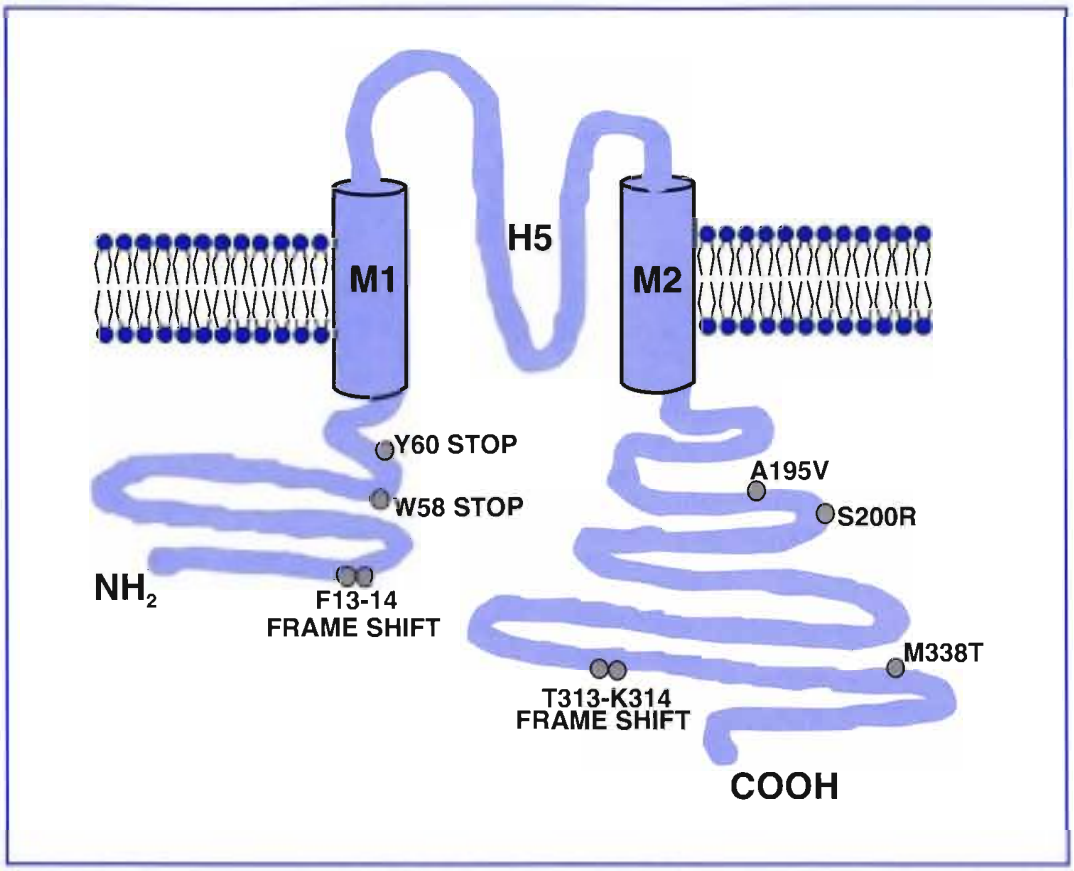


Fig 2. Proposed model of ROMK with associated mutations and consequences in Bartter's syndrome. Single letter amino acid codes are used. Adapted from Hebert (1995) and Simon et al. (1996c).

Bartter's syndrome

During the early 1960s it was found that in some neonates showing failure to thrive, muscle weakness, and polyuria there was an associated hypokalaemic metabolic alkalosis. Plasma renin and aldosterone were elevated but blood pressure was normal or even low. These patients were also hypercalciuric and often-displayed nephrocalcinosis. This disorder is known as Bartter's syndrome. A variant condition, Gitelman's syndrome is associated with late childhood or adult onset of neurological symptoms, polyuria and hypokalaemic alkalosis, but with hypocalciuria and hypomagnesaemia. The estimated frequency of heterozygotes for Gitelman's syndrome may be as high as one per cent.

The complicated pathophysiology of these two disorders suggests that the causes may be multifactorial. The similarity between the symptoms of Bartter's syndrome and those of loop diuretic abuse (often the cause of apparent Bartter's presentations) led to the idea that the basis of the disorder was a defect in salt reabsorption by the loop of Henle. Bartter's original hypothesis was that the condition resulted from a resistance to the pressor effects of angiotensin II, leading to chronic over stimulation of the renin-angiotensin system but relative hypotension. The consequent rise in plasma aldosterone would lead to renal K^+ loss and metabolic alkalosis. However, chemical blockade of adrenal release of aldosterone or even bilateral adrenalectomy was only partially effective in correcting the renal

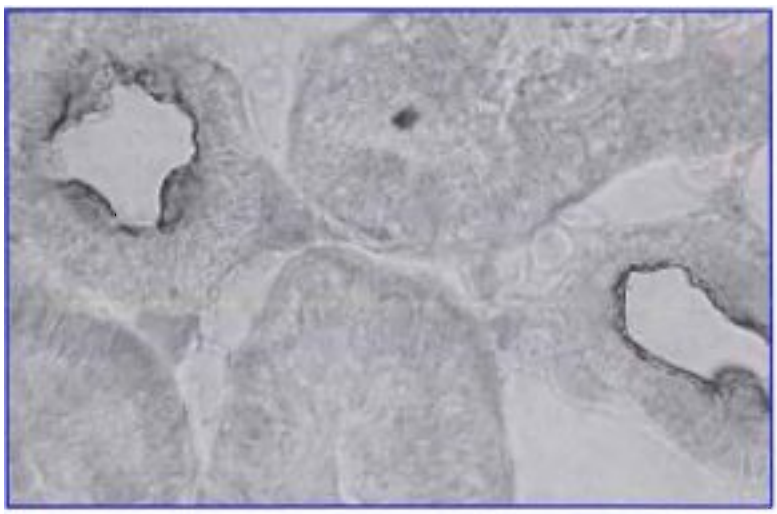


Fig 3. Horseradish Peroxidase visualised staining of an anti-ROMK antibody in Apical membrane of rat kidney distal nephron.

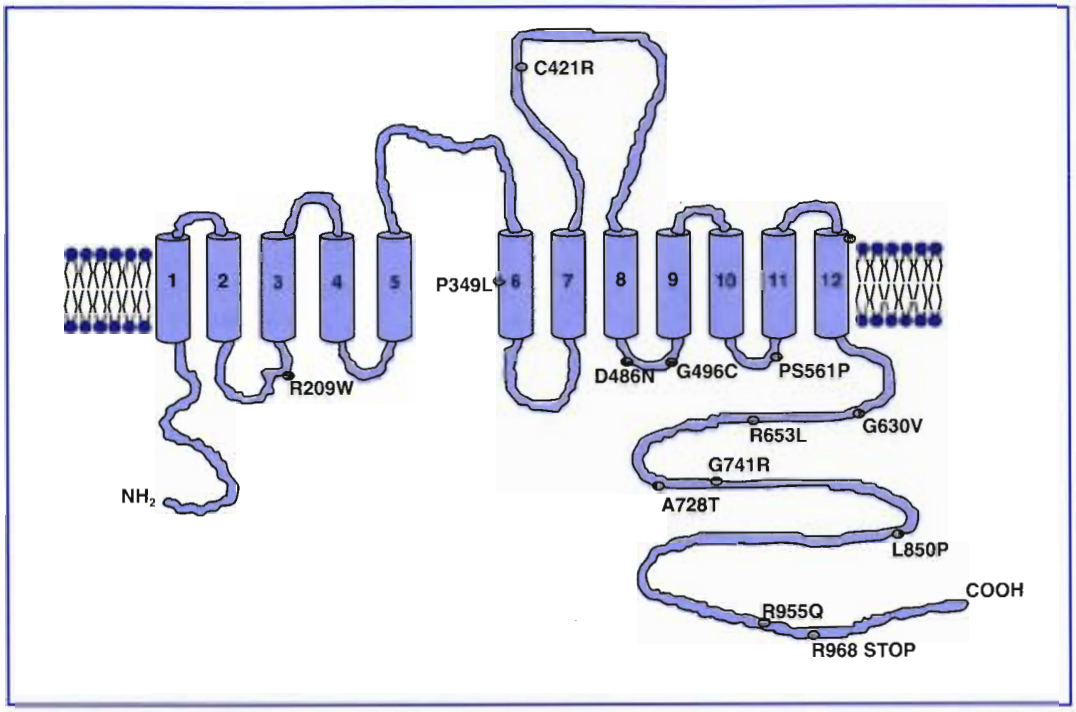


Fig 4. Proposed model of TSC with some associated mutations in Gitelman's syndrome. The consequences are shown as single letter amino acid code. Adapted from Gamba et al (1994) and Simon, et al (1996a).

wasting of K^+. Other ideas centred on the observed increased levels of prostaglandins in plasma and urine of Bartter's patients. The vasodilatory effects of prostaglandins could be responsible for the hypotension and secondary hyperreninaemia. Inhibition of salt reabsorption in the loop of Henle by prostaglandins would increase distal delivery of NaCl. This, in the presence of hyperaldosteronism would stimulate distal Na^+ reabsorption and augment secretion of K^+ and hydrogen ions.

Mutations in TSC, NKCC2 and ROMK are associated with Bartter and Gitelman's syndromes

Recent work from Richard Lifton's laboratory at Yale suggests that both disorders can be explained by mutations in the cotransporters or ROMK. Bartter's syndrome is associated either with mutations in the gene encoding NKCC2 on chromosome 15 or with ROMK on chromosome 11. The mutations in NKCC2 are of highly conserved amino acids or result in frame shifts. Mutations in ROMK (Fig 2) produce frame shifts resulting in premature terminations of the protein, and substitutions resulting in loss of conserved amino acids such as serine at exon 200 which lies within a Protein Kinase A phosphorylation site.

The gene encoding Gitelman's syndrome maps to a region of chromosome 16, which contains the TSC gene. Mutation analysis has so far revealed a variety of effects (Fig 4); most mutations alter the charge of amino acids or remove proline residues. Others delete heavily conserved amino acids which lie in a protein kinase C phosphorylation domain or introduce premature stop codons causing truncation of the carboxy terminus. These findings underscore the importance of the kidneys in control of blood pressure. Malfunction of these proteins lead to defective NaCl reabsorption in the distal nephron, resulting in renal salt wasting, hypovolaemia and hypotension. The details of the mechanisms by which these gene mutations lead to loss of protein function await detailed site - directed mutagenic studies in combination with heterologous expression and targeted knockout approaches. Exciting times lie ahead!

Stanley White
Department of Biomedical Science
The University of Sheffield

References:

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Simon, D B *et al.* (1996a) *Nature Genetics* **12:** 24-30.

Simon, D B *et al.* (1996b) *Nature Genetics* **13:** 183-188.

Simon, D B *et al.* (1996c) *Nature Genetics* **14:** 152-156.

VOLTAGE-GATED SODIUM CHANNELS: CLONES WITHOUT BONES

Molecular biology has revealed a large family of voltage-gated sodium channels, some of which have been identified physiologically. A "wonderful example of the two-way street of science". But what about all the other channels which have been cloned? Do they have other functions apart from generating action potentials? Reggie Docherty explains what we know and don't know about the different isoforms of sodium channels.

The action potential is a 'sacred cow' of physiology. No physiologist would challenge the proposition that activation of voltage-gated sodium channels is the main mechanism underlying the upstroke of the action potential in mammalian neurones or in cardiac or skeletal muscle cells. There is no compelling reason to do so. But what of the reverse proposition, that the physiological role of voltage-gated sodium channels is the generation of action potentials. This too is often held to be true without much thought being given to the matter. There is little doubt that the sodium channels give rise to action potentials - but is that all that they do ? The answer to this question is far from clear.

The efforts of molecular biologists over the past ten years or so have confirmed suspicions that the voltage-gated sodium channel is not one but a family of molecules. Indeed, they have shown us that voltage-gated sodium channels are legion. There are at least nine distinct genes for sodium channel α sub-units in mammals. The α sub-units are single, large glycoprotein (protein MW of about 200 - 250 kD) molecules with a common, characteristic structural topology incorporating a voltage-gated sodium selective pore. Two accessory sub-units (β1 in brain and muscle and β2 in brain) have been identified. These are each about a tenth the size of the pore-forming α sub-unit. The β sub-units may influence the kinetics of channels or their location in the membrane but they are not a prerequisite for expression of voltage-gated channel activity. Only the α sub-units are considered in the discussion below.

The table lists the accession numbers for a very limited selection of records from the EMBL / GenBank databases which contain sequence and bibliographic information about sodium channels. The records contain cDNA and predicted protein sequences for mRNAs for sodium channel isoforms encoded by 9 distinct genes. A fairly easy way to access information of this type is to register (usually free to academics) with the human genome mapping project at www.hgmp.mrc.ac.uk. A variety of other useful facilities and links are available at this site which is well worth a visit.

Accession number	species	channel type	description
X03638	rat	B1	Brain 1 (TTX-sensitive)
X03639	rat	B2	Brain 2 (TTX-sensitive)
Y00766	rat	B3	Brain 3 (TTX-sensitive)
M26643	rat	SkM1	Skeletal muscle 1 (TTX-sensitive)
M27902	rat	H1	Heart 1 (TTX-resistant; also found in developing + denervated skeletal muscle)
L39018	rat	NaCh6	Sodium channel 6
U79568* U35238 X82835	rat rabbit human	PN1 NaS NE-Na	Peripheral nerve 1, Schwann cell sodium channel and neuroendocrine sodium channel (TTX-sensitive)
U53833 X92184	rat rat	PN3 SNS	Sensory neuron sodium channel (TTX-insensitive)
M96578*	rat	NaG	Glial sodium channel

* partial sequence data

Matching molecules to mechanisms in muscle

The physiology and molecular biology of sodium channels in skeletal muscle complement each other well. It has been known for a long time that skeletal muscle cells express two distinct types of sodium channel activity. They are the rapidly activating TTX-sensitive channels of normally innervated, adult skeletal muscle and the relatively slow TTX-resistant channels seen in developing and denervated muscle. cDNAs encoding corresponding proteins with appropriate properties, named respectively SkM1 and SkM2 (or μ1 and μ2 for channels from human tissue), have been cloned. Thus, in muscle, the findings of physiology and molecular biology converge and present a good working model, at the molecular level, of the role of identified sodium channels in skeletal muscle excitability. So much so that significant progress has been made in our understanding of the pathophysiology of a variety of congenital muscular diseases which have been traced to mutations in the SkM1 gene (located on chromosome 17). This 'wonderful example of the two-way street of science' has recently been the subject of an excellent and comprehensive review article, from which I quote, by R L Barchi (1995).

Clones for cardiac currents

What about the heart? As for studies on skeletal muscle, the findings of physiology and molecular biology are convergent. The upstroke of the action potential and the sodium channel type which gives rise to this event in non-nodal cardiac muscle has slow kinetics and is resistant to TTX. A channel with the properties expected of a cardiac sodium channel has been cloned. This channel was first identified in cardiac tissue and is usually named H1. It turns out that H1 is the same as SkM2, the TTX resistant channel of developing skeletal muscle, which is interesting since the cellular mechanisms controlling expression of the H1 protein in the two tissues must be quite different. The general consensus in the literature points to H1 as the channel responsible for the upstroke of the cardiac action potential (see Fozzard & Hanck, 1996). A congenital cardiac dysrhythmia characterized by a long QT interval occurs due to mutations in the human H1 gene, which is located on chromosome 3. Thus the convergence of physiology and molecular biology again predicates a significant advance in our understanding of pathophysiological mechanisms.

There are a few untidy ends in the heart story. At least three other sodium channel isoforms are expressed in cardiac tissues albeit at lower levels than H1. First there is B1 (brain 1, see below) which is a TTX-sensitive channel, closely related to SkM1, but found predominantly in neurones (see below). The two others are called $Na_v2.1$ and CSC-1. Neither $Na_v2.1$ nor CSC-1 have been expressed in oocytes or other heterologous systems so their identification as functioning ion channels is uncertain. If corresponding proteins are expressed in cardiac muscle then their function is not known.

Bewildered by the brain

Numa, Noda and their colleagues in Japan (see reviews by Noda, 1993; Catterall, 1995) have cloned three voltage-gated sodium channel isoforms from rat brain called B1, B2 and B3. In humans, the genes for B1, B2 and B3 are located on chromosome 2. There is also a splice variant of B2 called B2a and growing evidence

To a molecular biologist

When you scan a nucleotide sequence or admire your banded gels, do you feel the same as we do when recording from our cells ?

When you tune your thermal cycler to get a crisp reaction, do you feel like us, when we get the buzz of a perfect leak subtraction ?

When you clone with RACE does your pulse keep pace, does your data come slow or like rain?
When you screw up your buffer does your boss make you suffer, And make you do it all over again ?

Can you persuade as much pleasure from a molecular measure as may be prised from a perfect patch ?
Do you curse and swear when there's nobody there and your gel bands and sequence don't match ?

Your gel and my cell must have the same tale to tell,
Their beauty is in the eye of the beholder.
I think we're the same, each playing the same game,
though I confess, I suspect, I'm much older.

We're now in a world where receptors abound and with ionic channels so thick on the ground, that it's hard to know which ones go where.
These homologous clones need physiological bones and it's our job to lay those bones bare.

Reggie Docherty

that alternative splicing may occur with all the sodium channel genes implying even greater channel diversity. These genes encode transcripts for sodium channel isoforms which are closely related to SkM1 and are TTX-sensitive. Transcripts for B1, B2 and B3 are found predominantly in neurones but may also be present at low levels in astrocytes and other non-excitable cells. Each transcript has a unique pattern of expression in CNS tissue. Their expression is developmentally regulated and is sensitive to tissue injury.

In addition to these 'neuronal' sodium channel isoforms two other putative sodium channel isoforms have been cloned whose transcripts are present in CNS tissue. One is NaCh6 which is expressed abundantly in neurones, astrocytes and Schwann cells. The other is NaG (closely related to $Na_v2.1$ from heart) which is found predominantly in glial cells. It is by no means clear which of the various transcripts for sodium channel isoforms are expressed as functional channels in CNS tissue. Nevertheless, if the only physiological role of voltage-gated sodium channels is the generation of action potentials then neurones are spoiled for choice and glia are working under a terrible misapprehension.

Perplexed in the Periphery

As well as the sodium channel isoforms found in the CNS (B1, B2, B3, NaCh6 and possibly NaG) peripheral neurones also express PN1. This is a TTX-sensitive channel which is the same (or the rat homologue) as NaS (cloned from rabbit Schwann cells) and NE-Na (from human neuroendocrine cells). The PN1 channel is expressed abundantly in sensory neurones and postganglionic sympathetic neurones. Sensory neurones have the privilege of an additional cell-specific isoform which is TTX-insensitive (but distinct from H1 - see above) and called either SNS or PN3. This last, the SNS/PN3 channel, is likely to be responsible for the TTX-resistant sodium channels in small diameter sensory neurones. Evidently the biology of sodium channels in peripheral neurones is at least as complicated as in their CNS cousins. With the possible exception of SNS/PN3 the channel isoform(s) responsible for physiologically identified voltage-dependent sodium channel activity in 'real' cells is not known at this time.

Identifying the particular sodium channel isoforms which are operational in neurones and glia in the brain and peripheral nervous system and distinguishing between translational and post-translational mechanisms controlling excitability and function presents a major challenge to neurophysiologists. Unless specific pharmacological probes become available this challenge can only be met by applying molecular techniques in a physiological context.

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Further reading:

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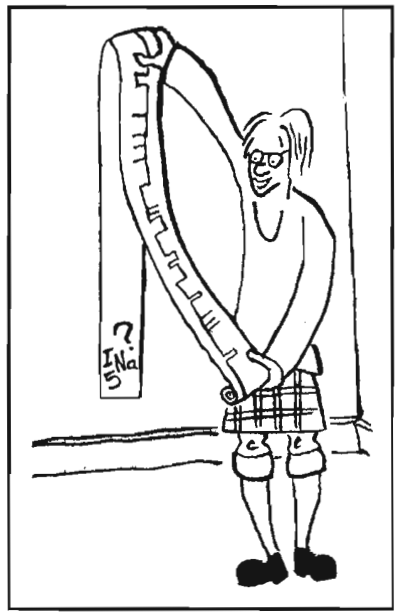

SEDA - PROMOTING IMPROVED STANDARDS IN TEACHING AND TEACHERS

Professor Phil Race began life as a scientist but soon moved into the field of Educational Development. In 1995 he took early retirement from his post as Professor of Educational Development at the University of Glamorgan. During his 24 years in Wales he led the development of one of the first SEDA-recognised programmes for lecturers. He now divides his time between leading the Certificate in Teaching in Higher Education Programme at Durham University, writing books on teaching and learning for both students and educators and organising various training workshops all over the country.

As with many other disciplines, a number of University Departments of Physiology have taken steps towards improving the learning experience of their students. The fact that a special interest group in Teaching Physiology was set up within the Physiological Society last year shows that your discipline is taking this matter seriously. This article looks at the role that SEDA (The Staff and Educational Development Association) can play in improving teaching quality.

Changing Universities

A Physiology degree course usually lasts three years, during which time students learn both basics of how the body systems function and state-of-the-art aspects of fields in which their lecturers are leading specialists. In the last two decades there have been significant changes to students' learning experiences at University, caused by factors such as:

- larger class sizes as a consequence of 30% of 18-21 year olds now participating in higher education.
- less funding for Universities, which results in fewer lecturers and tutors per student and a decrease in individual attention from staff.
- an increase in the financial pressure placed on students, many more of whom now take part time jobs to help them fund their studies.

There are two main ways that Universities are trying to help students to overcome the effects of such changes on their learning; improving the teaching quality that students receive and helping students themselves to become more skilled at the business of managing their own learning and preparing for assessment.

Can anyone who's an expert in a subject teach?

Until relatively recently, there was little thought given to the need to train university lecturers in teaching methods. Lecturers are employed on the basis of their research record, which means emphasis is placed on their research publications and past record in attracting grant funding. It was widely assumed that anyone bright enough to be appointed to a lecturing post was up to the challenge of putting the subject across to students. Many lecturers can remember well their first lectures and tutorials when they were effectively plunged in at the deep end, and exposed to groups of students without having received any advice, training or support regarding how to teach. Perhaps this situation worked without major disasters because there were then fewer students at university and more staff to help the students.

And what about assessment ?

Perhaps the most frightening aspect of all for new lecturers is the moment they find themselves with a red pen in their hands and shoulder for the first time the responsibility for assessing student's work. It is usually not long before some of the assessments they are involved in will influence students degree classification and can therefore make or break a student's ensuing career. Many lecturers remember talking on this responsibility without ever having had any training in how to assess and more important in how to design assessment tasks or exams for the students. Therefore programmes to train lecturers in how to assess fairly, reliably and consistently are long overdue.

Measuring the quality of teaching

For some years the quality of research in universities has been measured by the 'Research Assessment Exercise'. Whether you love them or loath them it is an inescapable fact that the results of this exercise now have a significant bearing on the amount of funding given to individual Departments.

In a similar way we now have Teaching Quality Assessment. This is not really new- the 'New Universities', when they were polytechnics, had very similar inspections

Table 1.

SEDA OBJECTIVES

The applicant should demonstrate they have achieved each of the following outcomes regarding the quality of their teaching:

- Designed a teaching programme from a course outline, document or syllabus.
- Used a wide and appropriate range of teaching and learning methods effectively and efficiently to work with large groups, small groups or one-to-one.
- Provided support to students on academic and pastoral matters.
- Used a wide range of assessment techniques to assess student work and to enable students to monitor their own progress.
- Used a range of self, peer and student monitoring and evaluation techniques.
- Performed effectively the teaching support and academic administrative tasks involved in teaching in their department in their institution.
- Developed personal and professional coping strategies within the constraints and opportunities of their institutional setting.
- Reflected on their own personal and professional practice and development, assessed their future development needs and made a plan for their continuing professional development.

under the auspices of the former Council for National Academic Awards (CNAA). However, for those Physiology Departments based in the 'Old Universities' the advent of teaching quality assessment means that for the first time lecturers are being faced with people from outside who come into their lectures, tutorials and laboratory classes and observe how they teach. The results cannot be ignored as they will have a direct effect on the levels of funding given to departments.

Are courses for University teachers sufficient?

Just attending a course on how to teach well is of limited value. Anyone could duly attend all the sessions in such a course, but remain unchanged regarding the quality of their actual teaching and assessment. It's not really possible to have an 'exam' in how good lecturers are at teaching and assessing. Even if such an exam could be devised, it would be possible for lecturers to swot up on the topics involved, write convincingly about them in the exam room and continue to teach as badly as ever! It would take too long to have someone look at everything that lecturers did after participating in a staff development course, so most universities are moving towards requiring lecturers on such courses to build up a portfolio of evidence of the ways that they approach teaching, learning and assessment. In this way lecturers can show they really have developed the desired skills.

One such course that I have recently been involved in setting up is that leading to the 'Certificate in Teaching in Higher Education' at the University of Durham. This programme for lecturers was introduced in 1996, intended mainly for new teaching staff but open to experienced lecturers as well, if the want to develop their teaching methods and to receive support and feedback on their teaching. The assessment of the course is based on portfolios put together by the participants, showing evidence of the ways in which they approach their teaching and assessment and also of their efforts to gather and analyse feedback from students. The lecturers at Durham have taken a considerable part in the design of the criteria for the assessment of their portfolios. One of their main concerns was that they did not want to have to do a large amount of 'extra work' in their already overcrowded schedules. This was overcome by asking them to include examples of their teaching materials and feedback forms with just a short commentary to lead the assessor through their evidence and to highlight specific problems and their solutions.

SEDA setting consistent standards

In recent years, the majority of universities have introduced induction programmes for new staff, and offer courses that cover the main principles of teaching, learning and assessment. However, the length and content of these courses varies widely between different institutes, and departments also vary in whether they make attendance at such courses compulsory. It is important therefore that there is an external body to ensure that desirable standards are consistently achieved across all the different programmes. Such external recognition will be important for Universities as they become required to show evidence of teaching quality. Accreditation will also allow staff who are moving between institutions to show they have already been trained to an acceptable standard.

Table 2.

SEDA VALUES
Applicants should demonstrate;
• Understanding of how students learn.
• Recognition of individual differences in learning.
• Concern for students' development
• Commitment to scholarship.
• Team working.
• Practising equal opportunities.
• Continued reflection on professional practice.

In the last five years, some significant work has been done towards establishing benchmarks for the quality of teaching and assessment in Universities. Much of the credit for this work is due to SEDA, a professional association to which many individual lecturers subscribe and where most universities are now institutional members. SEDA has developed an accreditation scheme for staff development programmes devised by individual universities or departments. Such programmes are 'recognised' or 'accredited' if it can be demonstrated that the programme produces lecturers who can show in their teaching and assessment that they have achieved the **SEDA objectives** (see Table 1) and are working towards excellence in teaching.

The SEDA recognition scheme also requires accredited staff development programmes to embrace each of a series of underpinning **SEDA values** or principles (see Table 2). These require the applicant to show understanding of the way students learn, including individual differences and potential difficulties. The Lecturer must also show a commitment to continued professional development and a willingness to seek out new ideas and to boldly go on trying new techniques.

Importantly, SEDA recognises that the types of teaching and assessment that are appropriate vary enormously depending on the specific discipline and also on the specific students involved. This is taken into account in any assessments. For example, while lecturers must show that they performed effectively their teaching support and academic administrative tasks, it is specifically stated in the objectives that these tasks should be relevant to the lecturers own department in their own institution. Account is also taken of the fact that in some Departments lecturers may be prevented from trying out new ideas.

At the time of writing this article, well over half of all the universities in the UK have either had their staff training programmes recognised by SEDA or are in the process of working towards such recognition. In addition. institutions in Singapore, Australia and New Zealand are also using the SEDA scheme as a basis for designing the training programmes they provide for teaching staff.

SEDA conferences- a chance to exchange ideas

In addition to accreditation of courses, SEDA also organises conferences on a variety of teaching related topics. This year their Staff and Education Development conference will be held in Birmingham on 1st - 2nd December. It seems highly probable that the Dearing enquiry will address the whole matter of appropriate accreditation both for teaching staff and for external examining. In response to this SEDA has organised two one day workshops entitled 'Staff development after Dearing' the first in York on 27th October and the second on Reading on 10th November.

Read all about it

Some of you may not have the opportunity to attend training courses or conferences on teaching. Others may have already completed such courses and still be looking for more ideas and helpful tips. You may find it helpful to consult some of the many publications aimed at university teachers. If you have a Staff Development Office they may well have library with a selection of books, tapes etc. As you might expect, SEDA produces an impressive range of the usual self help manuals for people wanting to try some different teaching techniques. In addition, SEDA also produces manuals covering more unusual aspects of the teaching and learning process, such as 'Leading Academic Programmes and Courses' and 'Making the Most of the External Examiner' both available in June 1997. Some titles from other sources are also suggested at the end of this article. If anyone feels they could produce a title specifically aimed at teaching and/ or assessing physiology students then contact SEDA - it is always interested in new projects.

SEDA and minimum standard for teaching

For a long time the standard of teaching in higher education has varied enormously between institutions and also between different lecturers in a department. As students and their parents gradually become more and more responsible for providing the funding for courses it is not unreasonable to expect that they, and the government, will want value for money. Minimum standards for teaching quality will be set and SEDA is playing an important role in this process.

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Further reading:

Details of the SEDA Teacher Accreditation Scheme for lecturers in higher education can be obtained from SEDA, Gala house, 3 Raglan Road, Edgbaston, Birmingham, UK., email office@seda.dmon.co.uk or visit their web page on http://www.seda.demon.co.uk for details of conferences and publications.

Details of the issues addressed in teaching quality assessments can be obtained in the 'Quality Assessors Handbook' published by the Higher Education Funding Council for England (HEFCE) and in 'Making the Grade' (UCoSDA) and Loughborough University. Examples of books aiming to help University Staff become better at teaching and assessing include;

- Race P & Brown S (1993). 500 Tips for Tutors, Kogan Page, London.
- Brown S & Race P (1995). Assess your own teaching Quality, Kogan Page, London.
- Brown S, Race P, & Smith B (1996. '500 Tips on Assessment', Kogan Page, London.

Technical and Educational Services produce a whole host of '53 interesting things to do' books (distributed by Plymouth Distribution Ltd, Plymouth) including;

- '253 ideas for your teaching'.
- '53 interesting ways to assess your students'.
- '53 interesting things to do in your lectures'.

The Oxford Centre for Staff Development, Oxford also produce a range of booklets including;

- Strategies for Diversifying assessment in Higher Education.
- Course design for resource based learning in Science.
- Developing student's transferable skills.
- Being an effective academic.

A SHORT HISTORY OF HEARING AND HAIR CELLS

Listening to a Physiological Society communication may trigger off a complicated set of responses (not all of which are fit topics for physiological investigation) but the ability to respond at all depends upon the proper functioning of the auditory system. Most textbooks give a reasonable account of how the inner ear and the auditory pathways operate without emphasising how much significant progress has been made in the past two decades. The problem has been that the inner ear contains small amounts of relatively inaccessible tissue (in the order of 15,000 sensory cells are present in each human cochlea). Choosing another species does not necessarily help, as the scale of the hearing organ of an animal is related to its hearing range (in octaves) rather than to its body size. What has happened since the late 1970's is that the neuroscience techniques to study single cells have developed and the cochlea should now be considered as a fertile ground for the mainstream neuroscientist. The molecular biology has also made enormous strides and, with the ability to work with small amounts of material, we are now on the brink of identifying cochlea-specific genes.

The sensory cell of the auditory (and vestibular) system is the hair cell. Hair cells are neuroepethelial cells with modified villi (termed stereocilia) about 2-6 microns long on their apical surface. When deflected by sound, stereocilia gates the opening of approximately 100 mechanoelectric transducing channels (estimates vary) and the resulting change in potential in the cell leads to controlled transmitter release (glutamate!) from the basal end of the cell. A large part of this picture has resulted from the work on the frog by Hudspeth and Corey and their colleagues in the US; from studies of the turtle by Crawford and Fettiplace in Cambridge; and from Ohmori working on chick hair cells in the Japan. Despite considerable effort and several promising leads, the molecular identity of the mechanoelectric transducer channel is still unknown. The mammalian system has proved yet more intractible because cochlear operation depends upon interaction between the mechanics of the cochlea and the hair cells.

Scanning electron microscopic view of the upper surface of the organ of Corti showing the three rows of outer hair cells, with their characteristic V shaped hair bundles, and one row of inner hair cells with their more linear bundles. Courtesy of David Furness, Department of Communication & Neuroscience, Keele University.

In mammals inner hair cells form the sensory cells and synapse onto the auditory nerve. The first recordings from cochlear inner hair cells with microelectrodes (by Russell and Sellick at Sussex) showed that the organ of Corti interacted with the mechanics of the cochlea as a whole. Subsequent studies of isolated cells, coupled with considerable theoretical effort in modelling, showed that the other population of mammalian hair cells, the outer hair cells, were responsible both for amplifying and altering the incoming sound vibration, allowing much more selective frequency information to be signalled along the nerve. At present, the description of auditory nerve activity in terms of the cellular physiology is reaching a reasonably mature state.

In the UK, research covers all areas of hearing, extending from the molecular basis of hearing through cell biology, cellular physiology, the structure and function of auditory pathways and to the formation of higher centre auditory maps. To list the departments where this work is carried out is open to the charge of selectivity. Despite that caveat, there are groups working on the cochlea and the physiology of the central nervous system at Bristol, Birmingham, Cambridge, Keele, Leeds, Leicester, London, Manchester, Newcastle, Nottingham (where there is the MRC Institute of Hearing Research), Oxford, Southampton and Sussex. But if you really want to know who is doing what and where, keep your eye on the Physiological Society meeting abstracts!

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MECHANOTRANSDUCTION IN SENSORY HAIR CELLS: AN OPEN-AND-SHUT CASE?

The mechanosensitive hair cells of the vertebrate inner ear and lateral line system possess an apical bundle of stereocilia that are arranged in rows of increasing height. The stereocilia are actually modified microvilli rather than true cilia, and contain a core of actin filaments (Fig 1). They behave like stiff rods pivoting around their insertions into the cell when they are deflected (Flock *et al.* 1977). Deflection of the bundle towards the tallest row of stereocilia increases the probability of opening of relatively nonspecific cationic channels located in the bundle whilst deflections in the opposite direction lead to hyperpolarisation (Corey & Hudspeth 1979a). The short time constants of the receptor currents imply that the channels must be mechanically operated (Corey & Hudspeth, 1979b), and have led to the suggestion that each channel is opened directly by a gating spring with an increase in tension caused by deflection towards the tallest stereocilia opening the channels and a reduction in tension produced by stereociliary movement in the opposite direction closing them. For a sustained deflection of the hair bundle, the mechanotransduction current adapts in a way that correlates to mechanical changes in the compliance of the bundle and suggests an element in association with the gating spring that maintains its resting tension but which is adjusted as the tension increases (Howard & Hudspeth 1987).

The tip-link hypothesis

The stereocilia are connected by two types of extracellular cross links; the **lateral** links (Flock *et al.* 1977) which run between the stereociliary shafts, and the **tip links** which run between the tips of the shorter stereocilia and the sides of the taller ones behind (Pickles *et al.* 1984). Pickles and colleagues proposed that the tip links are suitably positioned to act as gating springs, a suggestion that has become known as the tip-link hypothesis. Thus one would expect to find cationic channels at one or other end of the link. However this proved not to be the case.

These mechanotransduction channels are amiloride sensitive and this enabled us to undertake immunocytochemical studies using antibodies to the epithelial Na^+ channel from the kidney. Antibody labelling was not observed at the tip links but just below them and above the lateral links at the point where the shorter stereocilia come into closest proximity with the taller stereocilia (Hackney *et al.* 1992). This labelling is sensitive to other agents known to affect mechanotransduction (Furness *et al.* 1996) and membrane specializations have been observed in this contact region in both mammalian (Fig 1) and reptilian hair cells. This further implies that the mechanotransduction channels may be located in this region rather than at one or other end of the link.

To determine how stereociliary displacement might act upon mechanotransduction channels if they are in the contact region, a two-dimensional kinematic analysis of relative motion has been performed. The analysis assumes that contact between stereocilia is maintained during deflection and uses bundle geometry and dimensions from transmission electron micrographs of guinea-pig cochlear hair cells (Furness *et al.* 1997). It shows that if the channels are located in this position, they could be operated by shear between the sterocilia as efficiently as if they were at the ends of the tip links.

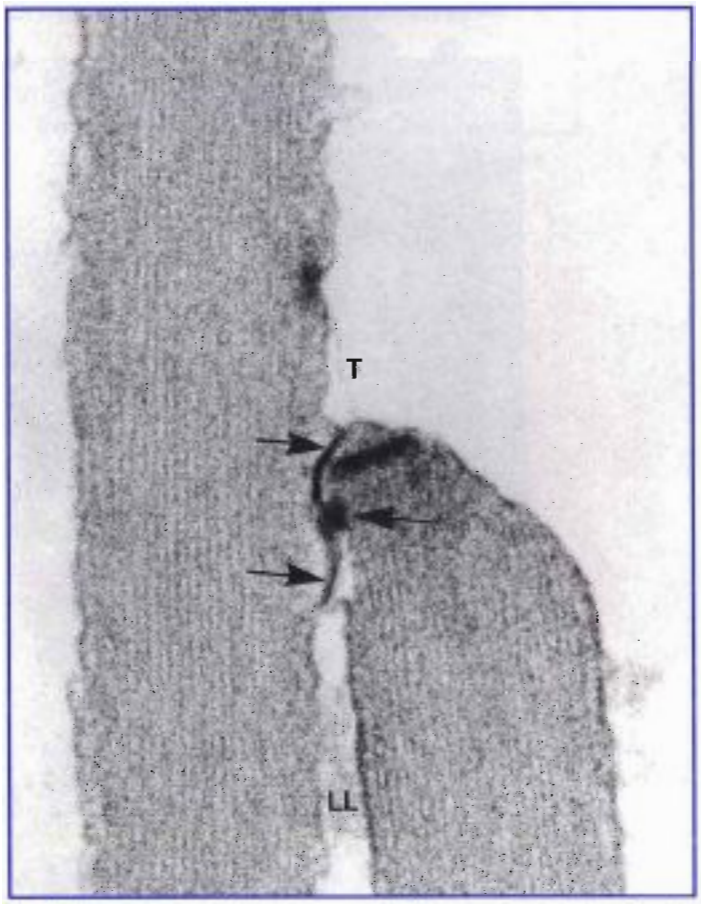

Fig 1. Transmission electron micrograph of longitudinal section through a tall and a short stereocilium on a guinea-pig cochlear hair cell. Note that they contain parallel arrays of actin filaments, and that there is a tip link (T) and some lateral links (LL) running between them. Note also the contact region between them (arrows). (Micrograph taken by Yukio Katori on a recent research visit to Keele from the Department of Otolaryngology, Tohoku University, Sendai, Japan.)

Modifying the hypothesis

If the antibodies to the Na^+ channel are indeed revealing the location of the mechanotransduction channels, rather than some hitherto unexpected cationic channels on the stereocilia, then the tip-link hypothesis requires modification. Rather than being directly responsible for the operation of the channels, the tip links may perhaps act as devices to maintain or adjust the precise position of the stereocilia thus playing the important role in adaptation that has also been proposed for them. Alternatively, stereociliary deflection may not open channels directly at the attachment points of the links but could stretch the membrane between the link insertions and the contact region thus opening mechanotransduction channels somewhat more indirectly than has been previously supposed. Perhaps hair-cell mechanotransduction is not quite an open-and-shut case after all!

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Biomedical Images Collection at the Wellcome Centre

Courtesy of The Wellcome Centre Medical Photography Library

Dr David Furness receives an Award of Excellence at the recent Biomedical Image Award ceremony at the 210 Gallery in the Wellcome Centre. His winning image - a scanning electron microscopic view of a guinea pig cochlea - is part of the new Biomedical Images Collection at the Wellcome Centre Medical Photographic Library. This collection focuses on the best images from modern biomedical research. It includes images obtained during the course of research, as well as pictures of scientists at work and of apparatus and techniques. Contributions are always welcome, especially in the fields of neurology, cardiovascular physiology, genetics and cell biology. Potential contributors should contact Jill Bailey (0171 611 8360, j.bailey@wellcome.ac.uk) or Mark Osmond (0171 611 8347, m.osmond@wellcome.ac.uk). The images are available at cost to academics for study, research or teaching. As with the photolibrary's other collections, of historical and clinical images, enquires about viewing or using images should be directed to 0171 611 8348.

The winning image - Scanning electron microscopic view of a guinea pig cochlea, showing the spiral organ with its rows of sensory hair cells. The whole spiral is only a few millimeters high.

ALL EARS AT BRISTOL

An ear for all

What is so interesting about the inner ear? Is it the astonishing sensitivity to sound across a broad frequency range or the fact that a single cell can detect sound vibrations of less than one nanometer? Could it be that some sensory cells work in reverse to refine the mechanical responses of the basilar membrane? Is it the extraordinary cytoskeletal architecture that governs the mechanics of the sensory epithelium or the genetic programming during development that leads to a cell pattern formation of exquisite precision? In fact the inner ear is a fertile meeting place for cell physiologists, systems physiologists, computer modellers, and molecular and developmental biologists. Research in these converging areas not only works towards the treatment and management of deafness but also illuminates some of the most fundamental aspects of human biology. And they are all brought together in the Department of Physiology at the University of Bristol.

A cell

The mechanism of mechano-electrical transduction by hair cells has challenged physiologists for some years. Although it appears to be the same in all hair cells there are substantial differences between the hearing and balance organs. Appreciation of the beauty of a Mozart concerto demands the highly sophisticated design of the cochlea. 'Heard' through the vestibular system it would probably make you sick. Corné Kros is studying the differences between the two systems at a cellular level by recording receptor currents from the hair cells when the hair bundles are stimulated with a fluid jet (Fig 1). The transducer currents turn out to be larger in cochlear outer hair cells than they are in vestibular hair cells. Moreover, measurements within the nanometer range with a laser interferometer reveal that the cochlear cells respond to much smaller displacements of their hair bundles than the vestibular cells. The cochlear cells thus appear to be more 'highly strung', so it is not simply the design of the organ that matters: a cochlea transplanted with vestibular hair cells would also fail to appreciate the Mozart concerto. Intriguing physiological differences also occur between cells at the high- and low-frequency ends of the cochlea and between cells at different stages of differentiation during development. The results from this work will be essential to our understanding of regeneration and the development of new therapeutic techniques.

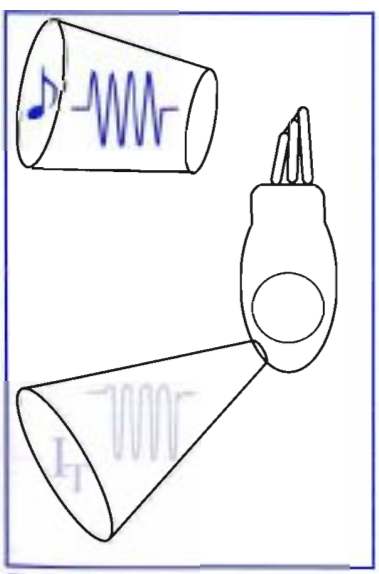

Fig 1. The electrical response (Transducer current I_T) of a hair cell following stimulation of the hair bundle by a fluid jet

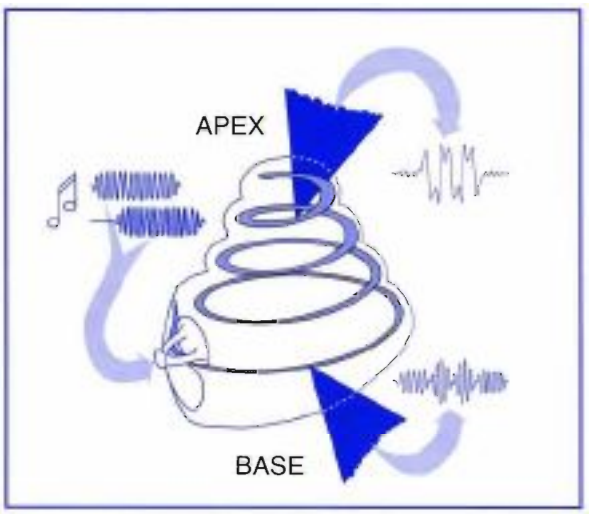

Fig 2. Complex sounds stimulate different responses from the apex and the base of the cochlea.

A system

One highly specialised group of cochlear hair cells, the outer hair cells, can not only sense the motion of the structures which stimulate them, they can actively control them. Mechanical measurements of the cochlea's various accessory structures, including the basilar and tectorial membranes, can hence be used to study the effects that the hair cells have on the cochlea as a whole. A laser interferometer is well suited to make these measurements and Nigel Cooper uses one such device to monitor sound-evoked displacements at various points along the length of the cochlear partition (see Fig 2). Given the cochlea's amazing ability to map different frequencies of sound to different places along its length, this means that the frequency dependence of the hair cell's activity can be studied. The intra-cochlear interactions that occur between different sound frequencies are also of interest, since low frequency sounds have to pass through the high frequency regions of the cochlea to reach their own characteristic places, whereas high frequency sounds never pass through the low frequency regions. The results of these system's studies show that the effects of the outer hair cells are different at the high and low frequency ends of

the cochlea. In the high frequency regions, both the sensitivity and the selectivity of the basilar membrane's vibrations are enhanced by the outer hair cell's mechanical activity. In the low frequency regions, however, the frequency selectivity remains unchanged and only the sensitivity is affected.

An ear in a computer

Physiological experiments cannot give us a complete understanding because every experimental intervention alters the mechanics. To overcome this problem Paul Kolston is aiming to re-create a cochlea on a computer. Since the cochlea must obey the laws of physics, it should be possible to replicate the motion of the cochlear partition by expressing the physical laws as a series of equations that describe how adjacent cells, membranes and fluids interact. If we get the equations right, the response of the real cochlea to any stimulus could be simulated and studied with much greater precision than is possible experimentally. Unfortunately, we cannot squeeze all the equations required to describe mechanical motion within the cochlea into a computer, so we must simplify the cochlear partition when formulating the model. But how much simplification should we use? We don't yet know the answer, so our aim is to minimise simplifications whilst retaining a realistic model that is solvable on present-day computers. Three-dimensional visualization techniques are used to probe what is happening within the model (Fig 3) and preliminary simulations have demonstrated that very small changes in the properties of individual cells can have profound effects on the way that the basilar membrane vibrates. The approach is flexible enough to simulate cochleae of differing complexity, so it could be used to predict the degree of mechanical amplification in regenerated sensory epithelia whose structure and properties are likely to be quite different from those of the normal mammalian cochlea.

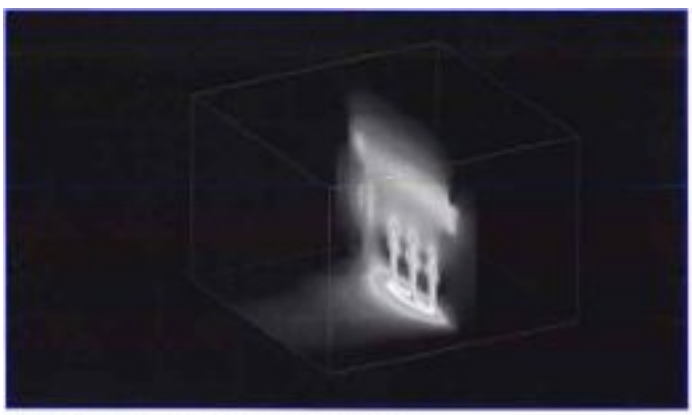

Fig 3. A slice through an ear in a computer.

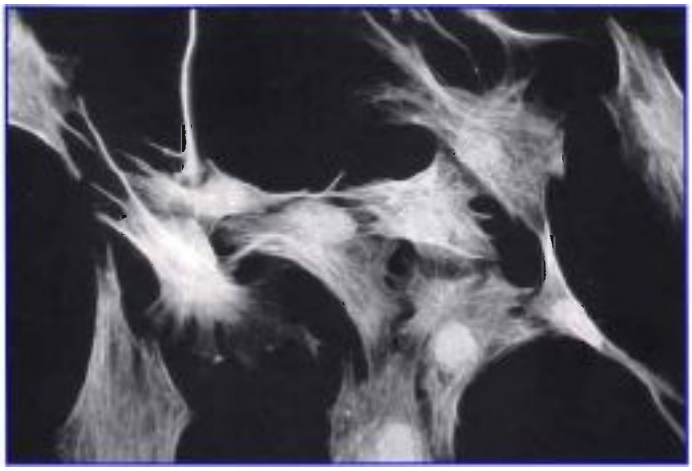

Fig 4. Conditionally immortalised cells from the inner ear. The raw material for an ear in a test-tube?

An ear in a test-tube

Building a cochlea in a computer leaves the operator in charge of every detailed element of its construction, but building one in a test-tube might be possible by simply tweaking a few genes. The mammalian ear has always been a challenge to experimental biologists because there are so few sensory cells and they are packaged in several layers of protective bone. What we really need is an ear in a test-tube, boned and as large as desired. Such a preparation would not only provide plenty of tissue but also help us to understand some of the most fundamental aspects of cell differentiation and development. This might in turn lead to methods of stimulating otherwise inactive natural repair mechanisms in the adult ear. Matthew Holley is tackling this problem by trying to derive conditionally immortalised sensory epithelial cells from the Immortomouse, a transgenic animal produced by the Ludwig Institute for Cancer Research. The aim is to establish cell lines that can be differentiated under controlled conditions to form a functional mechanosensory epithelium in vitro. We have recently cultured cells that express some of the features of differentiated hair cells (Fig 4) and intend to present some of the most exciting evidence at the Physiological Society meeting in Bristol in September.

A visit to Bristol

Hearing research in Bristol is as diverse and stimulating as the ear itself, and when you come to the meeting in September you will be more than welcome to see some of the techniques that we are employing to probe the mysteries of the inner ear.

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WHERE DOES THE SOUND COME FROM?

Alan Palmer explains how the auditory pathways process signals from the two ears to derive information of sound position.

Although the pioneer of auditory experiment and theory, von Helmholtz, didn't have much to say about binaural processing of sound, the study of binaural hearing has a long and distinguished history. One of the earliest and most influential investigators was Lord Rayleigh who, with the help of Lady Rayleigh, an assistant, several tuning forks and various lengths of tube, formulated the duplex theory of binaural hearing, (Rayleigh 1907). The essence of the theory is as follows: the effect of head shadowing, in reducing the sound level at the ear furthest from a sound source, is used to localize sources above about 1500 Hz, while the location of lower-frequency sources is computed from the difference between the phases of the sound at the two ears resulting from the longer path length to the remote ear.

Microseconds apart - exquisite sensitivity

Jeffress (1948) proposed a mechanism that could account for our sensitivity to differences of the order of microseconds in the time of arrival of sounds at the two ears. Direct evidence of this mechanism began to appear in the early 1960's and exquisite sensitivity to interaural time differences was demonstrated in neurones acting as coincidence detectors in the Medial Superior Olivary (MSO) nucleus of the brainstem (e.g. Goldberg & Brown 1969). Subsequently, further anatomical and physiological evidence has amply confirmed both the location and mechanism of interaural time sensitivity. The neural substrate for the Jeffress model is illustrated in Fig 1. When a low-frequency sound comes from directly in front of the subject, the path lengths are identical and the sounds at the two ears are in phase. Recording from either auditory nerve we find a prerequisite for sensitivity to interaural phase differences: the impulses in the nerve preferentially occur at a particular phase of the stimulus waveform. This "phase-locking" occurs only to low-frequencies and is the result of the periodic activation of the synapses at the base of cochlear hair cells by the depolarizing phases of the receptor potential, which follows the pressure waveform at the ear. The impulses in the auditory nerve are conveyed with high precision to the MSO via large calyx synaptic endings in the cochlear nucleus.

Axons of different lengths

The axons connecting the MSO with the cochlear nucleus of each side are not of equal length and the spikes arrive later from the side connected by the longer axon (the axon conduction time on the right side in Fig 1 is 300 μs longer then on the left). Since the MSO neurone only fires when spikes arriving from both sides are coincident, there is no output. However, when the sound source is located on the right side it takes the sound an extra 300 μs to reach the left ear. Thus the spikes arriving at the MSO neurone from the left are delayed and arrive at the same time as those traversing the longer axon from the right: the MSO neurone therefore fires maximally. As suggested by Jeffress, a population of such neurones with different axon lengths would signal the range of microsecond differences in sound arrival time,

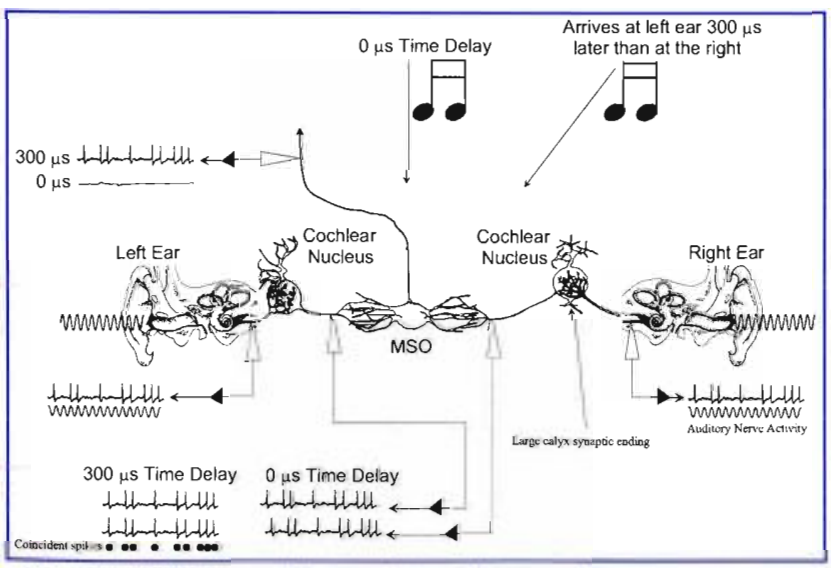

Fig 1. The sensitivity to small interaural time differences of a neurone in the Medial Superior Olive generated by coincidence detection fed by a delay line. The circuitry is reciprocated in the MSO on the other side of the brainstem. The cochlear nucleus and superior olive neurones by kind permission of Prof. J. Brugge.

which correspond to azimuthal sound positions. Evidence for such a neural architecture has been obtained from a variety of studies in a range of species, most notably in the cat and in the barn owl (see for example, Konishi *et al.* 1978).

Shifting the balance

The pathway for the analysis of the interaural level difference converges from each ear onto neurones of the Lateral Superior Olive (LSO) in much the same way as the pathway described above (see Fig 2). The major differences are that the path from one cochlear nucleus to the LSO is interrupted by a synapse in the Medial Nucleus of the Trapezoid Body (MNTB), and the interneurone from the MNTB onto the LSO is inhibitory. In Fig 2, sounds from the midline are of equal intensity at each ear producing both excitatory input to the LSO neurone from the right and inhibitory input from the left, resulting in only a few spikes at the output. Moving the sound to the left increases the discharge of auditory nerve fibres on the left and thus the inhibitory barrage from the MNTB to the LSO, which therefore exhibits low output rates. Moving the sound to the right shifts the balance toward the excitatory input from the right side, producing the highest LSO output rate. Thus while the signals traversing the auditory nerve from each side merely reflect the level at that ear, and contain no positional information, the output of the LSO is sensitive to the balance of the level at the two ears, which is a surrogate for the spatial position of the sound.

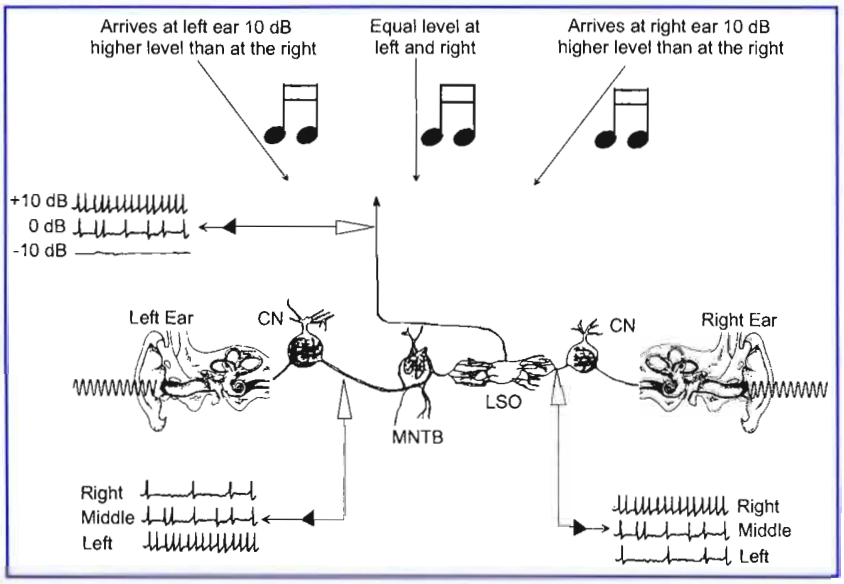

Fig 2. The sensitivity to the balance of sound levels at the two ears of a neurone in the Lateral Superior Olive generated by excitation from one ear and inhibition from the other. The circuitry is reciprocated in the LSO on the other side of the brainstem. The cochlear nucleus and superior olive neurones by kind permission of Prof. J. Brugge

Sensitivities to interaural differences based on these low-level brainstem mechanisms have been found at all higher levels of the auditory nervous system. In fact, other cues for the localization of wideband sounds also exist. Multiple reflections from the torso and within the pinna cause the spectrum of sounds reaching the two ears to be modified so that sharp spectral notches appear at different frequencies in the two ears, depending on the sound source location. Such cues can be used monaurally to localize wideband sounds, but also comparing the frequency of the notches in the two ears would provide an unambiguous positional cue (at least in the cat; see Huang ¶ & May, 1996).

Two ears also assist in the process of separating sound sources and one prominent binaural psychophysical effect, which depends upon this ability, is the binaural masking level difference. We have recently demonstrated binaural masking level differences in neurones sensitive to interaural time differences (Jiang *et. al.* 1996). Finally, in the external nucleus of the inferior colliculus and in the deeper layers of the superior colliculus neurones sensitive to the different values of interaural positional cues are organized topographically to produce a neural "map" of auditory space.

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PLASTICITY IN CENTRAL AUDITORY PROCESSING

Hearing begins before birth in some mammals, including humans, and after birth in others, although, in most species that have been studied the neonatal auditory system is far from mature. To a large extent, developmental improvements in auditory perception are due to changes that take place in the external ear, middle ear and inner ear. For example, the efficiency of sound conduction through the middle ear improves dramatically with age, and this in turn, leads to an improvement in the thresholds of central neurones. But, in addition to these peripheral factors, the maturation of the auditory system involves changes in the specificity of the terminal arbors and dendritic morphology of central neurones, in the distribution of the neurotransmitter receptors they express, and in their synaptic and sound-evoked response properties. Although much of the neural circuitry appears to be in place at an early age, it is now apparent that sensory experience also plays an important role in shaping the development of the central auditory pathway. Moreover, there are some instances where activity-dependent refinements of the coding properties of central neurones and of the representations to which they contribute continue into adulthood.

Activity - induced plasticity

The presence of topographically-ordered afferent pathways ensures that the tonotopic organisation of the cochlea is preserved at each stage of the central auditory pathway, including the cortex. Neurones in the central auditory nuclei of immature animals have broader frequency tuning than those in mature animals. Studies in which mice were reared in an acoustic environment of either repetitive clicks or two added tones in order to entrain different populations of the afferent fibres suggest that the relative timing of action potentials may be involved in eliminating inappropriate connections and the concomitant improvement of frequency tuning during normal development. Learning-induced plasticity appears to be present throughout life in the frequency map of the primary auditory cortex. Thus, training monkeys to perform a frequency discrimination task leads to an expanded representation of the frequency band within which the discriminations were made. Conversely, the restricted hearing loss produced by a partial lesion of the cochlea in mature guinea pigs causes an expansion in the cortical representation of adjacent frequencies.

Localising sounds - the role of sensory experience

Sensory experience appears to influence the development of binaural hearing and sound localisation more than other aspects of auditory perception. As described in the previous article by Alan Palmer, binaural differences in timing and intensity together with monaural spectral cues generated by the external ear contribute to the percept of sound location. Because these cues depend on the size and shape of the head and external ears, their correspondence with locations in space will change during the period of growth. A number of studies indicate that, at least at certain levels of the brain, sensitivity to auditory localisation cues can be modified to compensate for altered inputs.

Cochlear ablation

Because it is difficult to control the acoustic environment completely, most studies of auditory system plasticity have considered the effects of unilateral deprivation on the development of central neurones. Cochlear removal eliminates the direct input to the ipsilateral cochlear nucleus (CN) and the functional influence of that ear on neurones at higher levels of the pathway. When performed in infancy, unilateral cochlear ablation causes rapid degenerative changes both in the cochlear nucleus and the ipsilateral lateral superior olive (LSO) as a result of a loss of excitatory transmission. This procedure also eliminates activity in the inhibitory afferents from the medial nucleus of the trapezoid body to the contralateral LSO (see Fig. 2 in Palmer's article), disrupting the normal refinement of the presynaptic terminals and the maturation of postsynaptic dendritic morphology. The projection from the CN to the inferior colliculus (IC) and the responses of neurones in the IC that are driven by the intact ear are also altered by unilateral cochlear removal in infancy. Whether these changes contribute to the ability of animals to localise monaurally is unclear. However, it is of interest to note that studies in both humans and ferrets suggest that localisation of sounds using one ear can be more accurate if the onset of unilateral deafness occurs in infancy rather than later in life.

Ear plugging - a reversible alternative

In many ways, the effects of a unilateral conductive hearing loss, induced, for example, by occluding the external auditory meatus, are of more interest. This procedure is potentially reversible and is of clinical relevance given the prevalence among young children of otitis

media with effusion, which often involves an asymmetric conductive hearing loss. Plugging one ear in young barn owls and ferrets leads to a compensatory adjustment in the auditory space map in the superior colliculus, so that, while the ear is occluded, the auditory map remains in register with the map of visual space also present in this midbrain nucleus. Experience-induced plasticity in the auditory map seems to be restricted largely to development, as a similar period of monaural occlusion in adult animals does not alter the spatial tuning of these neurones. In owls, adaptive changes in sensitivity to binaural cues toward the abnormal values produced by the ear plug have been traced to the first site of binaural comparison in the brainstem and are accompanied by a corresponding adjustment in sound localisation behaviour. On the other hand, the reported effects of monaural occlusion during infancy on the responses to interaural intensity differences of neurones in the mammalian IC and cortex are less clear cut and there is only limited evidence for behavioural adaptation in spatial acuity and unmasking tasks that rely on binaural hearing.

Vision cues into the auditory system

Developmental plasticity in the auditory space map in the SC can also be induced by altered visual experience. Depriving animals of visual cues degrades the auditory map, whereas displacement of the visual field representation by rearing owls with prisms mounted in front of their eyes or by surgical deviation of one eye in young ferrets induces a corresponding shift in the auditory representation, so that the registration of the two maps is again preserved. Attention is now being focused on the site of action and the cellular mechanisms by which sensory experience calibrates the sensitivity of auditory neurones to sound localisation cues and recent work implicates NMDA receptors in aligning auditory and visual maps during development. These studies indicate that, when available, visual cues play a dominant role in multisensory integration. But, early loss of vision leads to morphological, physiological and behavioural changes in the auditory system, which can also be regarded as compensatory in nature.

To a large extent, experience-induced plasticity in the processing of sound localisation cues is restricted to a period of developmental sensitivity when growth-related alterations occur in the relative geometry of the sense organs. Nevertheless, some capacity appears to be retained throughout life to modify both the responses of auditory neurones and localisation behaviour following changes in the available spatial information.

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TINNITUS

Tinnitus - ringing in the ears - is a puzzle. The most common form is a high pitched (2-5kHz) noisy whistle which can be heard in quiet surroundings. When the reported sound becomes as loud as normal surround noise, it becomes a medical problem - and this does affect large numbers of individuals (the estimates for the UK exceed 1/300). Tinnitus is more common as normal hearing deteriorates. There are no effective drug treatments but there are some useful new animal models, particularly those developed by Jastreboff in the US.

It seems clear that sounds reported as a tinnitus do not originate in the cochlea: individuals with severe sensorineural loss or even physically damaged cochleas often report tinnitus. Drugs such as aspirin which induce a (reversible) tinnitus but which eliminate otoacoustic emissions (probably by reducing outer hair cell activity) also point to a central origin. For this reason tinnitus is often referred to as phantom sound (in analogy with a phantom limb). But it is not clear what tells the CNS to report such a 'virtual' tone or in which relay nuclei of the auditory system it arises.

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Cochlear Implants

In the past 20 years in particular, a revolution has occurred in the treatment of profound hearing loss (`total deafness'), in the invention of cochlear implants. Since it was first demonstrated that hearing could be induced by electrical stimulation of the exposed cochlear nerve (Djourno & Eyries,1957), tens of thousands of patients world- wide have received cochlear implants. With these devices, patients learn to hear meaningful sounds again, or in the case of infants, acquire spoken language, entirely through electrical stimulation and can live surprisingly normal lives as hearing persons, including using the telephone.

The basic nature of a cochlear implant is shown in Fig. 1. Sounds are transduced into electrical signals by a microphone, processed in a variety of ways in a control unit (typically worn in a pocket or on a belt) and transmitted across the skin by a radio-frequency link (typically behind the ear). The electrical signals acquired by the radio frequency receiver under the skin are transmitted to one or typically many more electrodes inserted surgically into the Scala Tympani of the cochlea.

The aim of the processing strategy is to recreate, as far as possible, the normal patterns of neural activity evoked by the corresponding sounds (particularly speech). This is done by electrical stimulation of the surviving fibres of the cochlear nerve. As such, it is an exercise in converting physiological knowledge into the design of hardware which is capable of being battery powered and cosmetically acceptable.

Ideally, one would wish to recreate the patterns of neural activity in space (place coding) and time (time coding) in each of the 30,000 fibres which constitute the human cochlear nerve. However, currently it is only surgically possible to insert only 22 electrodes or so into the region of the cochlea corresponding to the speech frequencies, namely 10 to 25 mm from the round window in the cochlear base. Furthermore, the electrodes are bathed in perilymph which drastically reduces the `place' specificity of stimulation by conducting signals from the intended place up and down the length of the cochlea, the so-called biological interface problem (Evans, 1985). In addition, electrical stimulation introduces abnormalities into the temporal discharge patterns.

In order to explore some of these uncertainties, we have recently adopted a good old physiological teaching tool - the sciatic nerve of the toad - for studying the neural consequences of simple and complex electrical stimulation (Morse & Evans, 1993, 1995). One of the most obvious differences between electrical

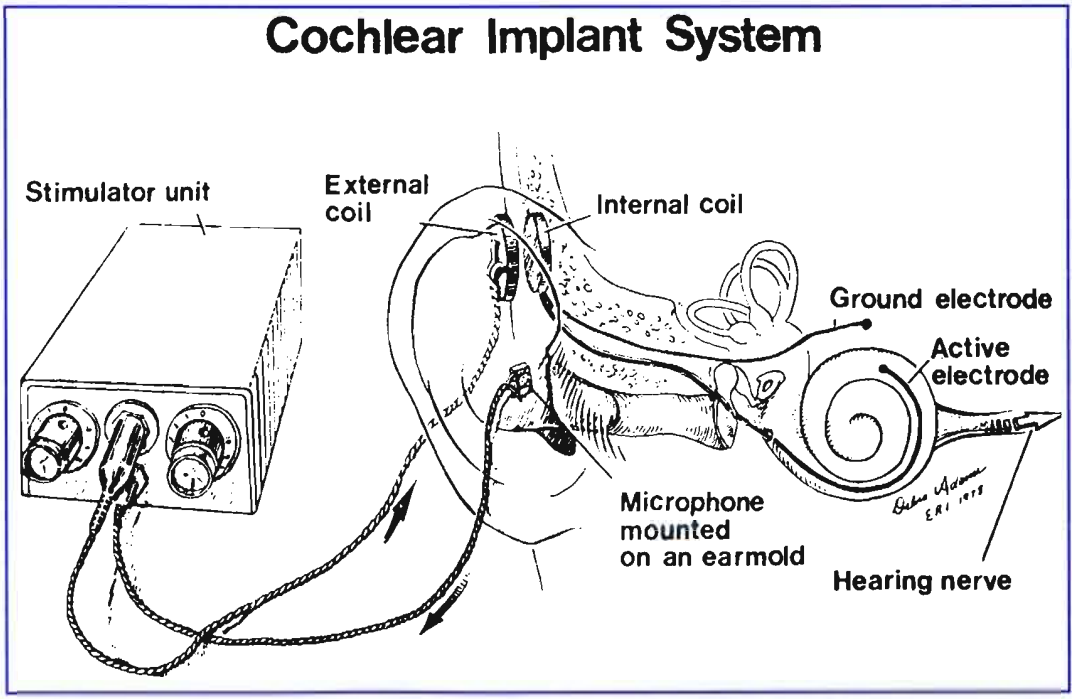

Fig 1 Diagram outlining basic features of a simple cochlear implant. While any one electrode is shown in the cochlea for simplicity, in practice up to 22 electrodes are inserted, evenly spaced along the speech frequency region of the cochlea.

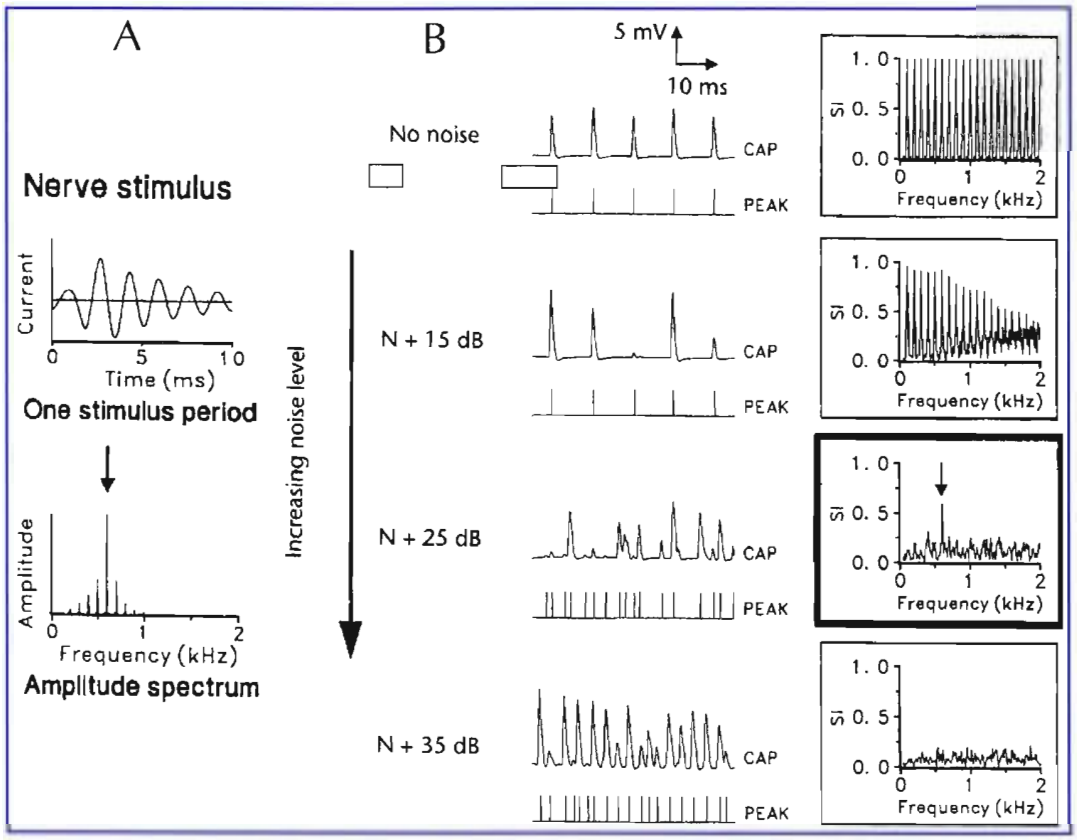

Fig 2 Demonstration of stochastic resonance in the firing patterns of toad sciatic nerve to a filtered speech stimulus. A: One period of the speech sound /ae/ (as in "hat") with fundamental frequency of 100 Hz as filtered by the lowest channel of a 4-channel cochlear implant. The amplitude spectrum below shows the most prominent harmonic at 600 Hz - the first speech formant. B: Responses of toad sciatic nerve to the stimulus in A with the addition of increasing levels of noise (from top down). The amplitude spectra (synchronization index plots) on the right change from reflecting the voice fundamental (peaks at 100 Hz spacing) when no noise is added (topmost), to clear enhancement of the 600 Hz formant (third down) with the optimal level of added noise.

stimulation of nerve and normal hair cell excitation is that the neural response to speech signals in the sciatic nerve model are dominated by the voice fundamental frequency. (This is presumably why even the oldest, single channel, cochlear implants were surprisingly successful). The question arises, how can we transform this excitation so that the information-bearing speech frequencies - formants - are included? The surprising answer has been too add noise (Morse & Evans, 1996)! The addition of Gaussian noise to each channel of stimulation converts the pattern of excitation from that of the voice fundamental to that of the speech formants most emphasised by the particular cochlear implant filter channel. At an optimal level of added noise, the formants can become even more prominent than in the original signal (as in Fig. 2). This turns out to be an example of a process called `stochastic resonance' (eg Wiesenfeld & Moss, 1995); many non—linear processes, physical and biological (specifically those embodying a threshold), can exhibit `stochastic resonance' with the addition of noise.

Whether in practice this strategy can benefit actual cochlear implantees remains to be seen.

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MEDICAL RESEARCH COUNCIL CHANGES ITS FUNDING POLICIES

As this issue of the Magazine went to press, the Medical Research Council announced that it was about to introduce major changes in the way in which it funds medical research in UK Universities. These changes are to be implemented from 30th May 1997 and are likely to have a major impact on most physiologists. They are briefly summarised here. For more information about the new funding schemes contact the New Funding Schemes Support Office, Medical Research Council, 20 Park Crescent, London, W1N 4AL. Tel: 0171-637 6003/6024 (9.00 am to 5.00 pm). Fax: 0171-636 6289. e-mail address: new.schemes@headoffice.mrc.ac.uk. Details are also available on the MRC's Web page at: http://www.mrc.ac.uk.

Major Changes

- The MRC project grant scheme will be discontinued and no new applications will be accepted after Friday, 27 February 1998. The existing project grants scheme will run for the 1997/98 academic year, which will be treated as a transitional year. However, the funding available for project grants during this transitional year is likely to be reduced compared to the current year.

- There will be greater flexibility in Programme Grants. For example, applicants will be able to request support for the salary of the principal investigator for up to three years. This change is intended to help universities attract high quality established researchers and the university will be expected to provide an assurance that the applicant will be appointed to an appropriate university post after the three years. The MRC will also consider applications for smaller scale Programme Grants than hitherto.

- There will be major changes in the way in which Grants are reviewed. The current system will be abolished and each grant will be reviewed by one of a panel of 200 experts. The precise details of this scheme have not yet been released.

New Schemes

- *Centre Grants.* for the support of multidisciplinary research Centres. Each Centre will comprise several independent research teams with complementary research programmes and will be led by a full-time Centre Director of interantional standing. It is expected that initially about four new Centre Grant awards might be made each year and that at steady state the Council might support about 20 Centres at any one time. Centre Grants do not replace MRC Units and the MRC will continue to fund institutes and units, where appropriate.

- *Co-operative Group Grants* to foster collaboration between independent researchers normally, but not exclusively, within a single University. Co-operative Groups may vary in size but should consist of at least three projects with three different principal investigators. At least two of the component projects must be MRC funded but the third may be funded by other organisations (such as charity or industry). Component grants are intended to be mainly short term (up to 3 years) and can provide support for infrastructure, including scientific and technical staff support and associated indirect costs, research facilities, major items of equipment and administrative support. Applicants are expected to hold established University appointments or to be Senior Fellows of the MRC, the Royal Society, the Wellcome Trust or other Medical Research Charities.

- *Development Grants* to help Universities get to the point where they can make competitive applications for funding under the Co-operative Group Grants scheme. Development Grants are not renewable.

- *Innovation Grants* to provide short-term funding for high-risk, speculative or innovative research. These are awarded on the basis of the applicant's track record of achievement in research supported by MRC funds. Innovation Grants will normally be awarded for one year and the maximum award will be £40,000 (including indirect costs).

- *Career Establishment Grants* to provide support for a fixed period for scientists recently appointed to University academic posts (within the last three years) to help them to establish themselves as independent research workers. Career Establishment Grants may be held for a maximum of five years and are not renewable. It is likely that between 20 and 25 Career Establishment Grants will be awarded each year.

- *Training and career development award schemes* continue largely unchanged.

The stated aim of the MRC in introducing these changes is to encourage greater scientific collaboration, both between individuals and between academia and industry. It is likely that many members of the Physiological Society will have strong views about the new scheme so use the Magazine as a Forum for such discussions and write in and express your views.

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University Laboratory of Physiology
Oxford

THE FEDERATION OF EUROPEAN PHYSIOLOGICAL SOCIETIES (FEPS) IS ON ITS FEET

After a 2-year period of preparation the Federation of European Physiological Societies (FEPS) was founded officially in Prague in June 1991. The most important aims of the Federation are to advance science and education related to physiology and to bring together physiologists in Europe to exchange expertise. At present 25 National Societies are member of FEPS.

Meeting places will be the FEPS main congresses, to be organized every 4 years in between the meetings of the International Union of Physiological Sciences (IUPS), joint meetings of two or more Constituent Societies and workshops and symposia on specific timely topics.

The first main congress of FEPS was held in Maastricht, the Netherlands from September 9-12, 1995, under the auspices of IUPS. The Maastricht meeting was attended by 574 scientists from 32 countries and the Executive Committee of FEPS was delighted to see that about 150 colleagues from Central and Eastern Europe were able to attend the congress. Thanks to our sponsors, the organizers were able to help these colleagues financially by (partially) waiving their registration fee or taking care of (part of) their local or travel expenses.

One of the plenary lectures at the Maastricht meeting was the FEPS lecture on "Latent excitatory interconnections between hippocampal neurones" by Professor O Krishtal from Kiew. FEPS lectures are not only given at the FEPS main congresses, but also at joint meetings of two or more Constituent Societies. The FEPS lecturers are selected by the Executive Committee of FEPS. Candidates can be nominated by the organizers of the meetings.

Although the first main congress can be considered a successful start, the scientific quality of these congresses needs improvement. At the next main congress, to be held in Prague from June 30- July 4, 1999, symposia on timely topics will be organized and internationally renowned scientists will be invited to participate in these symposia. The Executive Committee of FEPS is doing its utmost to raise funds to create a financial basis for this activity.

The workshops on timely topics will be accessible only to a limited number of scientists - currently we are thinking of about 60 participants - and should be a stimulating environment for scientific discussions between young scientists, for example, post-docs, and renowned scientists. This can be achieved by a format of relatively short introductions and extensive informal discussions. In addition, the organisation of symposia on specific topics is foreseen. The topics and the potential organisers of workshops and symposia can be proposed by Member Societies, or by individual members of these societies, to the Meeting Committee of FEPS, which is chaired by Dr Peter Bie from Copenhagen, Denmark. The organisation of workshops and symposia under the auspices of FEPS requires approval of its Executive Committee.

Through the coordinating activities of our Meeting Committee, proposals for workshops have been submitted already to the European Science Foundation (ESF) for funding. The first ESF sponsored workshop organized under the auspices of FEPS will be held in Maastricht in December 1997. The topic of this workshop is "Implications of cardiovascular specific gene expression".

Besides sponsoring through the ESF, the Executive Committee of FEPS is looking into the possibility of financially supporting workshops and symposia through other sources. In a stable situation we are aiming at 1-2 workshops and/or symposia per year. Hopefully this situation can be reached before the turn of the century.

Another important activity of FEPS concerns animal legislation. Following the symposium organized on this topic at the IUPS meeting in Glasgow in 1993, FEPS has installed an Animal Legislation Committee under the chairmanship of Dr Osmo Hänninen from Finland. Other members of this Committee are Dr N Thorn (Denmark) and Dr K Klinke (Germany). The main purpose of this Committee is to get involved in the discussions on animal legislation in Europe to defend the points of view of physiology.

In summary, the baby has started walking, but it needs a lot of effort to guide it safely through adolescence to adulthood. The help of all members societies is needed to accomplish this.

Robert S Reneman
President, FEPS
Maastricht

FORTY YEARS

Hilary Brown reminisces on her forty years of research studying the electrical properties of cardiac muscle cells.

As a zoology undergraduate I was most drawn to physiology, particularly that of invertebrates, about which relatively little seemed to be known. So I chose to study crustacean hearts as my graduate project. I was to be based in Oxford, but to work mainly at the Stazione Zoologica in Naples.

I spent my first six months in the Oxford Laboratory of Physiology learning electrophysiological techniques and investigating the effect of adrenaline on action potentials of frog ventricular cells. In the late 50's these techniques were relatively simple but even so I had a lot to learn. My first lesson was how to solder, then I built a simple pre-amplifier to use with the oscilloscope to which I had been introduced. Glass microelectrodes for intracellular recordings were a new development and the Laboratory workshop made me an electrode puller. Its somewhat erratic pull was a great advance over hand pulling (which I also tried). The electrodes were filled with 3M KCL by boiling under reduced pressure - a frightening procedure which would now ruffle some Health and Safety feathers. Successful electrodes were carefully labelled and stored for re-use. With perseverance and luck, stable records could be obtained. It was exciting to see cardiac action potentials, first recorded by Weidmann only a few years previously.

Neapolitan procrastination and exasperating charm

On the 36 hour train journey to Naples, where I was to start investigating the neuromuscular system of the heart of *Squilla mantis* (a large shrimp), my luggage included an oscilloscope and the faithful electrode puller. The Stazione Zoologica, founded in the nineteenth century so that northern European scientists could study Mediterranean marine creatures, provided bench space but not apparatus. Like the city of Naples itself, the Laboratory had many primitive features and an atmosphere of exasperating charm. I quickly learnt some essential Italian for communication with the technical staff - all experts in Neapolitan procrastination. When I complained at receiving a shock from an aged light switch, I was patiently shown the handy piece of wood I should have used to switch it on! It was quite a struggle to assemble even my simple electrophysiological set-up but despite obstacles, the most spectacular being the collapse of my laboratory's ceiling (fortunately, at night), I made progress and completed my thesis work.

An important career-shaping event had occurred right at the start of my time as a graduate student when I met a Michael Brown, then intercalating a research year into his medical studies. After qualifying (and marrying me) he returned to physiology research in Oxford. My own career then had to become quite flexible. I also worked at the Physiology Laboratory (where my husband became a Lecturer) first as a Departmental Demonstrator and then on grant supported posts, held part-time while our children were young.

To patch clamping and pacemaking

In land-locked Oxford I could no longer work on marine Crustacea so I switched to frog cardiac muscle, joining Denis Noble's group. Voltage clamp data were needed from cardiac muscle other than the Purkinje fibre which, because of its favourable geometry, had been the first cardiac tissue clamped. Using a sucrose gap method we found that frog atrial muscle showed pacemaker activity when given small depolarizations. Although our preparation was attacked as 'insanitary' in an American review article, we made progress in analysing the underlying membrane currents.

My interest in pacemaking was thus firmly established when Dario DiFrancesco joined us in the late 1970s, determined to study the mammalian sino-atrial node. With its small cells and abundant connective tissue, this had proved the most difficult cardiac region to voltage clamp. Dario introduced us to the 'small preparation' of sino-atrial node. Prolonged fine dissection gave a 250 μm diameter ball of tissue which (if still beating) was impaled with two microelectrodes. If these gave stable, virtually simultaneous, potential records, voltage clamping could begin (it was by then about 6.00p.m. after an 8.30a.m. start). Altogether, it was a highly demanding technique, but all the more exciting when it yielded results, showing clearly for the first time the hyperpolarization-activated inward current, i_f ('Look! there's that funny current again!').

We progressed to patch clamping single pacemaker cells, again more difficult to isolate and study than other cardiac cells. In Denis Noble's group, experiments have always had an extra stimulus and dimension through the incorporation of results into computer models. Now single 'cells' can be re-assembled into network models using parallel computers. The first of these was (appropriately) of the SA node.

Those rare moments

What have I enjoyed? The excitement of discovery (when it occurred); the companionship of the Laboratory, in particular that of talented and interesting visiting scientists from abroad; teaching; writing; the stimulus and interest of Meetings. I was fortunate to be able to work part-time when my children were young and then become full-time again, a pattern which is harder now with the fierce competition for grant money. Set against that has been job insecurity and the lack of university and college 'status' for those on soft money.

What were the best moments? The moment when my D.Phil examiners asked me to take tea with them and I knew they liked my thesis; when we realised the sucrose gap apparatus was not giving just noise, but clear records of atrial action potentials; the first records of i_f from the 'small preparation'; the successful isolation and study of healthy, spontaneously beating sino-atrial node cells.

My laboratory is currently looking at catecholamine action on potassium currents in SA node cells: isoprenaline causes faster decay of i_k and this contributes to pacemaker acceleration. Perhaps things do come round full circle: there's certainly a connection there to my much younger self using the spring-mounted, re-cycled microelectrodes to record frog ventricular action potentials during adrenaline action.

(This is a condensed version of an article which appeared in the Quarterly Bulletin of the British Society for Cardiovascular Research).

Hilary Brown
University Laboratory of Physiology
Oxford

THE ORIGIN OF THE QUARTERLY JOURNAL OF EXPERIMENTAL PHYSIOLOGY

The first volume of the Quarterly Journal of Experimental Physiolog y

In 1991 the Quarterly Journal of Experimental Physiology was renamed Experimental Physiology. It became a bi-monthly journal with a distinctive bright red cover. Now it has just become available in electronic format. (http://physiology.cup.cam.ac.uk/jep). Sharpey-Schafer could not have envisaged his Journal ever being 'sent down' a telephone wire but readers may be interested in these extracts from "The Origin of the Quarterly Journal of Experimental Physiology", written by David Whitteridge and published in 1983.

"The first number of the *Quarterly Journal of Experimental Physiology* appeared in January 1908, 75 years ago. Its birth was stormy... At the time the *Journal of Physiology* was the property of J. N. Langley, the Professor of Physiology at Cambridge. It had been founded by Sir Michael Foster, but in 1894 it ran into debt and Langley paid its debt and took over control. His methods of editing caused great resentment as in the interest of clarity he shortened and often completely rewrote papers...

The opportunity to start a new journal came when J. G. McKendrick, the Professor of Physiology in Glasgow, retired in 1906 from the Chair and from the editorship of the *Journal of Anatomy and Physiology*. Schafer was approached, and agreed to take on the physiological side of the journal, but when only four existing subscribers were in favour this plan was dropped. In June 1907, Sherrington urged Schafer to start a completely new journal, and his arguments must be given in full.

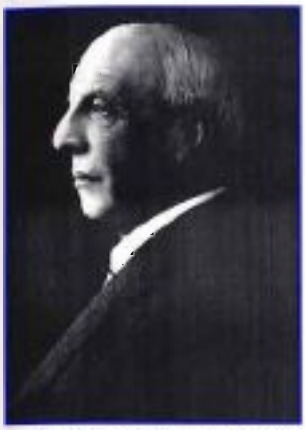
Dear Schafer,

...I could have preferred your starting something fresh *altogether than continuing a combination with what the Journal of Anatomy and Phys. has always understood by 'Anatomy'. I could have preferred it on the practical ground that Physiology has suffered much in prestige and loss of, or rather want of its share of wordly goods and 'endowment' from being constantly dragged at the tail of Anatomy and save the mark this miserable Anthropotomy! [Anthropometry?]. The mere sequence of the words 'Journal of Anatomy and Physiology' serves to prolong the inferiority of the position given to physiology, especially north of the border. The anatomists are well aware of this and this underlies part of their desire to resuscitate the moribund journal. How much more enthusiastically would physiologists embrace a new periodical if you would start one quite independent in* name *as* in fact *from the mediaeval 'Anatomy' which so many of them are sick of and find hampering their own legitimate sphere.*

A new Journal is wanted *and* you are the person to start it...

Yours sincerely,
C S Sherrington

PS: Please forgive my perhaps too free expression of opinion.



Sir Edward Sharpey-Schafer

Encouraged by this letter, Schafer sent circulars to members of the Physiological Society informing them of his intention. The response was satisfactory and Gotch, Halliburton, Sherrington, Starling and Waller gave Schafer their support. He sent the first number to press under the name of the *Quarterly Journal of Physiology* on 25 December 1907 (at that time Christmas Day was not a public holiday in Scotland). On 7 January 1908, Langley wrote to Schafer to say that he had just received a circular announcing the appearance of the new Journal and asking for a change in its title to avoid confusion with the *Journal of Physiology*. Schafer's answer is not extant, but on 10 January, Langley sent a telegram disapproving of a number of titles but recommending *'The Quarterly Journal of Experimental Physiology'*. In a letter dated 9 January, Langley swept aside Schafer's objections to changing the title of the new Journal on the grounds of expense, and added: 'The starting of the Journal is of course your scheme and I do not think it straightforward that you should have given me no notice with regard to it.' Schafer replied...

January 15th 1908
My dear Langley,
It has pained me that you should think that I and those engaged with me in the production of the new Journal have acted in any but a straightforward fashion:... I value your friendship too much to allow it easily to pass although I must own that my first impulse on receiving your last letter was to take no notice of it containing as it did an accusation which I felt to be unjust...

Schafer pointed out that he had twice circulated members advertising the new Journal, that there was ample material for the two journals from the increasing number of active laboratories and that the new journal would publish histological material...

Langley... wrote to Schafer on 15 February, saying that he disapproved of competing journals, which lowered standards and that it would have been better to have two specialist journals, leaving Histology or Neurology to Schafer's new journal... He went on to say that they would both be in a false position if Schafer remained on the list of those who assist in selecting papers for the Journal of Physiology, and thanked Schafer for his past support. As Langley made very little use of his Editorial Board, this had little effect apart from the disappearance of Schafer's name from the cover of the Journal of Physiology. Langley did not change his editorial methods, for in 1922 Alexander Forbes wrote to Adrian complaining that their joint paper had been 'Langleyized!'.

In his diary, Schafer said that his main intentions in starting the new journal were that accepted papers were to be published in the form sent in by the author or head of the laboratory, and that papers should be illustrated as fully as might be necessary...

The Quarterly Journal of Experimental Physiology has never had a circulation comparable with that of the Journal of Physiology, and there have been a number of financial crises, two of them in Sir Edward's lifetime. In 1935 Sir Edward Sharpey-Schafer retired, and transferred the Journal to three trustees, the Professors of Physiology, Anatomy and Pharmacology in the University of Edinburgh, who became personally responsible for its debts, but were not allowed to make personal profits. This became an uncomfortable position in the 'Fifties when costs were rising very suddenly, and the Journal became the property of a trust with limited liability. A few years later the Physiological Society provided a subsidy which kept it solvent for some years, and finally in 1979 (*sic 1981*) the Society acquired the Journal and took over its management. The desirability of continuing the Journal has therefore been debated about every 10-15 years, three times by the Committee to my knowledge. Each time the arguments and the conclusions have been the same. By providing a second channel of publication in this country, it has continued to obviate some of the consequences of Editorial eccentricity in the *Journal of Physiology*; it permits a wider definition of physiology and now includes cognate sciences; it allows authors a little more freedom in the presentation of their results, and it has always kept up the standard of its illustrations.

Extracts from D Whitteridge (1983) The Quarterly Journal of Experimental Physiology, 68: 521-523.

Companies may boycott universities

Adair Turner, director-general of the Confederation of British Industry, has warned that employers may boycott universities which fail to improve the quality of their teaching, and has asked Sir Ron Dearing to use his report next month to establish stricter quality standards

***Guardian** 5 June 1997 p.9*

Source: SPIN

No notice is carried for more than three successive editions. Notices are starred so that readers can see at a glance whether this is the first (one star) or final (three stars) appearance of the notice. Notices for the Winter 1997 edition (to be distributed on 7 November) should reach the Administration Office by 15 September.

THIRD INTERNATIONAL SYMPOSIUM ON RESEARCH FOR AQUACULTURE: FUNDAMENTAL & APPLIED ASPECTS

24-27 August 1997
Barcelona, Spain

Scientific sessions will include reproduction, nutrition & metabolism, growth & development, pathology, applied research on aquaculture, and a free session on comparative physiology & biochemistry. Sessions will comprise plenary lectures, state of the art, oral communications and poster presentations. There will also be workshops on specific subjects related to the sessions.
A satellite Symposium on Insulin and IGF superfamily peptides and related molecules is planned for 28 August 1997 in Barcelona.
Further information from Joaquim Gutierrez, Dept of Physiology, Faculty of Biology, University of Barcelona, 08028 Barcelona, Spain. Tel: +34 3 402 1532, fax: +34 3 411 0358, email: joaquim@porthos.bio.ub.es ***

Meeting of the British Society for Cardiovascular Research

MYOCARDIAL INJURY: PRESENT KNOWLEDGE AND FUTURE DIRECTIONS

5-6 September 1997
University of Bristol

Further information from Dr M-S Suleiman, Bristol Heart Institute, University Department of Cardiac Surgery, Bristol Royal Infirmary, Bristol BS2 8HW. Fax: 0117 928 3581, email: M.S.Suleiman@bris.ac.uk ***

THE NEURON IN TISSUE CULTURE

One-day symposium sponsored by Becton Dickinson (UK) Ltd, The British Neuroscience Association & the European Tissue Culture Society
5 September 1997
University of Bristol

Plenary and keynote lectures on progress in the physiology, neuropharmacology and developmental biology of the neuron *in vitro*. Free communications are invited for poster presentation; selected authors will be offered an oral presentation.
Further information about registration, submission of abstracts and accommodation from Dr L W Haynes, School of Biological Sciences, University of Bristol, Woodland Road, Bristol BS8 1UG. Tel: 0117 928 8656, fax: 0117 925 7374, email: L.Haynes@Bristol.ac.uk or Mr Paul Eros, Becton Dickinson (UK) Ltd, Between Towns Road, Oxford OX4 3LY. Tel: 01865 748844, fax: 01865 781578. ***

EUROPEAN WORKING GROUP ON CARDIAC CELLULAR ELECTROPHYSIOLOGY

21st Meeting
12-13 September 1997
Tours, France

Pre-registration forms and information from Professor Jorge Argibay, CNRS physiologie des cellules cardiaques et vasculaires, Faculté des sciences, Parc de Grandmont, 37200 Tours, France. Tel: +33 47 36 7012, fax: +33 47 36 7112, email: argibay@univ-tours.fr or from WWW address: http://www.univ-tours.fr/garnier/ccv_home.html ***

AUTUMN SCHOOL IN COGNITIVE NEUROSCIENCE

30 September - 3 October 1997
University of Oxford

A free course for third-year undergraduates, graduate students and post-doctoral scientists considering research in Neuroscience. Each day will be devoted to a particular area of cognitive neuroscience.
Further information and application forms from the Administrative Secretary, Oxford Centre for Cognitive Neuroscience, University Laboratory of Physiology, Parks Road, Oxford OX1 3PT. Tel: 01865 272497, email: cogneuro@physiol.ox.ac.uk, WWW address: http://www.physiol.ox.ac.uk/mcdp/autsch/ ***

BRITISH NEUROSCIENCE: A CELEBRATION TO COMMEMORATE THE RELAUNCH OF THE BRITISH NEUROSCIENCE ASSOCIATION

1 October 1997
Wellcome Building, London

Six eminent neuroscientists will talk anecdotally, humorously and inspiringly about their discoveries and the contribution these have made to British neuroscience over the past few decades. They are Professor Patrick Wall, 'A brief history of the Brain Research Association', followed by 'The evolution of thinking about pain mechanisms'; Sir Andrew Huxley, 'The axon, 1935-1952'; Professor Eric Barnard, 'Unnerving experiences on the path towards a molecular neuroscience'; Professor Marianne Fillenz, 'From the neuromuscular junction to the brain'; Professor Horace Barlow, 'Between the brain and the mind'; & Professor Elizabeth Warrington, 'The emergence of neuropsychology; forty years at the National Hospital'.

The event is free to BNA members and £25 for non-members. There will be a nominal fee for lunch and refreshments. Further information and tickets, which must be obtained in advance, from Dr Yvonne Allen, Dept Human Anatomy & Cell Biology, University of Liverpool, Ashton Street, Liverpool, L69 3GE. Tel: 0151 794 5449, Fax: 0151 794 5517, email: y.allen@liv.ac.uk***

Open Meeting at The Royal Society

DISCUSSION MEETING EPITHELIAL CELL GROWTH AND DIFFERENTIATION

22-23 October 1997

Organised by Dr M J Crumpton, Professor T M Dexter and Professor N A Wright. 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.britac.ac.uk/rs/ ***

Open Meeting at The Royal Society

DISCUSSION MEETING BRAIN MECHANISMS OF SELECTIVE PERCEPTION AND ACTION

19-20 November 1997

Organised by Dr J Duncan, Professor G W Humphreys and Professor A M Treisman. 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.britac.ac.uk/rs/*

TRAINING COURSE IN CELL CULTURE FOR NEUROSCIENCE

4-19 December 1997
University of Bristol

An intensive training course including lectures, seminars and 25 hours' hands-on practical work under supervision. Theory and application of good tissue culture practice, handling neural cell lines, instruction in dissection and primary culture techniques for the peripheral and central nervous system from basic to advanced level. Includes cell typing, transduction and hybridoma methodology. Suitable for neuroscientists with little or no experience in tissue culture methods.
Sample programme and further information from Dr L W Haynes, (address given above). **

NEW HORIZONS IN CGRP AND RELATED PEPTIDES RESEARCH

11-12 May 1998
Shaftesbury, Dorset

Further information from Sue Brain. Fax: 0171 332 4739, email: sue.brain@kcl.ac.uk *

Visiting Scientists

Foreign visitors of the status of at least post-graduate 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 L69 3BX.

For Office use:		

Confidential

The Physiological Society
APPLICATION FOR STUDENT ASSOCIATESHIP

Surname (IN CAPITALS) ..... Title* Mr/Mrs/Miss/Ms *Circle as appropriate

Forenames (IN CAPITALS) ..... Date of Birth ...../...../.....

Degree Title .....

*University/Institution ..... Tel .....

Department ..... Fax .....

Address.....

Postcode .....

Email .....

Photograph of Candidate

Current Address
Please give here the address to which you would like correspondence from the Society, including Meeting Programmes and Magazines, to be sent for the current academic year.

.....

.....

.....

Tel .....

Fax .....

Permanent (if different)
Please state your permanent address, at which we will be able to contact you after completion of your degree.

.....

.....

.....

.....

Tel .....

I enclose a cheque for £5 payable to The Physiological Society.

I confirm that the information given above is accurate and up to date and that I hereby authorise The Physiological Society to hold this, and such other personal information as is supplied to the Society by me or my authorised agents or representatives in future, in machine-readable form for use in accordance with the purposes registered under the Data Protection Act 1984.

Signed ..... Date .....

The Member of The Physiological Society proposing the Candidate should read the guidelines overleaf and sign the following statement.

I hearby confirm that the Candidate is registered for a first degree in Physiology or related science, and that *he/she is a suitable person for admission to Society Meetings.

Membership Number

.....

Name of Proposer (IN CAPITALS) ..... Signature of Proposer .....

Tel ..... Date ...../...../.....

Address .....

.....

.....

Please return this form to: The Physiological Society (Student Associatehip), PO Box 11319, London WC1E 7JF, (UK).

GUIDELINES FOR MEMBERS OF THE PHYSIOLOGICAL SOCIETY PROPOSING CANDIDATES FOR STUDENT ASSOCIATESHIP

Eligibility

Students registered for an undergraduate course in Physiology or a related science. Candidates will normally be expected to have completed their first year of study. Students are encouraged to associate at the beginning of their second year.

Proposal

Candidates must be proposed by a Member of The Physiological Society. The Committee has authorised the Committee Secretary and/or the Student Associate Liaison Officer to approve or reject proposals as they are received throughout the year.

Publications

Student Associates receive copies of Meetings Programmes, Notices and the Society's *Magazine*.

Fee

The mailing fee for Student Associates is £5 per academic year (or part thereof).

For Office use:		

Confidential

The Physiological Society
APPLICATION FOR AFFILIATION

Surname (IN CAPITALS) .....

Forenames (IN CAPITALS) .....

Field of Interest IUPS classes ...../ ...../ .....
(see overleaf for codes)

Work Address .....

.....

.....

Postcode .....

Email .....

Title* Dr/Mr/Mrs/Miss/Ms *Circle as appropriate

Date of Birth ...../ ...../ .....

Special Interest Groups .....
(see overleaf for guides)

Tel .....

Fax .....

Photograph of Candidate

Research Area (eg, give thesis or project title).....

.....

Present Course / Postdoctoral Position .....

Qualifications:

Degree	Date	Subject	Awarding Institution

I enclose a cheque for £..... payable to The Physiological Society (see overleaf for fees).

I confirm that the information given above is accurate and up to date and that I hereby authorise The Physiological Society to hold this, and such other personal information as is supplied to the Society by me or my authorised agents or representatives in future, in machine-readable form for use in accordance with the purposes registered under the Data Protection Act 1984.

Signed ..... Date .....

The Member of The Physiological Society proposing the Candidate should read the Guidelines overleaf and sign the following statement.

I hereby confirm that the Candidate is *a postdoctoral worker or *registered for a higher degree in Physiology or related subject, and that he/she is a suitable person for admission to Society Meetings.
*(*Delete as appropriate)*

Membership Number
.....

Name of Proposer (IN CAPITALS) ..... Signature of Proposer .....

Tel ..... Date ...../ ...../ .....

Address .....

.....

Please return this form to: The Physiological Society (Affiliation), PO Box 11319, London WC1E 7JF (UK).

GUIDELINES TO MEMBERS OF THE PHYSIOLOGICAL SOCIETY PROPOSING CANDIDATES FOR AFFILIATION

This form of association with the Society is intended for physiologists still in the early stages of their careers working in laboratories in the UK, Ireland **or abroad**. It is open to postgraduate students registered for a higher degree in Physiology or a related subject and to postdoctoral workers who are not yet Members of the Society. **It is expected that postdoctoral workers proposed as Affiliates will normally be within the first five years of attaining a first professional qualification (PhD or medical degree) or awaiting the outcome of their proposal for nomination for election to Membership of the Society.**

The Committee has authorised the Committee Secretary to accept or reject proposals as they are received throughout the year.

Affiliation must be renewed by payment of the appropriate fee at the start of each year (ie October). For administrative convenience, Affiliates registered after October will have to pay for the full year. The fees are determined from time to time by the Treasurer; they are currently:

	UK & Ireland	Rest of Europe	Rest of World
With Meetings Abstracts	£10	£30	£35
Without Meetings Abstracts	N/A	£15	£20

Affiliation is for a term of five years in the first instance. Exceptionally an Affiliate may be permitted to remain as an Affiliate beyond five years on payment of the subscription rate applicable to an Ordinary Member.

All Affiliates receive copies of Meetings Programmes, Notices and the Society's *Magazine*. Affiliates can attend Meetings in their own right but must be introduced by a Member of the Society when giving a Communication or Demonstration. Affiliates are not Members of the Society and do not have the right to vote at its General Meetings.

FIELD OF INTEREST
IUPS CLASSES

01	Anaesthesia
02	Anatomy & Embryology
03	Anthropology
04	Biochemistry
05	Biophysics
06	Biomedical Engineering
07	Blood
08	Cardiovascular
09	Cellular & Tissue
10	Comparative Physiology
11	Electrolytes & Water Balance
12	Endocrines
13	Energy Metabolism & Temperature Regulation
14	Environmental
15	Enzymes
16	Gastrointestinal
17	General Physiology
18	Gerontology
19	Immunology
20	Liver & Bile
21	Lipids & Steroids
22	Microbiology
23	Minerals, Bones & Teeth
33	Molecular Physiology
24	Muscle & Exercise
25	Neuroscience
26	Nutrition & Food
27	Pathology
28	Pharmacology
29	Radiation
30	Renal
31	Reproduction
32	Respiration

You may specify up to three Classes.

THE SOCIETY'S SPECIAL INTEREST GROUPS

AF	Autonomic Function
BB	Blood-Brain Barrier
CC	Cardiovascular/Respitatory Control
CI	Comparative & Invertebrate Neuroscience
CN	Cellular Neurophysiology
CP	Comparative Physiology
DP	Developmental Neurophysiology
EC	Endocrinology
EM	Epithelia & Membrane Transport
GI	Gastrointestinal Tract
HC	Heart/Cardiac Muscle
HI	History of Physiology
HP	Human Physiology
IC	Ion Channels
ME	Microvascular & Endothelial Physiology
MC	Muscle Contraction
MP	Molecular Physiology
NE	Neuroendocrinology
PP	Placental & Perinatal Physiology
RP	Renal Physiology
RE	Respiratory Physiology
SC	Sensorimotor Control
SF	Sensory Functions
SM	Smooth Muscle

You may specify as many Groups as you wish.

The Physiological Society

VACATION STUDENTSHIP SCHEME
APPLICATION FORM

Details of Host Applicant

Name ..... Membership Number .....

Address .....

.....

Tel ..... Fax .....

Three recent publications:

Details of Student

Full Name ..... Date of Birth .....

Degree or other course currently being studied:

Course Title .....

Department .....

Institution .....

Duration of Course: ..... Years of course completed by this summer .....

Previous Studies and Relevant Work Experience

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

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

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.....

Details of Proposed Research Project

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

Summary of Costs

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

Living expenses per week: £.....

Number of weeks for which support will be required .....

Other expenses (*please give details*) £.....

Funding sought or received from other sources for this project

TOTAL AMOUNT REQUESTED FROM THE PHYSIOLOGICAL SOCIETY £.....

If an award is made, to whom should the cheque be made payable?

.....

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

Signed ..... Dated .....

On completion, please return **SIX COPIES** of this form and of any supporting documentation (including a covering letter explaining your reasons for selecting this particular student) to the Administrator (Vacation Studentships), The Physiological Society, PO Box 11319, LONDON WC1E 7JF. The closing date for applications is **30 APRIL.**

Back cover: Detail of the stereociliary bundle of a single outer hair cell, showing the rows of neatly arranged stereocilia increasing in height across the bundle. The stereocilia are 1 to 2 micrometers high. Courtesy of David Furness, Department of Communication & Neuroscience, Keele University.