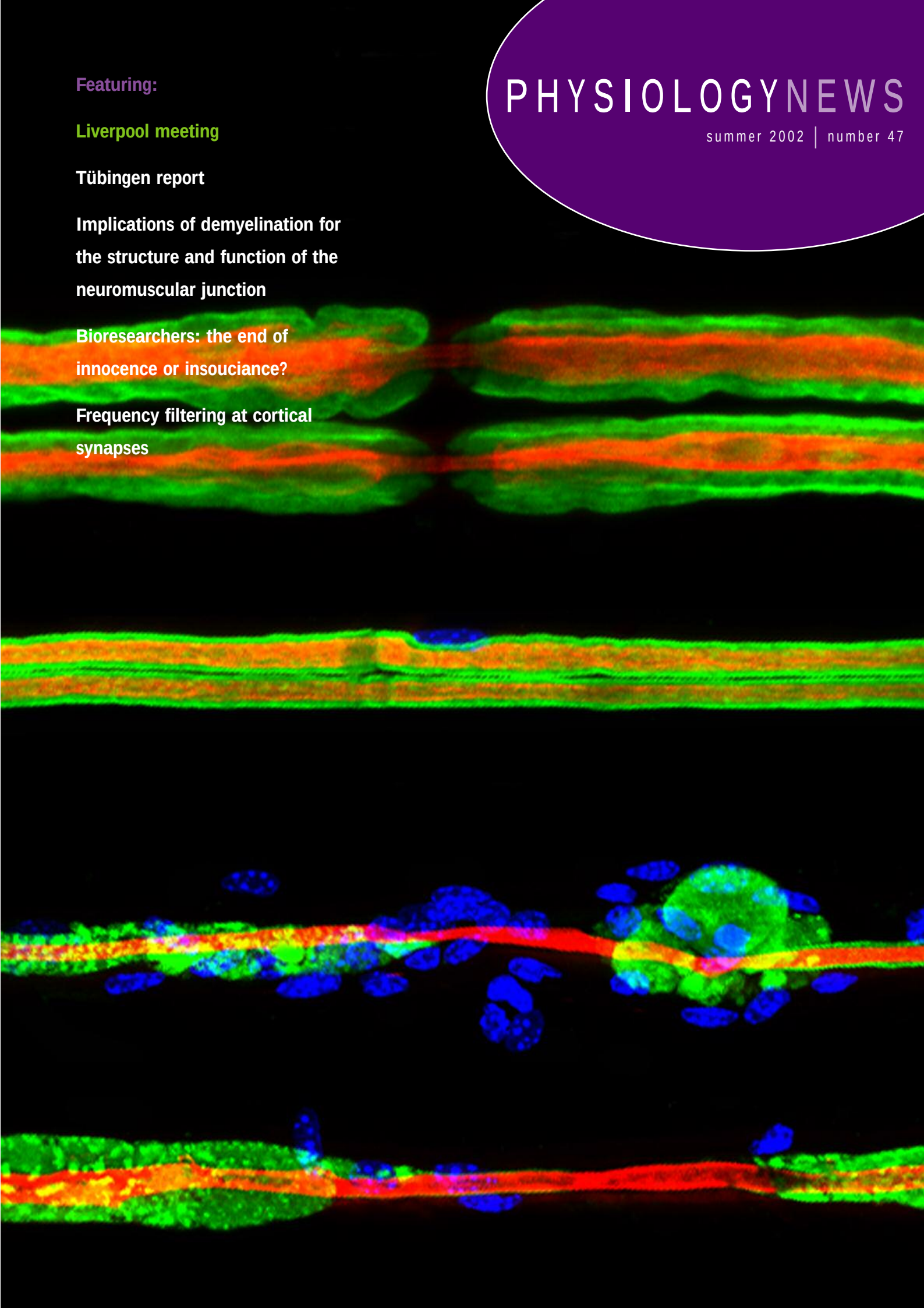
PHYSIOLOGYNEWS
summer 2002 | number 47

Featuring:



Published quarterly by The Physiological Society

Contributions and Queries

Executive Editor
Sheila Greaves
Tel: 020 7269 5725
Fax: 020 7269 5720
Email: sgreaves@physoc.org

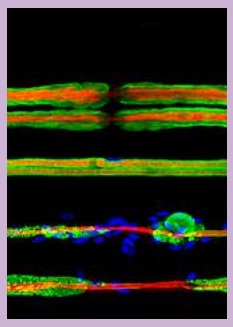
The society web server: www.physoc.org

ISSN 1476-7996

The Physiological Society is registered in England as a company limited by guarantee, No 323575. Registered office: PO Box 11319, London WC1V 6YB. Registered Charity No 211585.

Printed by The Green Tree Press Limited

Cover photo



Teased sciatic nerve fibres from 8-month-old wild and Prx$^{-/-}$ type mice. Image supplied by Felipe Court. See article p12

PHYSIOLOGYNEWS

Contents

Action Points

Affiliate Travel Grant Scheme:
The next deadlines for receipt of applications are 31 July and 30 September 2002.

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

Membership Applications:
The deadlines for receipt of applications for full membership are 30 June and 30 September 2002.

Change of Address:
Members should inform the Administration Office of any changes of address, telephone, fax or email addresses.

Changes can be emailed to: jgould@physoc.org

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

University College London (18-20 December 2002):
Abstracts must be submitted to the Meetings Secretary's Office by 25 September 2002.

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

Magazine:
Letters and articles and all other contributions for inclusion in the Summer issue should reach the Administration Office by 7 June 2002. Please cite all references in articles in the style of The Journal of Physiology.

Magazine Online

The magazine is now available on our website www.physoc.org.

Guidlines for contributors

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

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

Length of articles
This will be determined by the subject matter and agreed between the contributor and the commissioning editor. Articles will vary in length from 500 to 2000 words.

Submission of articles
Authors should submit text in the form of a disk accompanied by a printout wherever possible. Use of disks reduces the risk of introduction of errors during re-typing. It is helpful to give brief details of the computer, operating system and software package(s) used.

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

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

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

Digital photographs and images should be produced at a minimium of 350dpi.

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

Suggestions for articles
These should be made either to the Executive Editor or to a member of the Magazine Editorial Group (see contents page).

EDITORIAL

Foreword

Welcome to the third issue of Physiology News. We hope you will enjoy another packed magazine. This issue we have a profile of physiology in Liverpool (p 4), a meeting report from Tübingen (p 8), and a range of other features. Bill Parry discusses the social responsibilities of bioresearchers in the age of bioweapons (p 14), and also introduces us to Laura Cowell, a 16 year old with a very personal interest in Cystic Fibrosis research (p 22). Three scientific features (p 12, 17 and 20) all have a neuroscience theme. And to balance things out, we also asked Mark Cain, our resident satirist, to give us his thoughts on neuroscience (p 26). Finally, we have a large amount of Society news, including information on what the Society is doing on our behalf in the public and public policy arenas, calls for nomination of prospective Council members (p 33) and a plea from Maggie Leggett for volunteers to help take the science – and especially physiology – message into schools (p 30).

To paraphrase Bill Winlow's editorial: get involved – your society needs you!

IT'S TIME TO VOTE

This editorial is being written just a couple of days after the debacle of the first round of the French Presidential Election, when M. Lionel Jospin was beaten into third place by the right winger M. Jean-Marie Le Pen, who came second, raising the spectre of a government of the far right in France. Many French people, particularly Socialists, are now regretting not having tuned out to vote. Sadly we are seeing similar voter disinterest in some of our UK cities at local elections. It has surely never been more important for people to use their democratic rights, because if we don't use them we risk losing them in the long run.

Now I'm not saying that the Physiological Society is about to elect a right wing regime, but last year the society sent out 1800 ballot papers and we had only 300 returned for elections to the Council. In the years previous to that we had received 250, 169 and 100 ballot papers (in reverse order). I estimate that this was approximately 16.7%, 13.9%, 9.4% and 5.6% going backwards from 2001. So things really have improved, with last year's turnout up by almost 300% on that of 1998! That sort of figure would be meat and drink to psephologists on General Election night, but whichever way we look at it turnout in our Society elections is still pretty awful. Screaming Lord Sutch and his Monster Raving Loony Party probably elicited more interest. Lord Sutch was always an entertaining distraction at elections and amusement value has certainly declined since his death, but the bread and butter issues of politics still remain important to our lives, whether we are amused by them or not.

Society ballots don't raise much of a giggle, but if you have any observations on how we run our elections or on the appearance of those boring old ballot papers, then tell us through these columns. We'd like to hear your views and to see the expression of those views in the elections. As for the ballot paper, the design is the same as it always was, except that those nominated are placed on it in random order, no longer alphabetically, and also details of those elected to the Editorial Board of the Journal of Physiology don't appear on it any more. However, the election process has changed slightly, in that the ballot count occurs before the AGM so that results can be posted in a timely fashion, which at least is logical.

Too often we see voter apathy in society today, followed by those who often did not vote blaming those in power for perceived or even real iniquities in society in general. Democracy at its best should be about an interaction between the voters and the candidates and so it should be with the Physiological Society. As we approach the next set of Society Council elections, I must urge everyone who is a member to use their ballot papers when they arrive and not to dump them in the round file on the floor by your desk. I used to be a city councillor in Leeds and I often told people to vote, whether for me or not, because I believed the act to be important and to give the voter a sense of ownership of the process and a sense of political purpose. So come on everybody, give it a go. It doesn't take long. And while we are on the subject, take a close look at who is standing and consider what they have done for the society already or what their potential might be on the Council. Democracy matters, and it starts from the ground up.

DON'T FORGET TO VOTE

Bill Winlow

Welcome to the University of Liverpool

Professor Graham Dockray

Physiology in Liverpool first emerged through teaching in the Liverpool Royal Infirmary School of Medicine. Then, in 1878, it was incorporated into the new University College of Liverpool. In 1881, George Holt endowed a Chair in Physiology, and this provided the base from which the modern Department of Physiology developed. The first holder of the Chair was Richard Caton, who was a founder member of the Physiological Society and later became Lord Mayor of Liverpool. The second was Francis Gotch who left for Oxford within a few years. His successor was Charles Scott Sherrington.

Right (left to right) Nataly Fedirko, Nina Burdakova, Julia Gerasimenko, Rebecca Longbottom, Alexai Tepikin (wearing tie), Paul Johnson, Michael Ashby, Cristina Camello

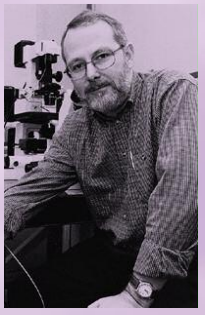
Below left (left to right) Andrea Varro, Lydia Wroblewski, Nicole Gennet, P-J Noble, Graham Dockray, Rod Dimaline, Lisa Flaherty, Felicity Ashcoft, Christopher Kirton

Below right Gül Erdemli (centre) with her group

Right Bob Burgoyne

Centre Bob Burgoyne with his group at a weekly meeting

Far right Barry Campbell



Sherrington was in Liverpool from 1895 to 1913. In recognition of his achievements and his contact with Liverpool, the University established the Sherrington Lecture in 1948. It is given biennially. On several occasions in the past, it has been possible to arrange the delivery of the lecture to coincide with meetings in Liverpool of the Physiological Society. It is a pleasure to be able do so again. During the forthcoming Physiological Society meeting this lecture will be given by Roger Nicoll (University of San Fransisco). Sherrington's link with Liverpool is also marked by the designation of the group of teaching and research laboratories that house the Departments of Physiology, Pharmacology and Human Anatomy and Cell Biology, as the Sherrington Buildings.

Research in the Department of Physiology is presently focused in five research groups. These are Mechanisms of exocytosis and endocytosis (Bob Burgoyne, Alan Morgan and Mike Clague); Epithelial signalling (Graham Dockray, Rod Dimaline, and Andrea Varro); Ion channels and pumps in secretory cells (Ole Petersen, Alexei Tepikin, and Oleg Gerasimenko); Control of smooth muscle (Sue Wray and Ted Burdyga) and Cell and molecular neuroscience (John Quinn, Judy Coulson, Gul Erdemli and Debra Gawler). All groups use cellular and molecular approaches to tackle physiological problems, and there are common interests in cell signalling and secretory cell biology. Research in the department is mostly supported by grants from the MRC, BBSRC and The Wellcome Trust, including several programme grants, an MRC Research Professorship held by Ole Petersen, and an MRC Co-op in Cellular biology of the gastrointestinal tract and pancreas in health and disease. Recent research achievements including major papers and new grants are listed on the departmental website (http://www.liv.ac.uk/~gdwill/physiol.html).

The Department has grown considerably in the last few years: in the RAE of 1992, 8 academic staff were returned, and in the RAE of 2001, 16 staff were returned (5*A). This expansion has been helped by a gift in memory of a former member of academic staff, David Roberts and his wife Marjorie, which allowed the construction of additional laboratories, seminar, meeting and common rooms. In addition, a JIF award from The Wellcome Trust to the Departments of Physiology and Medicine has supported refurbishment of laboratory space, and the purchase of a two-photon confocal imaging system, flow cytometer and other equipment. These laboratories were formally opened in Feb 2001 by Professor Erwin Neher.

Physiology in Liverpool is focused in the Department of Physiology, but there are also physiologists in Veterinary Preclinical Sciences and in clinical departments. The 4-year Ph.D. programme supported by the Wellcome Trust was formulated as a joint venture between the Departments of Physiology and Veterinary Preclinical Sciences, and the two departments jointly deliver the MSc course in Physiology. Links with other departments have been an important feature in recent staff appointments. For example John Quinn and Judy Coulson who arrived in spring 2001 hold joint appointments in the Departments of Physiology and Human Anatomy and Cell Biology, and Oleg Gerasimenko (presently supported by a JIF award) has a joint appointment in Physiology and Medicine.

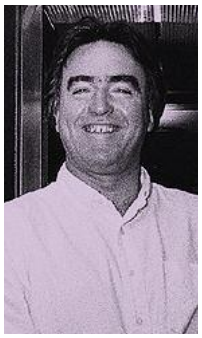
The opportunities for physiological research at this stage of the post-genomic era are as exciting as at any time in the history of the subject. However, establishing the mix of skills required to take full advantage of these opportunities is a formidable challenge. The importance of the core expertise of physiologists with interests in integrative biology, as well as in cell and molecular mechanisms, is clear. But proteomics and functional genomics,

Entrance to the Physiology building

Right John Quinn (Professor of Neurobiology)

Far right The George Holt building

Below (left to right) Dermott O'Callaghan, Margaret Graham and Jamie Weiss



Above (left to right) Ethel Wilkins, Iain Kirk (Technical staff) Rob Gayton (centre)

Right Beverley Fairfoull (Departmental Adrninistrator)

A practical class

the associated skills of bioinformatics, and the testing of new physiological hypotheses through genetic modification of organisms, are all important ways to enhance work in mainstream physiology. The network that promotes these activities in Liverpool includes the infrastructural support made possible through an MRC Co-op grant to develop transgenesis, and facilities for proteomic and gene array work supported by grants made through the NorthWest Science Review.

The expansion in research activity that has take place over the last decade has been matched by increased teaching (but any consequent increase in resource is more difficult to see). The Department of Physiology now delivers courses to over 800 students per academic year. Courses are organised through three different faculties (Medicine, Science, and Veterinary Science) and are at every level from year 1 to post-graduate. They have had consistently high ratings from the QAA, including scores of 23/24 for Physiology and Anatomy, 24/24 for Medicine, and 24/24 for the MSc course (reviewed with Veterinary Science). At the post-graduate level, the Department has vigorously pursued a policy of innovation in the methods of research training. The first of the Wellcome Trust 4-year PhD courses was introduced in Liverpool (Cell and Molecular Physiology). The key feature of this course was the development in the first year of serial attachments to several different research laboratories, coupled with some formal training in research skills. Similar approaches have since been adopted elsewhere. Amongst other clear benefits, this type of course allows students to be active and informed participants in the selection of their main research project. The course has been hugely successful. The experience gained in delivering the first year of the 4-year PhD course has now been used to inform the design of an MRes degree which started in 2001.

The forthcoming meeting of the Physiological Society in Liverpool will be held jointly with the Società italiana di Fisiologia. It will be a great pleasure to welcome our Italian colleagues to the UK, and all participants to Liverpool. There is much to do and see in Liverpool, and the science promises to be excellent too.

Graham Dockray
Head of Physiology Department
University of Liverpool

LETTERS TO THE EDITOR

Dear Editor

What do we mean by plasticity?

Is 'plasticity' becoming the new fashion word of physiology? In recent seminars and in the pages of 'Physiology News' I have noticed phenomena being described as 'plastic' that might previously have been regarded as examples of regulation, modulation or simple cause-and-effect. Although the language of science has to evolve, imprecise usage deprives us of the value of a word for describing a specific phenomenon or set of phenomena. I think it would be helpful if we agreed on a definition of plasticity, which we could all apply when writing or refereeing papers for the Society's and other journals.

It seems to me that such a definition should contain at least two essential elements. The first essential element is to distinguish plasticity from normal developmental processes. It is a response mounted in a mature organism, in cells that have already undergone differentiation.

The second essential element is a long-lasting phenotypic change. This of course raises the question: how long-lasting? In the example that is most familiar to me, fast-twitch muscle becomes slow-twitch muscle over a period of weeks in response to the stimulus of a sustained increase in motor activity. This transformation is stable for as long as the stimulus is present, but if the stimulus is removed the different components of the response revert slowly over weeks or months. There is therefore an element of stability about a plastic response that distinguishes it from phenomena that develop or disappear in hours.

Plastic changes involve re-expression of the genome. In a clear-cut case, genes are switched on that were previously off and genes are switched off that were previously on. In the fast-to-slow muscle transformation, for example, this is true of genes encoding the myosin heavy chain isoforms. However, long-lasting phenotypic changes could be brought about in other ways, such as alternative splicing, changes in translational efficiency, post-translational modification, and targeted breakdown, which must be encompassed by the definition. What about phenotypic changes that are quantitative rather than qualitative? In the muscle example, the activity of an enzyme of oxidative metabolism, such as citrate synthase, may increase by several hundred percent, and that of an enzyme of anaerobic glycolysis, such as lactate dehydrogenase, may decrease by eighty percent. In the current state of knowledge it seems reasonable to include in the definition marked up-regulation or down-regulation that forms part of a long-lasting pattern of change. On the other hand it would not be sensible to include changes resulting from a global non-specific increase or decrease in protein synthesis and/or breakdown, such as muscle hypertrophy or atrophy, because under these conditions the protein profile of the tissue remains essentially unchanged.

It may be difficult to be precise about the nature of the stimulus involved: for example, it may or may not be related to the primary function of the tissue. The fast-to-slow muscle transformation is an adaptation to a change in functional demand, but features of the muscle response are also elicited by changes in thyroid status. We may wish to exclude, however, genetically engineered changes in phenotype.

With these points in mind, I could suggest the following definition: '*Plasticity is the capacity of fully differentiated cells to undergo, in response to a stimulus, a long-lasting change in phenotype that modifies their properties or responsiveness to the same or other stimuli*'. As more is learned about the intracellular signalling pathways underlying such changes it may be possible to evolve a more mechanistic definition. Incidentally, the suggested definition would embrace plasticity of behaviour, because it is presumably underpinned by fundamentally similar changes that modify the efficacy of synaptic transmission.

I would welcome other views. Are the essentials too prescriptive or too broad? Is the definition too precise or too vague? Can it be improved?

Stanley Salmons
Department of Human Anatomy and Cell Biology
The Sherrington Buildings
University of Liverpool

VACANCIES ON THE EDITORIAL BOARD FOR *PHYSIOLOGY NEWS*

Have you ever fancied becoming involved in media or are you interested in journalism and writing and commissioning articles? If so, how about becoming involved in the production of *Physiology News*? We are especially interested in hearing from younger people who are not yet full members of the Society, or who have been newly elected.

As you know the Society's magazine underwent a very successful re-launch at the end of last year, and to continue to build upon this success the existing Editorial Board are looking for a couple of interested and bright individuals who think they have something to offer. The task is fun and rewarding and an excellent opportunity to see your own ideas and articles in print. The Editorial Board meets 4 or 5 times a year, depending on the magazine production schedule, to discuss ideas for future articles or new features, and whilst it is an unpaid role, travel expenses are reimbursed by the Society. If you are interested in becoming involved, or would like further information please contact Sheila Greaves as soon as possible at sgreaves@physoc.org.

Nachrichten aus Tübingen:
Joint scientific meeting of the German, British and Scandinavian Physiological Societies, Tübingen, Germany, March 15th-19th 2002

Above The *Physiology News* correspondent in journalistic disguise

Below Meeting organiser Florian Lang attends to business

Welcome to Tübingen

Tübingen is a delightful medieval city. Historic buildings, cobbled pedestrian streets, a hill-top castle, an ancient University, a market square, pavement cafes. What more could you ask for a Spring scientific meeting? Only good weather – and the 200 or so British physiologists who made the trip to Tübingen got that too. Despite dire warnings of icy winds or even snow – "Take your warmest jacket" said one German friend – the weather defied the gloomy predictions, with sunny skies and temperatures of 18°C plus throughout the meeting.

Not IUPS but EUPS?

The Deutsche Physiologische Gesellschaft (DPG) only holds one scientific meeting a year, and this was it, combined for this year with both the Physiological Society and with the Scandinavian Physiological Society, and supported by the Federation of European Physiological Societies (FEPS). The single annual meeting meant a large turnout of German physiologists, so the total number of participants was nearly 1300, with over 800 communications (see Table 1). The international character of the meeting meant – luckily for the UK participants – that the meeting language was English. I always feel slightly shamed as a Brit hearing delegate after delegate from other countries give presentations in near-flawless English, but there is no denying it makes conferencing in Europe easy work for us monolingual English speakers.

The large scale of the Tübingen meeting lent it the air of a sort of mini-IUPS (EUPS, anyone?), complete with a very superior trade exhibition, nifty conference bags and a thick abstract book. The poster sessions in particular were mammoth undertakings, with a couple of hundred posters on display simultaneously on Saturday, Sunday and Monday. This did mean a fearsome crush, since the space available for poster display was pretty restricted. However, the free food and drink (non-alcoholic, since you ask) at the poster sessions helped keep us fully-fuelled.

Food Glorious Food

The catering was, in fact, one of the memorable features of the joint congress. I am not referring here so much to the formal dinner (of which more later), as to the drinks and nibbles available free throughout the meeting, morning, lunchtime and afternoon. Apart from never-ending supplies of first-rate coffee, there were trays of the sort of sweet bakery products for which Germany is famous, as well as pizza, quiche, *Bratwurst* and delicious hot pork rolls. The provision, and re-provisioning, of all this was extremely efficient. A measure of how seriously the organisers were taking the catering was that on occasion Florian Lang could be seen himself doing the rounds carrying a tray of pastries.

One feature of the meeting I particularly liked was the provision adjacent to the free coffee service of a large number of benches and tables where delegates could sit, drink coffee, catch up and discuss. Would it be too fanciful to catch an air of the coffee-house culture of old Vienna in this? Even more splendidly, each table was equipped with a tray of free pastries (note to self: must cut down on pastries). I was struck by the fact that a tray-load would sometimes sit for hours without anyone eating a single item. I suspect that, at a UK Physiological Society meeting, a table-full of goodies of this kind would have lasted precisely

Communication

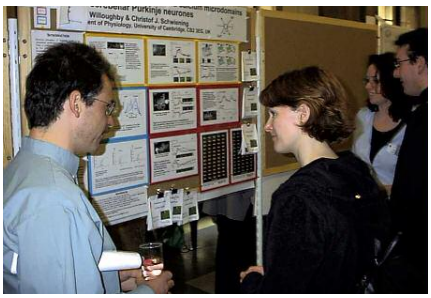


Table 1

Plenary Lectures	8
Symposium Lectures	98
Oral communications	234
Poster communications	577

Numbers of abstracts submitted for the 2002 joint congress

30 seconds before being devoured by a locust-like horde of half-starved and hung-over Ph.D students.

Overall, I felt the "in-meeting coffee-house" style of refreshment was vastly superior to the sort of 30 minute-long scrum-down for stewed tea that sometimes characterises our UK meetings. I think we could learn something from the DPG here. Of course, it must be admitted that the DPG charges each of its members a 50 Euro fee to attend the annual meeting, which probably explains the greater air of comfort/luxury compared to our "home" Physiological Society meetings. But it might be worth considering a similar small charge – say £ 10 or £ 20 – for at least the bigger Society meetings in the UK.

Size isn't everything

Big meetings have a lot to be said for them in terms of well-attended scientific sessions (and conversely, and more importantly, no really poorly-attended sessions). They also give all physiologists the chance to find just the right session for their paper or poster. However, there are other advantages apart from just "critical mass". It will clearly be easier to attract sponsorship and recruit trade-show exhibitors if the sponsors/exhibitors know this is the one time in the year when all the members of a scientific society – their potential customers – will be present, and that there will be 1000+ of them. One meeting a year also means that virtually every graduate student and postdoc hopefully has something new to present. Against this one could argue, with some justification, that it is harder to make contacts than at a small meeting with, say, a couple of hundred participants. This is, of course, why big international meetings tend to spawn satellite Symposia. Another issue is that, if everyone in your lab has their own poster at a meeting, you can all end up grouped together in a single poster session, which can leave your corner of the poster hall feeling uncomfortably like just another lab meeting.

A favourite poster

Because the meeting spanned the whole of physiology, there was a (sometimes rather overwhelming) variety of science on offer, from hard-core molecular biology to hard-core human physiology. Talking of which…

"Favourite" might be the wrong word, but among the most eye-catching (eye-watering?) things I saw were two posters in the human neurophysiology session from the surgeons and radiologists of Tübingen University. Both posters employed the fashionable technique of functional magnetic resonance imaging to identify areas of brain activity during different tasks. The first poster dealt with areas of the brain activated during voluntary contraction of the human external anal sphincter. I am sure you don't need me to tell you where the balloon device (which was helpfully illustrated by a photograph) was placed. In fact, the placement of a

Above, top to bottom The evening reception; Physiological Society stand with (*left to right*) Stan White, Maggie Leggett, Jeremy Ward, Melanie Rees and David Brown; Mark Boyett (Leeds) risks strangulation at the poster session; Mark Dunne reluctantly accepts his award for the meeting's most verbose abstract!

TÜBINGEN'S SCIENTIFIC AND INTELLECTUAL HISTORY

The presence of the university, founded in 1477, has given Tübingen a rich intellectual history, and a number of significant scientific discoveries were made in the city. The early physiologists of the University worked in the unusual setting of the Tübingen castle. The castle, sited high on a hill overlooking the river Neckar, passed to the University early in the 19th century, with the kitchens becoming the University's chemistry laboratory. Felix Hoppe-Seyler, one of the fathers of German biochemistry was Professor here in the mid-19th century. Hoppe-Seyler, who did important work on the chemistry and optical properties of haemoglobin, was an early scientific European; he was known for the international character of his laboratory, which contained both German and non-German speakers and had links with laboratories in France and the UK. Hoppe-Seyler left Tübingen for Strasbourg in 1872, and later founded the Journal of Biochemistry which still bears his name (*Biological Chemistry Hoppe-Seyler*, ISI Impact Factor 2.98).

The most famous discovery made in the castle labs was made by one of Hoppe-Seyler's students, the Swiss scientist Friedrich Miescher. In 1868, Miescher succeeded in isolating cell nuclei and detected in them a phosphorus-containing substance that he named "Nuklein" (*below right picture*). Miescher separated his "Nuklein" into an acidic substance and a protein-containing basic substance. The acidic substance he had isolated was a nucleic acid – DNA – while the basic protein fraction consisted of the histones which package DNA. Later Miescher also isolated "Nuklein" from the heads of trout sperm from the River Rhine. Although Miescher is remembered in the names of several scientific institutes in his native Switzerland, his discovery of DNA – more than 80 years before Crick and Watson solved its structure – is not as widely known as it might be.

Incidentally, scientists in those days had to have strong stomachs. The starting material for Miescher's preparation of "Nuklein" was the pus from discarded surgical bandages. This pus contained many neutrophils and macrophages, from whose nuclei the DNA was derived.

Tübingen also has a rich non-scientific cultural history. Goethe wrote his earliest works here, and was also particularly renowned for seeking "inspiration" in the local bars (*see below; note*

kotzen = vb. to vomit). Another latterly famous inhabitant of the town was the philosopher Hegel (dialectics), who shared a room at the Tübingen Seminary with the poet Hölderlin in the early 19th century. Hermann Hesse, the Nobel Prize-winning author of *Siddharta* and *Steppenwolf*, trained as an antiquarian bookseller at the Hechenhauer bookshop, which is still in the same building in the Holzmarkt (*see below*).

balloon device was common to this communication and the other one from the same group of authors, which dealt with the brain response to anal sensory stimulation (sic). I was left musing that the main methodological difference between the two papers could be summarised as being that, in the second paper, the subject was simply required to brace him- (or her) self, rather than having to clench on command.

Dessert after Dinner – Hölderlin, Rachmaninoff or Satie?

The DPG, like the Physiological Society, has its own unusual traditions. The most striking of these was revealed at the conference dinner. There were no speeches, or at least only very brief ones. Instead, however, there was an after-dinner musical interlude, not to mention some poetry reciting. The special feature of this event, an old tradition of the DPG, was that the performers were all congress participants. The musical performances were of an amazingly high standard, especially given the stress involved in playing in front of several hundred of your peers, including people you might have to face in a Ph.D. defence/viva. I am not sure it would work at a UK meeting, though. Somehow I find it hard to see several hundred "well-watered" UK physiologists sitting quietly after dinner for a recitation of poetry. Off-colour limericks, maybe.

Although almost all the performers were from German labs, the Physiological Society was not totally unrepresented, since Stuart Wilson from Dundee manfully "kept the British end up" with a rendition of one of Satie's *Gnossiennes*. A measure of how seriously Stuart took his representative responsibilities was that he (even more manfully) refrained from taking any alcoholic drink prior to

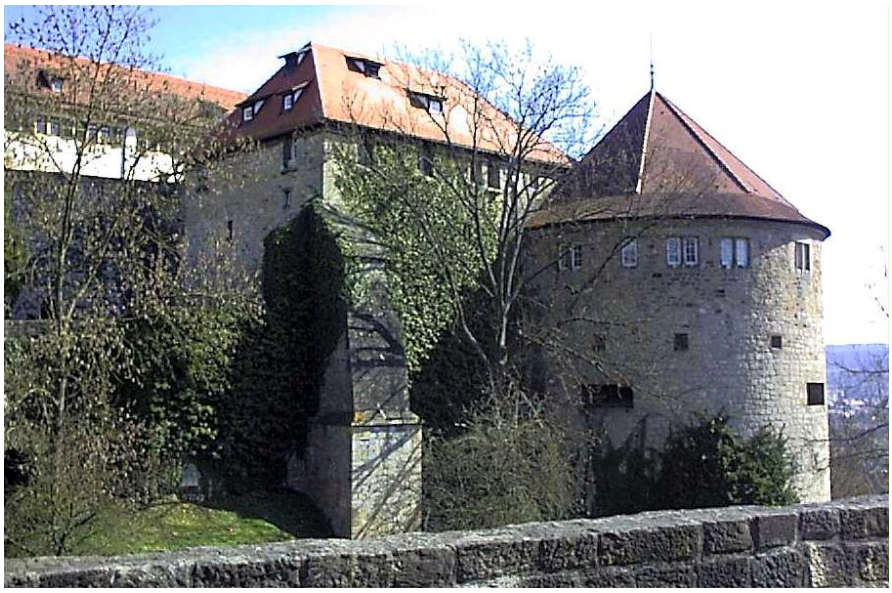
his performance. However, I can report that he made up for this afterwards.

Vive la difference – but is there one?

Apart from the musical and literary recitals at the dinner, and the free food, there was no obvious difference between the conduct of the meeting and of the home Physiological Society meetings we are all familiar with. A scientific session is a scientific session is a scientific session, I guess. Somehow, though, German scientists seem more polite than their English counterparts. Thus I did not see a single serious disagreement during the questions after talks, and the one time a debate seemed likely to break out the Chairman rapidly closed the session! Perhaps it is too fanciful, but I had the impression that a public disagreement – even about the science – would have been regarded as a touch inappropriate. Of course, older members of the Physiological Society can sometimes be heard opining that the questioning after communications at home meetings nowadays is "not what it was" or has "gone soft", so perhaps the Germans are just a little bit ahead of us.

In summary, we owe a tremendous vote of thanks to the organisers of the joint congress, and particularly to Florian Lang and the local Tübingen organising committee, who had obviously worked like crazy to get such a huge show on the road. They put on a splendid meeting, and one which leads me to think that "de facto pan-European" joint meetings of this kind ought to become a regular feature of the European physiology calendar.

Austin Elliott
University of Manchester



Top Tübingen castle

Above left A Tübingen house

*Above righ*t Town Hall clock

Left Cultural (and physiological) overload

Implications of demyelination for the structure and function of the neuromuscular junction

Recent studies of neuromuscular junctions in animal models of demyelinating disease suggest that glial-axonal signalling plays a crucial role in stablising synaptic form and function.

Felipe Court

Charcot-Marie-Tooth (CMT) diseases comprise a group of hereditary neuropathies heterogeneous in their clinical and molecular features. They were first described by Charcot and Marie, in France, and Tooth, in England, in 1886. The clinical phenotype of CMT, although showing considerable variability, is characterised by progressive muscle weakness and distal sensory dysfunction. Several genes have been associated with CMT and the original classification, mainly based on the disease phenotypic expression, has been reformulated; autosomal dominant demyelinating forms are referred as CMT1 and CMT3 and recessive demyelinated as CMT4. The CMT2 subclass represents those related to axonal gene mutations. In addition, a number of animal models representing different forms of CMT have been generated by genetic engineering or have arisen by spontaneous mutation. These are often excellent models of the correspondent human syndrome; hence they provide valuable information about disease mechanisms.

Aspects of the research in Peter Brophy's lab focus on CMT conditions produced by defects in genes associated with Schwann cells, the myelin-forming cells of the peripheral nervous system. Specifically, the lab is interested in the effects of protein disruption on the formation and maintenance of myelin. Recently, axonal degeneration has been recognised as an indirect consequence of demyelinating conditions. This fact emphasises the dependency of the axon on its associated myelin forming cells and opens a valuable way to unveil the biology associated with axon-Schwann cell signalling. In addition, the recognition that axonal damage is not only an integral part of myelin disorders but also a major contribution to the pathology of the disease, may redirect the strategy of future therapeutic approaches.

My Communication to the Physiological Society at the Bristol meeting last year[1] presented results of experiments I carried out in Richard Ribchester's lab, relating to the involvement of neuromuscular junctions in neuropathic changes accompanying demyeli-

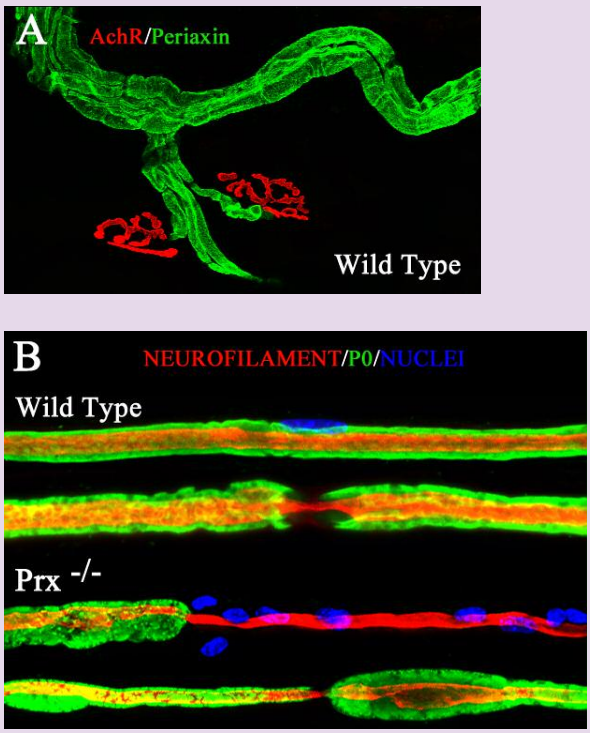


Figure 1 Peripheral demyelination in Prx $^{(-/-)}$ mice.
(A) Immunostaining for periaxin protein (green) together with AchR staining (red) shows that periaxin is present in myelinating Schwann cells but not in perisynaptic ones.
(B) Teased sciatic nerve fibres from 8-month-old wild type (upper panel) and Prx$^{-/-}$ mice (lower panel) were immunostained for myelin protein P0 (green), neurofilament (red) and nuclei (blue). The null mutant shows focal thickenings of the myelin sheath flanking demyelinated segments and increase of nuclei, correspondent to Schwann cells attempting to remyelinate demyelinated fibres (observed as "onion bulb" formations in ultrastructural images[3]).

nation. Our initial aim was to seek possible changes in the functional and structural characteristics of the neuromuscular synapse as a consequence of demyelinating disorders. In so doing we hoped to evaluate the contribution of motor end-plate plasticity to the phenotype of demyelinating conditions. The rationale for this was the fact that axonal degeneration, described in several demyelinating forms of CMT conditions, could be a consequence not only of the lack of trophic support from neighbouring Schwann cells, but might also be elicited by the interruption of trophic signals originated in the muscle fibre, some of them known to be critical for neuronal survival. We used the periaxin knock-out mouse ($Prx^{-/-}$), an animal model of CMT (autosomal recessive demyelinating, classified as CMT4F) to explore the consequences of a demyelinating condition in the neuromuscular junction.

The expression of the Periaxin proteins (L- and S-periaxin) is restricted to myelinating Schwann cells in the peripheral nervous system. $Prx^{-/-}$ mice initially produce compact myelin, but later demyelinate due to disruption of a novel dystroglycan complex[2] (Figure 1). Phenotypically, the mice show tremor, inappropriate clasping reflexes, reduced peripheral nerve conduction velocity and pain behaviour[3]. I used intracellular recording from muscle fibers to evaluate the physiological characteristics of neuromuscular transmission in the $Prx^{-/-}$ mice and immunohistochemistry together with confocal microscopy in order to compare the morphological features of axons, myelinating and terminal Schwann cells, and postsynaptic apparatus of $Prx^{-/-}$ and control mice. End-plate potential (EPPs) recordings at low frequency of stimulation (1 Hz) revealed that most of the mutant junctions showed normal synaptic responses, with amplitude, time course and quantal contents of EPP similar to wild type at all ages. In addition, miniature end-plate potentials (MEPPs) were not different in the $Prx^{-/-}$ compared with the control values in terms of amplitude and frequency (Figure 2). However, EPP latency increased significantly with age (Figure 2A). As shown in figure 2B, EPP latency in wild type mice decreased over a period of 2 months (from the second to the fourth months of age). This is probably related to the maturation of axons and myelin sheaths. In the periaxin null mutant mice, however, latency increased over the same 2 month period, reflecting the fact that $Prx^{-/-}$ Schwann cells initially myelinate axons normally, but this is followed by derangement of the sheath.

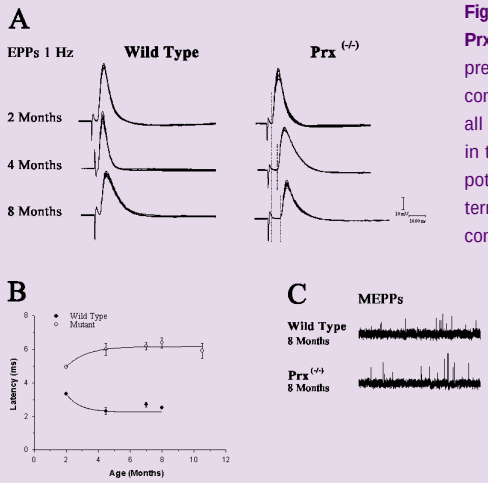


Figure 2 EPP latency increases with age in Prx (-/-) mice. (A) EPPs in the mutant strain present amplitude, time course and quantal contents of EPP are similar to wild type at all ages but the EPP latency increase with age in the Prx (-/-) mice (B). Miniature end-plate potentials in the Prx (-/-) were not different in terms of amplitude and frequency when compared with control animals (C).

When stimulated at higher frequencies (30 Hz; Figure 3), 40% of $Prx^{-/-}$ endplates responded intermittently, contrasting with the complete response exhibited in wild type animals. Our preliminary immunocytochemical data (not shown) suggest that the intermittent failure of synaptic transmission in the $Prx^{-/-}$ mice is associated with structural abnormalities in the neuromuscular junction, consistent with branch-point failure of nerve conduction.

We are currently performing electrophysiological recording from identified neuromuscular junction using vital staining together with acetylcholine receptor staining (using rhodamine-conjugated α-bungarotoxin). We are using the vital stain FM1-43 to visualise nerve terminals by staining the recycling synaptic vesicles. This dye also stains the preterminal axon passively. Using this approach, we are attempting to correlate the morphology of the axon and postsynaptic end-plate with electrophysiological recordings from the correspondent muscle fibres[4].

In conclusion, our observations suggest that demyelinating conditions,

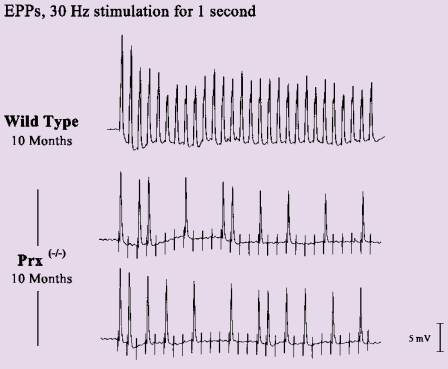


Figure 3
Intermittent block of synaptic transmission in Prx (-/-) mice. Following a 30Hz stimulation for 1 second, many $Prx^{-/-}$ end plates (10 month old mice) responded intermittently compared with a 100% response in control animals.

in addition to the known effect in proximal axons and Schwann cells, produce functional and structural changes at neuromuscular synapses. The data obtained thus far are consistent with the hypothesis that intermittent synaptic transmission, due to branch point failure, may explain several aspects of the physiological abnormalities that accompany demyelination, including the phenotypic signs of muscle weakness and tremor.

I am supported by a Wellcome Trust Prize Studentship. I thank my supervisors, Prof. Peter Brophy and Dr. Richard Ribchester for their advice and helpful comments on this article and Mr. Derek Thomson for technical assistance with my electrophysiological recordings. I am very grateful to the Society and to Pfizer for the award of a Pfizer Prize for my presentation of some of the work described in this article at the Bristol Meeting of the Society, September 2001.

Felipe Court
University of Edinburgh
Department of Neuroscience and Preclinical Veterinary Sciences

References

1 Court, FA, Brophy, PJ, & Ribchester, RR, (2001) Effects of peripheral demyelination on neuromuscular transmission and glial cell organisation in periaxin gene-deficient mice. *J Physiol Proceedings* 536P, 118P.

2 Sherman, DL, Fabrizi, C, Gillespie, CS & Brophy, PJ (2001) Specific disruption of a schwann cell dystrophin-related protein complex in a demyelinating neuropathy. *Neuron* 30, 677-87.

3 Gillespie, CS, Sherman, DL, Fleetwood-Walker, SM, Cottrell, DF, Tait, S, Garry, EM, Wallace, VC, Ure, J, Griffiths, IR, Smith, A & Brophy, PJ (2000) Peripheral demyelination and neuropathic pain behaviour in periaxin-deficient mice. *Neuron* 26, 523-31.

4 Costanzo, EM, Barry, JA & Ribchester, RR (1999) Co-regulation of synaptic efficacy at stable polyneuronally innervated neuromuscular junctions in reinnervated rat muscle. *J Physiol* 521 Pt2, 365-74.

Bioresearchers: the end of innocence or insouciance?

Bill Parry

The scientific community was stunned last year after a team of Australian researchers announced that they had inadvertently developed a highly pathogenic strain of mousepox when trying to create a contraception vaccine for mice. The same manipulation attempted in smallpox could, theoretically, create a similarly lethal strain of the disease that could be used by states or terrorists. After consulting widely with colleagues and the Australian government and military, they went public because they felt they had 'a duty' to be up-front about their discovery and to alert the world that simple genetic manipulations could produce unexpected and potentially devastating effects. That was months before the anthrax attacks in the United States. Would they have gone public if the discovery had been made *after* the attacks? Alistair Ramsay, now Professor of Medicine at Louisiana State University, was part of that team. He says that, although the balance of opinion might have advised that they did not publish, he feels that 'it still would have been right to publicise our findings to alert society to the very real possibility that genetic engineering can produce these potentially nasty outcomes'.

Alistair Ramsay

Physicists and chemists have already had to deal with this issue, and now, more than ever before, many bioscientists are having to as well. Although biomedical research will continue to make impressive and far-reaching beneficial strides in the coming decades, like all technology this progress could be (and if history is anything to go by, will be) misapplied with potentially calamitous effects. So, should bioscientists show more ethical responsibility for the potential ramifications of their research? If so, how so?

The issue attracts a spectrum of opinions. Many, such as Sir Joseph Rotblat, the 1995 Nobel Laureate for Peace, believe that science, at least temporarily in some instances, should 'not have a completely free run'. On the other hand, Lewis Wolpert, Professor of Anatomy and Developmental Biology at University College London, cherishes 'the openness of scientific investigation too much' to regard any research as too dangerous to approach. Between these opinions fall the views of those who express the need for some degree of regulation and monitoring but with a minimum of intrusion.

Rotblat says in his essay 'Science and Humanity in the Twenty-First Century' that 'the need for such responsibility [for one's actions] is particularly imperative for scientists, if only because scientists understand the technical problems better than the average citizen or politician. And knowledge brings responsibility'. He suggests that scientists adopt, like medical doctors, a type of Hippocratic Oath, and believes that ethical review committees should review research projects, particularly ones that have 'a direct impact on the health of the population', such as genetic engineering.

This latter idea is supported by many, including Malcolm Dando, a biological weapons expert and Professor of International Security at the University of Bradford. Given the uncertain future of the Biological and Toxins Weapons Convention (BTWC), Dando proposes an internal ethical review committee system, internationally binding and nationally implemented, that includes academia, industry and government. Under this system, there would be four levels of regulation, separated by the level of toxicity or danger of the research involved, from potentially highly dangerous techniques (e.g. viral vectors) and lethal pathogens (e.g. small pox) to pathogens deemed dangerous, though less of a public threat. The levels of regulation and monitoring, concerning both research and publications, would be correspondingly adjusted to the potential threat involved. The fourth level would consider odd and unexpected findings, such as the super-virulent mousepox virus.

Dando emphasises that this is just one possible system and he encourages bioscientists to think of other possibilities. A similar call was made at a recent summit in New York, called 'Preserving an open society in an age of terrorism'. Charles Curtis, President of the Nuclear Threat Initiative, told bioresearchers there that they must be 'the authors, the implementers and the enforcers' of common sense safety procedures, and that they should do so promptly and publicly.

Whatever system is considered, says Dando, it has to be 'the least onerous and minimally intrusive' so that 'we can preserve most of the free exchange of science. We're trying to find things that we have to put fences around; we want the number of fences kept as low as possible; but we want to design the best fences we can'.

Many though feel that safety and ethical checks already exist, at least within academia. Alistair Ramsay says that for most publicly-funded research, the peer-review process already weeds out most potentially dangerous or ethically dubious research proposals. His experience includes research in New Zealand, Australia and now the USA. He adds: 'Within institutions, there are safety committees, which are often quite rigorous in terms of what you're doing. There is a significant level of control – I wouldn't call it "censorship". It's not infallible, and these committees are not constituted to address direct issues of research ethics, but certainly any work that was overtly threatening would not get through these systems, I don't believe.'

Wolpert believes that, while scientists have the same moral duties and social obligations as any other citizen, censoring or restricting scientific understanding should not be countenanced, no matter how noble the intention:

> The main reason is that the better understanding we have of the world, the better chance we have of making a just society, the better chance we have of improving living conditions. One should not abandon the possibility of doing good by applying some scientific idea because one can also use it to do bad. All techniques can be abused and there is no knowledge or information that is not susceptible to manipulation for evil purposes.... Once one begins to censor the acquisition of reliable scientific knowledge, one is on the most slippery of slippery slopes.

Dr Annabelle Duncan is the molecular science chief at the Commonwealth Scientific Industrial Research Organisation and a former deputy leader of a UN team that investigated bioweapons in Iraq. She has reservations about the internal ethical review system: 'To apply this on a very wide scale may be problematic; I fear that they could easily become politicised... I favour widespread debate around issues. The open debate ensures that all views are brought to the fore and also has, in the longer term, an important educational element.' She concurs that censoring potentially dangerous findings is not the answer either. She told me that there was certainly a need for more control and transparency: 'We need to know who's working with dangerous pathogens and doing what with them.' She says that while the modified mousepox virus paper drew attention to the fact that unexpected results could be misused and modified for maleficent purposes, the results could also be used – and were more likely to be used – for beneficial purposes.

Several governments, however, are less confident with present safety checks. Dando has repeatedly warned academics that if they do not proactively design and implement some

form of an ethical review committee system, governments will: 'Those people who say that biology is neutral, that there is nothing we can do, and that research has been and is likely to be misused in the future – I just don't think that will work. Legislators will constrain them, and I don't think that biologists are going to get away with that argument for very much longer. In fact, they aren't.'

They aren't, because legislation has already been drafted and passed in the UK in the wake of the terrorist attacks in the US last year. Academic and industry concerns surrounding the Anti-Terrorist Act were raised in this magazine ('Defusing the bioweapons time bomb', Spring 2002). Many British academics have since expressed alarm over the Export Control Bill, presently making its way through Parliament, saying that it could restrict academic freedom. A recent article in the *Economist* ('Secrets and lives', 9th March 2002) examined government measures being considered in the US primarily to balance academic enquiry and national security. It states:

> It certainly seems that federal agencies will—quite reasonably—place more emphasis on assessing the risks of a piece of research before agreeing to fund it. More worrying, from the scientists' point of view, is that new areas of bioscience may become classified, that the government is considering reviewing work prior to publication (with an option on refusing permission to publish) and that it might insist that the methods section of some research papers are removed.

The US government has already recalled nearly 7000 technical documents that pertain to chemical and biological weapons production. The White House has also asked the American Society for Microbiology (ASM), with a membership of over 44,000, to limit information that could potentially be misapplied to biological weapons from the 11 journals that the ASM publishes. The society's president, Dr Abigail Salyers, recently wrote: 'Terrorism feeds on fear, and fear feeds on ignorance,' adding that information that can improve public safety was the best defence against bioterrorist threats.

Alistair Hay, Professor of Environmental Toxicology at the University of Leeds, emphasises the need for academics to shape and implement a scheme, and soon: 'Academics should begin to think about what they would like to see, what they would hope to avoid in any legislation, and to shape it from the outset. We need to run an initial scheme past the government before something [they devise] gets too far down the road.'

Alistair Ramsay reflects that scientists, as a whole, generally act in an ethically responsible way. He notes, however, two gaps in the present peer-review committee system: dealing with scientists who are going to do negative research; and dealing with serendipitous findings. Greater transparency could help alert colleagues to suspect or be suspicious of research or behaviour and discourage your typical 'mad scientist'. Concerning serendipitous findings, he says: 'I'm fully prepared that we shouldn't "publish and be damned", that we have a responsibility to discuss our findings where we sense there's a potential for misuse. I don't know the best paradigm for that. What we need now is to put in a mechanism, which scientists will have some input into shaping, that will deal with unexpected findings and how best to potentially control their misuse.'

And many, including Ramsay, add that any review system should involve the public in some capacity. Wolpert states his view unequivocally: 'I do not believe that scientists, or any other group of experts, should have the right to take ethical decisions on their own that affect the lives of the public. Their ethical beliefs may not reflect the public view and that is why I have always argued that their responsibility is to put their knowledge, and its possible applications, in the public domain.'

The recent anthrax attacks, the current war on terrorism and chilling Al-Qaeda documents discovered that reveal their willingness to use biological weapons, have put bioscientists and the dark potential of their research into the public spotlight. In response, our governments have warned that some freedom will have to be sacrificed for greater security from these threats. While many bioscientists might feel that the current systems adequately keep a check on research and the potential misapplications of it, governments and the public seem less comfortable with their claim: risks over which individuals have little personal control are far less readily embraced, especially with something as terrifying as a biological weapons attack. Moreover, recent events show that there is clearly a need to deal with unexpected results, terrorist attacks and, if possible, aberrant scientists.

While I found little consensus over the specific nature of an internal ethical review committee system, there was overwhelming support for a strengthened BTWC. This internationally binding agreement prohibits the development, testing, production and stockpiling of biological weapons via a monitoring mechanism that promotes transparency and confidence building measures. Negotiations to jump-start this convention will resume in November after talks last year broke down.

In the meantime, legislation is being considered or drafted that could have a significant bearing on many bioscientists' research and careers. It seems that, like it or not, many bioscientists will be forced to be ethically and professionally more active in containing that risk. Bioscientists can influence that process now or wait for it to influence them.

Bill Parry is a freelance writer and also works at the Institute of Biology

Frequency filtering at cortical synapses

Combinations of presynaptic molecular mechanisms result in frequency-dependent patterns of transmitter release from pyramidal axon terminals that can be unique to a given class of target cell. Inputs to other pyramidal cells and to one class of inhibitory interneurones display a complex time course of recovery from paired pulse depression that results in a selective depression of transmission at gamma frequencies.

In a communication to the Society last year we reported a novel presynaptic frequency filter apparent at the synapses made by cortical pyramidal cells with some classes of postsynaptic targets. The frequencies filtered by this mechanism are those that appear in the cortical EEG during arousal and attention (the gamma frequency band), the oscillation in the population activity being due to the synchronous firing of neurones in phase with the rhythm. Pyramidal cells do not typically fire on every cycle, however. It is the fast spiking interneurones and the connections between them that appear to drive the rhythm and provide the temporal framework for the synchronous, if more sporadic, activity in the pyramidal population (Traub *et al*, 1998). The synchroneity is proposed to result in temporary cell assemblies that form, disassociate and reform in different configurations with each cycle, representing coherent features of the cortical representations of images or events (Singer 1999, 2001). Indiscriminate, reverberating activation of large populations of interconnected pyramidal cells at gamma frequencies would not only obliterate information coded by these assemblies, it could be dangerous. Mechanisms that prevent such indiscriminate recruitment are therefore likely to be important and this communication focussed on a presynaptic mechanism for which we coined the term 'notch filter'.

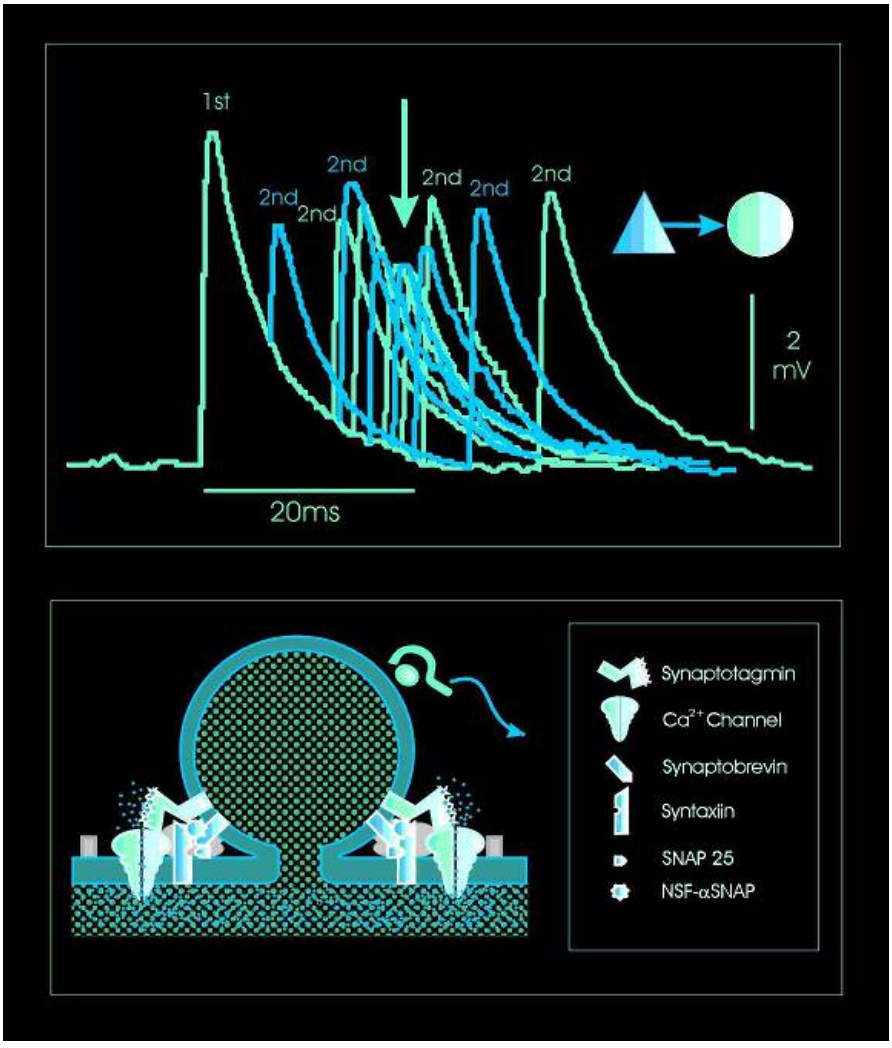
The release of transmitter into the synaptic cleft involves an extremely sophisticated series of interactions between proteins and lipids in the vesicle membrane and in the plasma membrane (Thomson 2000, for review). Before fusion can occur, a vesicle must become attached to an appropriate release site. Proteins whose interactions are essential for the subsequent maturing or priming process are thereby unleashed from the molecular brakes that retard their energy-consuming interactions when they are not attached to an appropriate site. A fusion core complex consisting of proteins in the two membranes forms, binds an ATP-ase and, possibly via cyclical formation and dissociation of the core complex with the resultant expenditure of ATP, primes the vesicle so that it becomes ready for immediate release. The availability of fully mature, primed vesicles forming this immediately releasible pool of transmitter is therefore an important factor in determining whether a release can occur, especially during continued activity. The small synaptic terminals made by pyramidal cell axons in the cortex contain relatively few vesicles, estimates varying between 40 and 60 and only a small proportion of these are in the immediately releasible pool at any one time. Depletion of this pool, factors that retard the entry of vesicles into this pool, or that withdraw primed vesicles from the pool can therefore have a powerful effect on release. The mechanism that probably contributes most significantly to paired pulse depression, release site refractoriness (Betz, 1970), appears to involve the retardation of other primed vesicles by a factor made available during Ca^{2+}-dependent fusion of a vesicle with the plasma membrane. It is therefore a mechanism activated by the release of a vesicle and does not operate in the absence of a release. Terminals that

Alex M Thomson

have released transmitter are refractory, while those that did not release remain available and may be facilitated. A mechanism that results in the release-independent depression of subsequent release at very short interspike intervals has also been identified, but appears to be expressed at only a minority of connections, those made with some subclass(es) of interneurones (Thomson and Bannister, 1999).

Another essential component of the release machinery is the population of presynaptic Ca^{2+} channels. The activity of these channels appears to be regulated by other proteins at the release site so that Ca^{2+} influx is greatest close to fully mature vesicles. A brief influx of Ca^{2+} in a spatially restricted region, or micro-domain, triggers fusion of the vesicular and plasma membranes and the release of transmitter (Llinas, Blinks and Nicholson, 1972). The release may be an 'all or none' phenomenon, but it does not occur with a probability of 1, nor with equal probability at all release sites or even on every trial at a single site. Four Ca^{2+} ions must bind to each vesicular membrane bound Ca^{2+} sensor protein (synaptotagmin), for fusion to be triggered. Small differences in the number of Ca^{2+} ions that enter during an AP, or in the affinity of the synaptotagmin binding sites for Ca^{2+} produce dramatic differences in release probability. This requirement for four Ca^{2+} ions underlies facilitation (and augmentation). Where a single AP does not trigger sufficient Ca^{2+} entry for a release to occur, some of the Ca^{2+} nevertheless binds to synaptotagmin. The requirement for a subsequent Ca^{2+} entry is reduced, since some sites are already occupied and the probability of release for a second AP within a brief period is increased.

In the simplest model proposed to account for the very different patterns of transmitter release at the terminals of pyramidal axons, those with a high release probability exhibit paired pulse (and brief train) depression because they become refractory for a period after each release, while those that have a low release probability exhibit facilitation because they rarely release in response to a single AP and do not experience refractoriness. This model accounted for the differences observed between the typically 'depressing' EPSPs elicited by pyramidal cells in other pyramids, and in some classes of inhibitory interneurones and the strongly facilitating EPSPs elicited in other classes of interneurones. It forms the basis for the proposal that connections between pyramidal cells are phasic, responding strongly to novel inputs, but reporting little detail about maintained activity. In striking contrast, facilitating synapses report little or nothing at the beginning of a presynaptic spike train, but respond increasingly powerfully as activity continues; both types of connection retaining a short term memory for



Top In this dual intracellular recording in neocortex, a pyramidal cell (triangle) was presynaptic to a parvalbumin immuno-positive interneurone. EPSPs were elicited in the interneurone by pairs of APs in the presynaptic pyramid with a range of interspike intervals. Responses to spike pairs at each interval were averaged and are superimposed, with green and blue traces alternating. The green arrow indicates the 'notch'.

Bottom Cartoon of a synaptic release site during fusion of its vesicle with the plasma membrane. The proteins that form the fusion core complex plus bound NSF-alpha-SNAP are in blue. Ca^{2+} microdomains are indicated by the blue spots representing Ca^{2+} ions. A modulatory complex such as Rab-Rabphlin can be seen to be dissociating from the vesicle and may be the signal that retards other mature vesicles in the immediate vicinity. Other proteins involved in docking and in controlling the availability of fusion core proteins (or SNARE's) are indicated in grey (Modified from Thomson, 2000).

preceding activity.

To study the time course of recovery from short interval paired pulse (and brief train) depression, dual intracellular recordings were made in slices of adult rat and cat neocortex. The presynaptic neurone was driven to fire with different patterns and at different frequencies with a range of injected current pulses and postsynaptic responses recorded. Cells were filled with biocytin and processed histologically for identification, and where appropriate, with immuno-fluorescence for parvalbumin. At the connections made by pyramidal axons with some types of interneurones, the early recovery from paired pulse depression appeared adequately described by a single exponential. This could, for example, represent the time course of removal of a/the factor that retards primed vesicles. That this time course is slower when the recovery of later EPSPs in trains is studied might result simply from accumulation of the factor. In these connections, therefore, existing models adequately fit the data. The mechanism responsible for a residual slowly recovering phase of depression, apparent when this curve is extrapolated and equivalent to 10-20% of the 1st EPSP amplitude at intervals >50ms, has not been identified and may be of postsynaptic origin.

At the majority of connections between pyramidal cells and at the pyramidal inputs onto parvalbumin immuno-positive interneurones, however, the picture was rather more complex. At very short interspike intervals (5-10ms) these connections exhibited powerful depression. Recovery from depression was at first rapid and some connections even displayed modest facilitation at intervals around 15ms. This early recovery (or the facilitation) was then interrupted by another phase of depression, peaking at around 20ms and declining again rapidly (half width around 5ms), to be followed at some connections by another phase of modest facilitation. Fluctuation analysis demonstrated that the mechanism underlying this 'notch filter' is of presynaptic origin. The proportion of failures of transmission increased during the 'notch' and the proportional change in CV^{-2} (inverse square of the EPSP coefficient of variation = np/[1-p]) was greater than the change in M (mean EPSP amplitude = npq). The 'notch' was equally apparent in all EPSPs in brief trains of 3-7 EPSPs, representing therefore a true frequency filter. It was, however, relatively insensitive to the size of the preceding EPSP or to the probability of release at low frequencies, differing therefore from the release-dependent components of depression.

The functional relevance of this 'notch' was tested by depolarising the postsynaptic neurone close to firing threshold. The probability of an EPSP initiating a postsynaptic AP correlated with its amplitude at more negative membrane potentials, with EPSPs occurring at very short interspike intervals and those coinciding with the peak of the 'notch' being less effective than those at intermediate, or longer intervals. Without significant coincident activity and summation, therefore, or unless some chemical modulator reduces the power of the 'notch', the only cells that will respond repeatedly to a presynaptic pyramidal cell firing at gamma frequencies will be certain classes of non-parvalbumin interneurones.

Although much of what we currently understand about synaptic transmission results from studies of the neuromuscular junction in the 40's 50's and 60's (McLachlan, 1978 Katz, 1996, for reviews), we are only just beginning to understand the complexities of the synaptic release machinery, and to provide tentative suggestions for the molecular mechanisms that might underlie each of the frequency-dependent properties observed in electrophysiological experiments. Some of these mechanisms may produce only subtle changes in release probability, or in the availability of the immediately releasible pool, but these subtle differences can result in powerful changes in population activity when many synaptic inputs are involved.

Alex M Thomson
Department of Physiology
Royal Free and University College Medical School, London

References

Betz, WJ (1970). Depression of transmitter release at the neuromuscular junction of the frog. *J. Physiol.* 206: 620-644.

Katz B (1996) Neural transmitter release: From quantal secretion to exocytosis and beyond The Fenn Lecture. *J. Neurocytology* 25: 677-686.

Llinas, RR, Blinks, JB and Nicholson, C (1972) Calcium transients in presynaptic terminal of squid giant synapse: detection with aequorin. *Science* 176: 1127-1129.

McLachlan EM (1978) The statistics of transmitter release at chemical synapses. In "International Review of Physiol., *Neurophysiology III*, Vol 17. Ed R. Porter. Baltimore, MD. University Park. pp 49-117.

Singer W (1999) Neuronal synchrony: a versatile code for the definition of relations? *Neuron.* 24:49-65, 111-125.

Singer W (2001) Consciousness and the binding problem. Ann N Y Acad Sci. 929:123-146.

Thomson AM and Bannister AP (1999) Release-independent depression at pyramidal inputs onto specific cell targets: dual recordings in slices of rat cortex. *J. Physiol*. 519: 57-70.

Thomson AM (2000) Molecular frequency filters at cortical synapses. *Prog. Neurobiol.* 62: 159-196.

Traub RD, Spruston N, Soltesz I, Konnerth A, Whittington MA, Jefferys JGR (1998) Gamma-frequency oscillations: A neuronal population phenomenon, regulated by synaptic and intrinsic cellular processes, and inducing synaptic plasticity. *Prog. Neurobiol.* 55:563-575

Melatonin: an antioxidant in phagocytic cells

In this article Carmen Barriga and Ana Beatriz Rodrigues discuss how melatonin favours phagocytic activity at the same time as neutralising free radical levels.

Phagocytosis is an important element of the non-specific immune response and represents a fundamental mechanism of defence against infection. The leukocytes responsible for carrying out the process are attracted to microorganisms by the chemotactic substances that the latter release. They engulf their target (phagocytosis) and then destroy it by the action of enzymes which form oxygen-derived free radicals by means of a series of oxidation-reduction reactions which lead to what is known as the "respiratory burst". In this process, various chemically aggressive species are formed, such as superoxide anions, hydrogen peroxide, or hydroxyl radicals. Their function is to injure and eventually destroy the microorganism.

The presence of free radicals in these phagocytes is beneficial for the organism, since it is thanks to their formation within those cells that pathogenic microorganisms are destroyed – an effective adaptation and solid defence adopted by the organism in its natural habitat. Evidently, a lowering of free radical production in phagocytes, or their neutralisation by antioxidants before these cells can do their work of destroying antigens, would hardly represent an immunological advantage. What would really be an advantage would be if once the radicals had fulfilled their goal they were then sequestered and/or eliminated from the phagocytes, as this would have the effect of guaranteeing the integrity of these important cells.

In recent years, many reports have shown that melatonin is a broad-spectrum antioxidant due to its ability to scavenge free radicals and to stimulate antioxidant enzymes[1] (Tan *et al*. 2000). We have observed that, in ring dove (*Streptopelia risoria*) heterophils, pharmacological concentrations of melatonin (23 x 10^6 pg/ml) reduce superoxide anion levels by modulating the activity of the enzyme superoxide dismutase, and at the same time induce a marked decline in lipid peroxidation[2] (Rodríguez *et al*. 1999).

In light of these results, we asked ourselves the following question: Could melatonin both favour the phagocytic activity of heterophils, and subsequently neutralise the free radicals formed in the phagocytes to avoid causing them cellular damage? With this in mind, we performed an *in vitro* study, evaluating the effect of different incubation times with the hormone melatonin on phagocytosis, and the formation of superoxide anion levels in heterophils after the ingestion of microorganisms. We used the diurnal (50 pg/ml) and nocturnal (300 pg/ml) physiological concentrations of melatonin that had previously been detected in our avian model, ring dove[3] (Rodríguez *et al*. 1999). We also used pharmacological concentrations of 23 x 10^6 pg/ml melatonin, a value that had previously been determined as highly effective in the modulation of the phagocytic process and the free radical levels following phagocytosis[2] (Rodríguez *et al*. 1999). The phagocytes, in this case heterophils, were isolated from ring dove blood by brachial vein puncture followed by density gradient centrifuging. We used *Candida albicans* as the antigen to be ingested in evaluating the capacity for ingestion, destruction, and free radical formation. We determined the phagocytic index (no. of candidae phagocytosed in 100 heterophils), the candidicide power

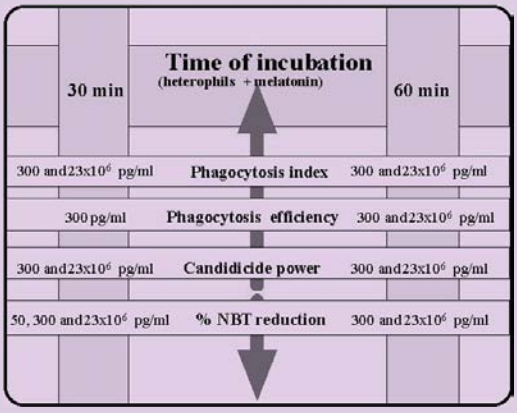


Figure 1 The melatonin concentrations at which there was stimulation of the phagocytosis index, phagocytosis efficiency, and candidicide power, as well as the melatonin concentrations at which there was observed a decline in the reduction of nitroblue tetrazolium (NBT, used as an indicator of the superoxide anion levels) with respect to the control and the diurnal concentration of the hormone, in ring dove (*Streptopelia risoria*) heterophils.

50 and 300 pg/ml = diurnal and nocturnal physiological concentration attained in ring dove plasma, respectively.

23 x 10^6 (100 µM) = pharmacological concentration of melatonin.

(no. of candidae killed of the total phagocytosed), and the superoxide anion production following the ingestion by the heterophils, using the nitroblue tetrazolium reduction technique. The determinations were made after 30 and 60 min of incubation.

Figure 1 gives a summary for the different tests carried out in this study of the melatonin concentrations that were found to be significant with respect to the control (free of hormone), and to the diurnal melatonin concentration (50 pg/ml). We observed that, in the presence of nocturnal and pharmacological concentrations of melatonin, the antigen-ingesting capacity of the heterophils was stimulated due to their greater efficacy in engulfing and phagocytosing antigens. Both melatonin concentrations also stimulated the candida-killing capacity (candidicide power) of the heterophils at both the shorter (30 min) and longer (60 min) incubation times.

With respect to the superoxide anion levels formed after ingestion in the heterophils incubated with melatonin, there was a clear decline in these levels following 30 min incubation of the heterophils with all three concentrations (diurnal, nocturnal, or pharmacological). The lowest superoxide anion levels were obtained after 60 min incubation and at the maximum (nocturnal) physiological and pharmacological concentrations, with the latter concentration giving the lowest levels of the free radical. Therefore, as indicated by the results of the 60 min incubation trials, the effect of melatonin on phagocyte oxidative metabolism seems to be concentration and time dependent. The finding that at greater hormone concentrations and longer incubation times melatonin has a greater effect on the suppression of superoxide anion levels could be explained on the basis of the possibility that, at short incubation times, the hormone probably acts alone when the other antioxidant mechanisms of the phagocytes are only partially activated, while at longer times the results may point to a sum of the effects of the melatonin and of other enzyme systems and antioxidant cellular components (catalase, superoxide dismutase, vitamins C and D, glutathione, etc.) which protect the cells against the activated forms of oxygen deriving from the respiratory burst.

It is therefore of interest that extraction of the pineal gland in the ring dove leads to a rise in superoxide anion levels[4] (Rodríguez & Lea, 1994), and these levels are observed to fall following *in vitro* incubation with melatonin at pharmacological concentrations using inert particles as antigen to be ingested[5] (Rodríguez *et al.* 1997). The present findings also complement the negative correlation that we have recently observed between serum melatonin concentrations and superoxide anion levels[3] (Rodríguez *et al.* 1999). Also, as was noted above, incubation of ring dove heterophils with the pharmacological concentration of the hormone (23×10^6 pg/ml) led to a modulation of different biochemical parameters, all related to the respiratory burst, such as the superoxide dismutase activity and lipid peroxidation.

This is thus corroboration that melatonin in phagocytes behaves as an antioxidant *in vivo* and as a good scavenger *in vitro* of both free radicals and non-free radicals alike[6] (Reiter *et al.* 2000). In view of the present results, we can conclude that melatonin favours heterophil phagocytic activity at the same time as neutralising superoxide anion levels when the hormone acts at the greatest physiological concentration (which is attained during the hours of darkness) or at pharmacological concentrations, with its effectiveness increasing with greater incubation time.

Carmen Barriga and
Ana Beatriz Rodriguez
Department of Animal Physiology
Faculty of Science
University of Extremadura

REFERENCES

1 Tan, DX, Chen, LD, Poeggeler, B, Manchester, LC & Reiter, RJ (1993). Melatonin: a potent endogenous hydroxyl radical scavenger. *Endocrine Journal*. **1**, 57-60.

2 Rodriguez, AB, Nogales, G, Marchena, JM & Barriga, C (1999). Suppresion of both basal and antigen-induced lipid peroxidation in ring dove heterophils by melatonin. *Biochemical Pharmacology*. **58**, 1301-1306.

3 Rodriguez, AB, Marchena, JM, Nogales, G, Duran, J & Barriga, C (1999). Correlation between circadian rhythm of melatonin and phagocytosis and superoxide anion levels in ring dove heterophils. *Journal Pineal Research*. **26**, 35-49.

4 Rodriguez, AB & Lea, RW (1994). Effect of pinealectomy upon the nonspecific immune response of the ring dove (Streptopelia risoria). *Journal of Pineal Research* **16**, 159-166.

5 Rodriguez, AB, Ortega, E, Lea, RW & Barriga, C (1997). Melatonin and the phagocytic processor heterophils from ring dove (*Streptopelia risoria*). *Molecular and Cellular Biochemistry* **168**, 185-190.

6 Reiter, RJ, Tan, DX, Manchester, LC, Karbownik, M & Calvo, JR (2000). Pharmacology and physiology of melatonin in the reduction of oxidative stress in vivo. *Biol. Signals Recept* **9**, 160-171.

Putting a human face on animal testing

It's easy to be a victim. But it's extremely difficult not to be one, and Laura Cowell has been doing this for as long as she can remember. Laura is attractive, precocious and articulate, and at first seems like your typical 16 year old.

But Laura has cystic fibrosis (CF), a congenital disease that mainly affects the lungs, pancreas and intestines, and which strikes one in 2000 newborns. With the complications that accompany it through life, Laura can expect to live to be 30, and will likely require a lung and heart transplant to help her reach that young age. She is also diabetic.

I first met Laura at a launch of publications by the Research Defence Society (RDS), an organisation that supports the humane use of animal experimentation for medical research. Laura, who was there as 'the patient', was one of several participants who was present to put an individual and human perspective on this volatile issue. Nervously, she told the audience 'If it wasn't for medical research, I wouldn't be here talking to you. I owe my life to the researchers and animals. That's why I'm here today.'

Now in her home in Devon, and much more at ease, she tells me about her current infatuation with the electric guitar, and her hopes to play in a band with her friends. 'I'm trying to learn some Nirvana tunes. I like Muse, too.' Trying to relate, I ask about the Smashing Pumpkins and Radiohead. 'Oh ya, they're great, too.'

Laura is taking media and film studies at a local college and relishes every aspect. Her favourite directors? She smiles. Kubrick, Guy Ritchie, and Tarantino. When I ask why she wants to be a radio or TV presenter, she briefly looks to the air for the answer: 'To get my point across. You often only hear one side of the story, and that's often misinformed.'

Which is why I'm here. To get her side, and why she has accepted the personal risk involved in supporting humane animal experimentation. I am one of many who have come to hear her side, a list that has recently included the BBC (whom she first started working with when she was six), a number of broadsheets and the *Evening Standard*.

Laura Cowell: just your typical 16-year-old, right?

What strikes me about their home is how normal it seems. *Is*. No signs of Laura's condition. Her childhood was characterised by pills, injections, inhalers, drips, doctors and hospital stays. At 10, Laura spent two months in hospital on antibiotics to improve her lung function. As soon as she had regained her strength, she had her appendix and gall bladder removed. By this age she'd had more medical attention than most of us ever experience. Then, two years later, she was diagnosed with diabetes.

I ask her when she was first aware of her condition. 'I don't remember a day of not having medicine. It's always been with me. I've grown up with it. I learnt to understand it as I got older.'

Most 16 year olds endure a number of daily ordeals which, to them, are a matter of life and death – spots, love and break-ups, hormone-swamped angst, parents who just don't understand. Yet Laura, on top of these, endures a regime of medication that really is a matter of life or death. Each day she takes between 40 to 60 pills, two insulin injections and two nebulisers (heavy-duty inhalers that dispense antibiotics).

Laura may be a victim of her genes, but she certainly has no time to feel victimised. When I ask in what ways her condition limits her day-to-day routine, she promptly and determinedly replies: 'It fits into my life, and not the other way round. It fits into what I'm doing.'

Her mental approach is more positivity than bravado, however. 'I'll have to keep an eye on my alcohol and insulin,' she admits, 'but otherwise it doesn't really affect me on a daily basis.'

She also has to take more care in winter, when she's more susceptible, which, she says, requires a daily IV drip

of antibiotics. She impassively indicates the mark in her arm.

Since the age of six, Laura has been in the media spotlight, doing her bit for CF research whenever she could. Her mother, Vicky, pulls out a photo album of Laura. Not your typical family photo album: this one shows Laura at different ages with a different mouthful of teeth, always smiling brightly with various television casts and presenters and world renowned specialists in the CF field.

Her participation in the production of the RDS's new publications is just the latest effort. These are intended to correct misinformation about animal experimentation in medical research and to show the public a factual, human, and humane side to the research – the side which struggles against the grisly, inhumane and outdated (or foreign?) images and fallacious information 'the Antis' (anti-vivisectionists) use in their high street displays and websites.

Several of the participants in the publications withheld their names for fear of being targeted by extremists. Is she concerned about possible attacks? She is unequivocal in her reply: 'No, not at all. It's worth it.' Not at all? 'Being the patient, I can't see how–'. She begins again: 'I can see how the researchers might be worried, but not the patient.'

Yet her mother, Vicky, Chair of Seriously Ill for Medical Research (SIMR), wouldn't give me their address via email, just in case. And Andrew Blake, founder of SIMR and their close friend, has CCTV at his home. Andrew gets round in a wheelchair. Laura concludes: 'If it happened it would be quite a shock. But it's getting an important point across, so it's worth it.'

As her condition is part of her life, she has made discussing animal experimentation a part of her life, too. Amongst her friends and in RE and science lesson debates, Laura has informed teachers and classmates of her dependence on animal experimentation – and their dependence too.

Does she have any moral qualms about humane animal experimentation? 'No, it hasn't troubled me. I'm not mean,' she says emphatically. Looking at Safka, their aged dog, she says, 'I don't hate animals; I'm an animal lover.' (She insists I note that Safka receives anti-arthritis medication, which was derived from animal experimentation – as is half the medication prescribed for animals, according to the RDS publications.)

Has she been to a lab to see it for herself? She has, and she was 'pleased' – a word she qualifies – with what she saw. 'Everyone was very friendly, very caring. I was pleased with the treatment I saw there.' She adds that anti-vivisectionists should be allowed to visit labs: 'I think they'd be quite surprised.'

Like all of us, Laura would rather that animals weren't required for medical research, but accepts it for the benefits it brings us. She asks a fundamental question: 'When it comes down to it, would they ['the Antis'] take the odd painkiller? Or deny their children antibiotics? I don't think so.' (Incidentally, non-animal studies account for 90% of all medical research in the UK.)

Laura feels that 'programmes on TV with debates are the best way to address the issue, to get the facts out'. She would also like to write for HOPE, the magazine of SIMR, featuring interviews with researchers who visit schools to discuss why humane animal experimentation is still necessary. She would like to visit schools herself, if possible, to express her point of view and experience.

Laura's media studies beckon. She's got to devise a four-minute opening sequence for a suspense short. I leave her, certain that she will continue to fight for what enables her to fight. More than CF, it's in her genes.

PRESS RELEASE

Patient Monitoring and Physiological Measurement Network

A new EPSRC funded Life Sciences Interface Network has been launched which will focus on patient monitoring and physiological measurement.

Current research into patient monitoring and physiological measurement is fragmented due to its multi-disciplinary nature. Workers in the field come from a variety of disciplines and institutions and have to draw on methods and solutions gathered from a wide range of physical and computing sciences.

The **Patient Monitoring and Physiological Measurement Network** will provide a focus for individuals and organisations involved in patient monitoring and non-invasive physiological measurement, to discuss development and research needs and obtain state of the art advice.

The Network objectives are to:

- Hold a series of strategic research workshops where groups of researchers and potential users identify areas for generic research.
- Provide cross-platform implementations of measurement and signal processing techniques for rapid evaluation by industry.
- Provide certified data-sets so new methods can be evaluated quickly and easily.
- Offer distance learning for education in new techniques.
- Produce literature reviews in specific areas to help disseminate novel techniques rapidly and encourage discussion.
- Facilitate interdisciplinary collaboration and networking between industry professionals.

Membership of the Network is FREE and applications are welcomed from academics, clinicians, student researchers and workers in the medical engineering industries.

Our first workshop will be held at 'Chancellors Conference Centre' in Manchester, 18-19 June 2002. Themes will include: anaesthesia and critical care monitoring, cardiac monitoring, processing and interpretation technologies, and home and outreach monitoring.

Further information about the Network including how to join and details regarding the workshop are on our website at www.pmpm-network.org or you can contact Dr Paul Beatty on 0161 275 5714

How the Edinburgh Medical School 'WENT ON LINE'

New College in Oxford is hundreds of years old; American visitors are sometimes astounded by this anachronism. The Venetian Cinquecento complex of the New Medical Buildings in Teviot Place is however only about 125 years old. The first Professor of Physiology there, William Rutherford had a fine voice, was a singer of repute and evidently a very good teacher. Rutherford had an imposing appearance and there exists on the second floor of the Medical Buildings a fine marble bust of him. He is also portrayed in an engraving. Conan Doyle qualified in medicine at Edinburgh. When he wrote *The Lost World* his description of Professor Challenger is said to have been based on his knowledge, gained as a student, of Rutherford.

Rutherford was interested in the science of acoustics. He was impressed by the invention of the telephone and conceived that the ear operated in a similar manner. At that time it was known that nerve signals were electrical but there was little knowledge of the frequency limitations of this form of transmission. However, for low frequency limitations the discharges of individual fibres in the auditory nerves are to some extent phase locked to the incoming sound, so Rutherford may have been partly right.

In 1886, Rutherford was a member of the House Committee of the University and he proposed that telephones should be installed between the Medical Buildings and the Old College. The matter was considered at meetings on 4th March and 26th November. At the latter there was "Approval of the proposal to set up three wires between the Old and New buildings with one pair of telephones and two pairs of electric bells at a cost of £34.10 in all".

When the BBC started broadcasting in Edinburgh in the 1920s, the chimney of the Medical Buildings was used to support the aerial. I have been told that on lifting a telephone at that time, the programme was clearly heard! At least it will have been better than the dreadful jingles we may now be enforced to listen to whilst 'on hold'. I am a member of *Pipedown*, an organisation that believes that we have a right to choose silence, that we should not be subjected to 'wallpaper music' on such occasions and also in public places such as swimming pools, restaurants etc (e-mail: pipedown@btintenet.com, web: http://www.btinternet.com/~pipedown/choose.htm).

After the introduction of the telephone, the demand grew in Britain to such an extent that it was felt that ultimately the whole adult population of employable women might need to become switchboard operators. The surge in demand is documented in *The Electrician* for 28th August 1891:

> 'A matter which has never yet been seriously faced, is how the demand for telephonic exchange connection, which, after the lapse of a few more years is bound to arise in all large cities, is to be met. What is possible in this direction under the influence of moderate rates and a reasonably efficient service, has already been demonstrated in certain localities – chiefly in Scotland – where towns boasting of next to no manufactures or staple trade, possess exchanges far exceeding in importance those of many English towns of three and four times the population. The principal supporters of such exchanges, after the manufacturers and merchants, being professional men such as doctors, solicitors and accountants; householders and shopkeepers such as grocers, butchers and druggists. The efficiency and the readiness with which a large town or city can be telephoned so as to meet the ever increasing demands of the inhabitants will depend in a very great measure on how the work is laid out and set about in the initial stage. If London were telephoned in the same proportion as Galashiels, it would possess 28,000 subscribers, but that number does not nearly represent the possibilities – far from it. We must certainly anticipate one telephonic exchange connection for every 50 inhabitants in time to come, a modest estimate, if we consider there is already one for every 200 inhabitants in Galashiels and some other towns, which are the merest hamlets in comparison. With London's present population of 5,600,000 such a proportion would represent 112,000 subscribers, and, as the population increases and the boundaries extend, more and more will grow the demand, until even that great number will appear inadequate and insignificant"

There were detractors; dissimulation may be easier when speaking, hence the word 'PHONY'. New technology with automatic switching eventually obviated the need for telephonists. Strowger, an American undertaker, invented an electro-mechanical system that was widely used until recently. One hundred years ago the telephone system was growing, now with mobile phones it still is, *Toujours la change, toujours la même chose.*

E Geoffrey Walsh
Edinburgh
http://www.ed.ac.uk/—gwalsh
(First published in 'Transmitting', The Museum of Communication Foundation Members' Newsletter)

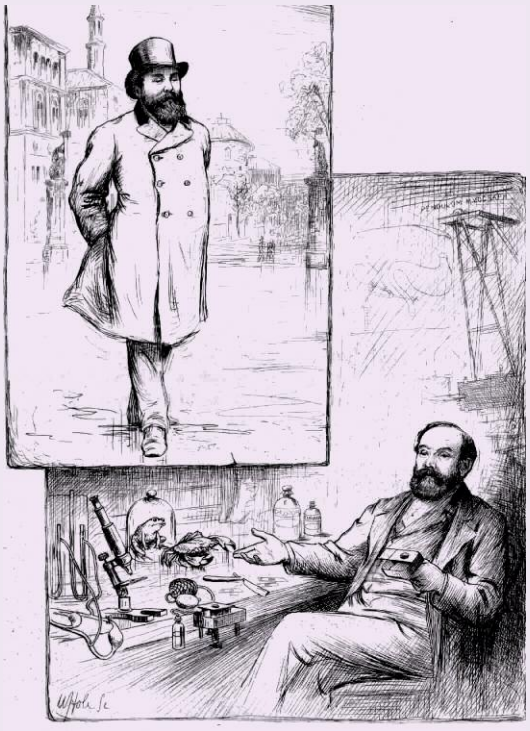
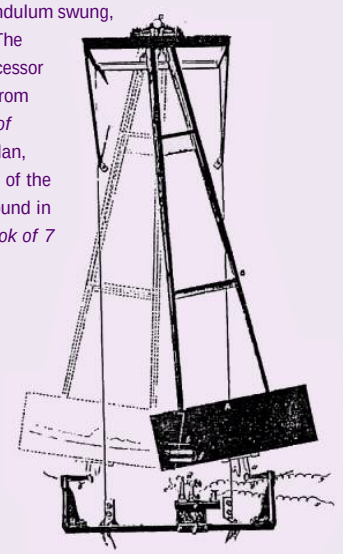


Figure 1 *Top* Rutherford in front of the Medical Buildings at the top of Middle Meadow Walk. *Bottom* Rutherford in the laboratory. The structure on the wall behind him is the pendulum myograph

Figure 2 *Below* The Pendulum Myograph, an ingenious 19th Century device for recording waveforms, partly designed by Helmholtz. The pendulum carried a glass plate which was blackened by soot. It was released to make a swing and then – caught by a catch. As it moved, a physiological event such as the contraction of a muscle from a frog moved a lever and inscribed a line on the plate giving a record – a myogram. The contraction of the muscle was due to an electrical stimulus, a circuit being completed as the pendulum swung, a form of triggering. The system was a predecessor of an oscilloscope. From Foster, M, *Textbook of Physiology*, (MacMillan, 1891). Other details of the instrument can be found in Landois, L, *A Textbook of 7 Physiology* (1888).



The Benevolent Fund – support when needed

Contrary to popular belief, the Benevolent Fund exists to help anyone who is, or has been employed in the field of physiology, not only Members or former Members of the Society. Because of the relative pay scales, it is more often the families of technical or other support staff, or of young postdoctoral workers, who benefit from the Fund when in need, for example after a death in the family, or personal illness. On average, one serious case a year is brought to the attention of the Trustees.

We realized last year that many of our stalwart supporters had retired or died, and our income was declining, so in the summer we approached many senior members of the Society for help.

At the end of the financial year, The Trustees would like to thank most warmly the generosity of several new donors, and the renewed generosity of many previous donors. Members have pledged £710 a year in standing orders made under the Gift Aid scheme, in addition to the £230 a year in existing covenants. Single donations provided a further £1,925 of which £1,270 was given under Gift Aid.

There are many ways in which the Fund can be used to help people “in necessitous circumstances” as the Trust Deed puts it. Examples include contributions (or loans) towards funeral expenses and emergency travel, medical costs, childcare arrangements, relocation costs and other unexpected bills. Following a family crisis, children may fall behind with school work or miss out on school trips – the Benevolent Fund may be able to help with the cost of extra tuition and fares. If you know of someone who the Benevolent Fund might help, then please contact the Trustees in confidence, directly, or via Jo Hancock, at the London Office.

Lynn Bindman (chairman, 2000-2002) and Jo Hancock (Benevolent Fund Administrator). The current Trustees are: Ann Silver (chairman) Alison Brading, Peter Ellaway, Trevor Smart, ex-officio Chris Fry, Jeremy Ward.

email jhancock@physoc.org

Telephone (020) 7269 5710

It's a no-brainer!

After much soul-searching, I have taken a tough decision. No more letting my heart rule my head. Instead, I've decided to start using my brain.

In short – I am going to become a neuroscientist.

There are just too many advantages to ignore:

First, I will be able to feel better about myself, as it is well known (at least among neuroscientists) that we neuroscientists are the crème de la crème of contemporary biologists, working at the frontiers of the brain revolution. Not like the sad lot who work on the rest of the body.

And there are other things. I will be able to tell people what I do at parties. All I will have to say is "I do brain research". They'll know what it means, because they've seen it on the telly. Neuroscience is trendy, you see.

Next, I will be able to apply to the Wellcome's separate Neuroscience panel, instead of slumming it with the whole of the rest of the body in Physiology and Pharmacology. Or I can apply to the BBSRC Neurone special initiative, or even to the MRC, who spend as much on neuroscience research as on the rest of physiology combined.

Plus, I will be able to start my grants, seminar, and talks to admiring students and members of the lay public with ringing phrases such as:

"This is the age/decade/century* of the brain"

"Understanding the brain is the greatest challenge left for bioscientists"

"The key challenge of 21st century bioscience is to understand the nature of consciousness"

"To boldly go where no man has gone before"

I admit I stole that last one.

Of course, I will have to work on my sincerity skills. It isn't all that easy to look someone straight in the eye and tell them that studying a network of three cultured neurones in a dish is going to help explain the nature of consciousness. Not without giggling, anyway. I think the trick is to learn to THINK the right way first. After that the required neurocentricity comes naturally. Thinking the right way means remembering to start each day by reciting the following, sometimes known as the "Neuroscience Creed":

- Research done on the nervous system is by definition more important than research NOT done on the nervous system.
- Therefore, if essentially identical phenomena are reported in the nervous system and in a non-nervous system cell, the nervous system paper is clearly much more important and significant.
- Furthermore, when an observation first made in a non-nervous system tissue is subsequently repeated in the nervous system, then the nervous system paper counts as the first observation of the phenomenon and should be cited as such.
- Therefore: all important physiological observations were first made in the nervous system. QED.

Even better, there is always a NEW bit of the nervous system to work on. This is because of a further basic tenet of brain research, namely:

- All brain regions can be subdivided ad infinitum, and the sub- regions, however small, are equally incredibly important, and are taken to be physiologically different to each other in incredibly important ways until proven otherwise.

So with any luck I will be able to find myself an obscure and vanishingly small neuro-anatomical region of the brain to specialise in (I will, of course, learn to call this a "nucleus", in order to spread maximum confusion among non-neuroscientists).

Then I shall settle down to repeating some other lab's experiments – easy enough to find a template in some paper in the Journal of Twitch and Spike, known to non-neuro-specialists as the Journal of Physiology – but on a different brain region. Hopefully this should keep me in business indefinitely.

There is a slight fly in the ointment. This is the sheer success of neuroscience in the last twenty years, which means that there are just TOO MANY neuroscientists (for instance, attendance at the annual Society of Neuroscience meeting now tops 20,000, and rises each year). Because of this glut of us, some of my neuro-colleagues are worried that we will run out of brain sub-regions. Which would be bad news for a Johnny-come-lately bandwagon-jumper (or recent convert to the neuro-supremacy cause, if you prefer) like me.

However, I have come up with what I think is a masterly solution. In the unlikely event that we neuroscientists run out of real nuclei, the solution will simply be to make up a plausible-sounding name, such as "nucleus recumbens" or "nucleus tractus polemicus", which can then be turned into an opaque three-letter abbreviation (such as "NCR" or "NTP"). With any luck, no-one should be able to figure out that it doesn't exist. They'll just think they haven't heard of it, because they're not a neuroscientist.

Anyway, must sign off now.

I'm off to write that grant proposal about integrative signal processing in the nucleus fatuus. And the nature of consciousness, of course.

Mark Cain

* Delete as applicable

The Voice of the Future 2002

Stuart Honan

On the 19th March, young scientists from a range of scientific and engineering societies attended a meeting with politicians to present their views on issues affecting their future careers. It had been several years since such an event (organised by the Royal Society of Chemistry), had been held, and I had volunteered as the representative for the Physiological Society. In the morning, a panel comprising several members of the House of Commons Select Committee on Science and Technology and Lord Lewis of Newnham fielded a range of questions put to them by young scientists, while in the afternoon Tony Benn (a former Cabinet Minister responsible for industry, energy and technology) addressed us on a range of issues before we had the opportunity to question him too.

A few topics dominated the morning session: money, prospects for women, and the public perception of science. Unsurprisingly, much was said about the perceived lack of funding available in science. Initially, this was noted in the context of the recent Research Assessment Exercise with concerns raised that the shortfalls in funding would affect the ability of departments to fund tenured posts for new academics. Later on, the likelihood of undergraduates pursuing a postgraduate course was questioned given the average debts currently being incurred by students. The low pay and poor job security for junior scientists were also noted, however, one scientist felt that he did not need to be paid much as he was doing what he loved! Although the chairman of the committee, Dr Ian Gibson, acknowledged that the audience was "pushing at an open door" with respect to the committee, one has to wonder how scientists will persuade those in charge of the public purse to give them more money when so many other groups are clamouring for what is a limited resource.

The career prospects for women in science was the topic of many questions with one Royal Society research fellow wanting to know what action was being taken to tackle discrimination against women. Indeed it was noted that most PhD students in science are women yet few are in senior positions. Beyond ensuring that promotion was based upon meritorious performance, and that sexual discrimination was prevented, the only particularly novel suggestion was to encourage career breaks for men, as well as women, in the belief that sexism regarding this would be offset. As for positive role models in the physical sciences, it was believed that this would be provided if more women scientists in physics and chemistry taught in the classroom.

The other major topic from the morning session was the public perception of science. Members of both the panel and audience commented that science as a profession has a poor image in the U.K. with beliefs that one needs to be a 'nerd' to engage in it, and that it is 'damaging' to society. One audience member felt such that he exhorted: "What can we do to make people love us?" This was contrasted with the attitude in continental Europe where one young scientist found the public response in the Netherlands such that, if possible, the next stage of her career would be pursued there. The public were also felt to have an uneasy grasp with the concept that scientific research yielded results that were not absolute. Indeed both the panel and Tony Benn noted that scientists and engineers rarely offered 'black and white' answers of the sort that politicians would want, and that a range of views were often held by experts. This lead Tony Benn to recall an instance when he was involved with overseeing the Concorde project in which, when he asked an engineer whether a certain component should be used was instead given a string of specifications. From what was said, the importance of the ability to clearly and openly communicate scientific information, and its limitations, to a lay audience is evident. The 'trust me, I'm a scientist' attitude would not do.

The ethical aspects of science were also noted in Tony Benn's speech, with an acknowledgement that research can yield products with the ability to affect many people adversely. Such moralising was also reflected in some of the questions asked by the audience, whether it was concerning scientists being employed by the military, or if life scientists should have their own form of the Hippocratic oath. In his replies, he commented upon the importance of involving ethics, and the responsibility we have to others (with or without an oath).

What can be concluded from the discussions held at this event? It seems that many of the issues raised by young scientists have been raised before by other members of the science community, but have obviously not been resolved. Although few novel solutions appear to have been generated from the event, hopefully the politicians will realise what concerns pray upon the minds of young scientists. As for communicating science to society, we in science can play a large part in changing attitudes through education. Indeed, events such as National Science Week give scientists the chance to tell the public about their work and the benefits of science, and they can hopefully be built upon. Anyhow, it will be interesting to know if these same concerns will still be felt by the 'voices of the future' when current young scientists become 'voices of the past', or if other issues will have since replaced them.

Stuart Honan
Department of Pharmacology
University of Cambridge

Glasgow Fluorescence Microscopy Workshop

On the 22nd November, 2001, 14 physiologists from many parts of the UK, stretching from London to Aberdeen, arrived in the Centre for Biophotonics at the University of Strathclyde to participate in a workshop focussed on fluorescence microscopy. The participants were postgraduate students, postdoctoral fellows, lecturers or senior lecturers. As there were more applicants than places available, participants were selected who already had some experience of fluorescent imaging techniques. The overall aim of the workshop was to introduce scientists to advanced fluorescence microscopy, and in particular, a comparison of camera-based and laser-scanning methods.

After registration and some tea or coffee to warm everyone up on a typically fresh, Scottish November morning, the next 3 hours were spent in a tutorial session in which a number of experts provided short talks on aspects of the hardware associated with the various imaging systems. Dr John Girkin provided an overview of the range and capabilities of confocal and multiphoton systems, Dr John Dempster gave an informative talk on the designs and abilities of a variety of CCD cameras and this was followed by a helpful presentation on microscope objective selection from Mr David Wokosin. Each presenter provided handouts, which included references to relevant reading material.

Lunchtime provided the opportunity for participants to get to know each other, gossip about old friends and discuss various points of interest from the morning's tutorials. As well as all this, the postgraduate students had their first "non-pot noodle" hot meal since beginning their PhD studies and are very grateful to the Physiological Society for its generosity! After lunch, the afternoon was spent in the Centre for Biophotonics where the features of camera-based vs laser-scanning imaging were demonstrated on the different imaging systems. The advantages of using multiphoton microscopy when imaging deep into intact blood vessels were demonstrated by comparing directly with conventional confocal imaging. Calcium sparks and waves were recorded from cardiac ventricular myocytes using both a fast, camera-based system, and a rapid, laser-scanning confocal microscope. The strengths and weaknesses of each system were highlighted during the afternoon and there was ample opportunity to discuss specific issues.

Nikon UK chose the course to demonstrate their new C1, modular confocal microscope and TE2000 inverted microscope for the first time in the UK. *Bio-Rad* provided a Radiance 2000 confocal, which had bi-directional scanning capabilities and specific software for rapid imaging acquisition. The workshop ended about 6pm and after some Christmas shopping in Glasgow City Centre by a number of participants, everyone met up for a meal in a local Chinese restaurant.

The next day was spent in the Institute of Biomedical and Life Sciences at the University of Glasgow and began with a series of tutorials on software issues relating to image analysis. Dr Francis Burton introduced issues concerning quantification of image elements, Professor Godfrey Smith provided an informative talk on the analysis of calcium sparks and waves and Dr Craig Daly concluded the series with a very useful review of the wide range of image processing packages commercially available. After some refreshments, there were small group sessions where the various image-processing packages were demonstrated on computer workstations, including the analysis of 2D and 3D structures using Zeiss KS400 by Dr Matt Neilson. Lunch and a feedback session followed, in which participants were encouraged to share their opinions on the workshop and in particular to suggest improvements for the next time. Some of their written comments were as follows:

"I think that overall, the workshop was great – really, really helpful – I learned a lot"

"It was so nice of you to pay for the food – particularly for poor PhD students who can't afford to eat!"

"The workshop could have been improved by extending the duration"

Karen McCloskey
Centre for Biophotonics
University of Strathclyde

Undergraduate Booklet on Using Animals – What the Students Thought

In September 2001 the Physiological Society launched a new booklet on the use of animals in medical experiments. It was designed for undergraduates to help them understand why we still use animals for experimentation, the laws that are in existence to protect the animals, and what the future holds for undergraduates – the next generation of physiologists. The mailing of the booklet was an extensive affair, and it is estimated that over 180 Universities and Institutes received around 20,000 copies.

We have now received feedback from the students themselves and that the response itself was overwhelmingly positive. '*Very informative*' advised a student from Edinburgh. '*It was brilliant*' said a student from Newcastle, and '*Extremely helpful and interesting, a tremendous effort*' recommended an undergraduate from Strathclyde.

We received feedback from a large number of students over a wide selection of courses including: Physiology, Biochemistry, Pharmacology, Nursing, Physiotherapy, Veterinary Science and many others. It is interesting to note that overall 65% of the students expected to do work on animals as part of their course.

The students held varying views on animal usage in experiments. Nearly half (47%) thought that animals should only be used in essential medical research, 32% said that they should be used if there is no alternative and 27% said that animals should be used in research as required. Pleasingly none thought that animals should never be used.

In a world where the Media plays a significant role, especially when it comes to such emotive topics as the use of animals, it would be hard for our students not to have experienced some kind of opposition to vivisection. Indeed, in our survey just over 50% had had exposure to the arguments against animal experimentation, whereas only 10% had seen any kind of pro-experimentation literature. The Society's booklet therefore tries to address some of the questions that young physiologist may one day have to answer for themselves. For example: 'Why experiment on animals at all?,' 'What are the alternatives?,' 'What about human volunteers?' and 'What are the laws and regulations in the UK?'

So what was the reaction to this kind of literature? Well again, the students that we heard from were very

enthusiastic. They said that they found the information useful and highly interesting. Some said that it broadened their views, others that it gave them a deeper insight to the subject. And others still, that it provided them with a lot of information that they wouldn't otherwise have known.

Throughout the booklet, we tried to present a balanced view of animal experimentation. The majority of students (72%) felt that the arguments were rounded, and the pros and cons well explained.

I would like to thank all of you who helped with this feedback process by handing out questionnaires and sending them back to me. We will be doing a reprint this year with a few minor alterations to incorporate some of the suggestions received. I shall be writing to Heads of Departments and departmental representatives in June to find out how many copies you would like for next year, and of course any Member is welcome to request copies as required at this or any other time.

Natasha Moses
Maggie Leggett

We were pleased with the very positive and unsolicited review of the booklet in 'Hope', the quarterly Newsletter for SIMR (Seriously Ill for Medical Research).

Visiting Local Schools

Last December, I circulated a questionnaire to discover which of you were already visiting local schools, and also to try to encourage more of you to find the time for this important activity. Whilst many scientists do have relationships with local schools, there are many more schools out there who would gladly welcome visiting speakers. The idea, in conjunction with other societies who are members of the UK Life Science Committee (UKLSC), is to build up a database of scientists willing to go into schools, and to hold this database in a central location which would be freely available to teachers and easy to search.

We are indebted to Peter Robinson for his help in developing the database. Peter is a senior lecturer at the University of Central Lancashire and a member of the UKLSC Education Group – many of you will have seen his picture in the last issue of *Physiology News*. Over the last four years he has developed the Biology4all.com web-site, from which the database will be accessible. This website is already visited regularly by biology teachers from over 500 schools, a number which is growing all the time.

Constructing this database is the Science Year initiative for the UKLSC Education Group, and was developed in conjunction with the Government's Science and Engineering Ambassadors Scheme (SEAS) launched last January. SEAS will provide an 'umbrella' for all schemes that attempt to encourage more young people to study science and technology from the age of 16. It is also hoped that this Government involvement will result in proper recognition and support from employers for all scientists, working in academia or industry, who wish to take part in promoting science.

There are of course many problems with giving up time to go into schools. There may be the aforementioned lack of support from supervisors/Head of Department etc, and also a feeling of being under qualified to address youngsters. However, there are a variety of ways in which a visitor can be useful to a school – practical demonstrations or taking part in careers fairs can be a less daunting starting point. Equally, teachers will be supportive before and during the event – and always present. I taught in a secondary school for 5 years and would be delighted to talk to any Member or Affiliate who is considering putting their name forward.

If your name is on the database all it means is that teachers can contact you. If, as a result of a discussion with a teacher, you decide that you would rather not help after all there is no compulsion.

The database will be launched at the British Association Festival of Science in September this year, at which we hope to attract some media coverage. Much as I am very grateful to those of you that replied to the survey already, currently there are fewer physiologists listed than those from other disciplines. So, please put your name forward and contact me as soon as possible.

Maggie Leggett

If you wish your name to be added to the database, please send your name, the age group you would prefer to address, and likely AV requirements to mleggett@physoc.org. *Please also indicate how far you would be prepared to travel. The Society will reimburse reasonable travel expenses on production of receipts.*

Robert W Berliner

1915-2002

Born on March 10th 1915 in New York, Bob Berliner graduated from Yale College in 1936 and completed his medical training at Columbia University. His early medical staff positions were spent in New York at the Presbyterian Hospital and the Goldwater Memorial Hospital. It was at Goldwater where he began his research career. Following a further period at Columbia as an assistant professor, in 1950 he was invited to join the National Institutes of Health to develop the Laboratory of Kidney and Electrolyte Metabolism. He was director of the Laboratory for 12 years. It was during this period that Berliner attracted to NIH many outstanding colleagues including Knut Aukland; Barry Brenner; James Dirks; Rex Jamison; Frank Knox; Trefor Morgan; Fuminori Sakai and Fred Wright, all of whom went on to become leaders in the field. Berliner was also a driving force in forming the NIH into one of the leading biomedical scientific institutions in the world. Between 1954 and 1968 he served as director of intramural research and in 1969 was appointed as the first NIH Deputy Director for Science.

A combination of thorough theoretical scrutiny and practical application of whole kidney clearance approaches were the hallmarks of Berliner's work, which was central to the formation of early concepts of how potassium, sodium and hydrogen are transported by the kidney. Berliner's many contributions provided the foundations for later work on single tubules and isolated cells of both the proximal and distal nephron. His analysis of the possible rates of hydration of carbon dioxide in the tubular lumen was an important input to the then strong debate surrounding the mechanisms by which bicarbonate is reabsorbed by the proximal tubule. Berliner also demonstrated that the process of potassium secretion is induced by dietary potassium loading and that this is the major pathway for potassium excretion by the kidney. Potassium is secreted in exchange for sodium; a process that is sensitive to alterations in acid base balance.

In 1973 he left the NIH to return to New Haven as Dean of the Yale University School of Medicine until his official retirement in 1984. His retirement undoubtedly allowed him more time to indulge his fondness for bird watching. In this context, "fondness" may be something of an understatement. His passion for this activity is signified by his official portrait in the Yale Medical School in which he is pictured not in one of the stereotypical academic poses, but standing next to an open window, a pair of binoculars in hand.

His many scientific contributions were emphasised by numerous honours and awards. These included election to membership of the National Academy of Sciences, receipt of the Homer Smith Award of the American Society of Nephrology; the Raymond C Daggs Award of the American Physiological Society; the AN Richards Award of the International Society of Nephrology and the George M Kober Medal of the Association of American Physicians. Yale University honoured him by endowing the Robert W Berliner Chair of Cardiology and Diagnostic Radiology. His close links to Physiology at Yale were emphasised by the creation of the Robert W Berliner Lectureship in Renal Physiology. Bob Berliner was a physician scientist who undoubtedly was one of the founding fathers of modern renal physiology. He will be missed by all who have had the benefit of scientific or social interaction with him. He died on February 5th aged 86 and is survived by his wife, Leah, and their four children, Robert Jr., Alice, Henry, and Nancy.

Stan White
Department of Biomedical Science
University of Sheffield

The BA Festival of Science University of Leicester 9 -13 September 2002

After the success of the Physiological Society's workshop last year, we will once again be taking part in the British Association Festival of Science. The theme of this year's festival is 'Science and the Quality of Life' and the workshop will take place on 11th September at the University of Leicester.

Our four distinguished speakers will be:

Professor Tom Kirkwood, from University of Newcastle who will be speaking on **Ageing and Immortality**. Professor Kirkwood will describe how the ageing process occurs and the key to understanding longevity.

Professor James Malone-Lee, from UCL will speak on **Science and Incontinence** and the great improvements that have been made in this area in the last few years. A gentle and humorous approach to this subject will mean that a nappy should never seem the same to you again.

Dr. Olga Rutherford from King's College London whose talk is entitled **Exercise for Healthy Bones**. As the amount of exercise we do decreases, bones become more fragile. Dr Rutherford will be explaining some of the patterns of targeted exercise that could be of great benefit to us all.

And finally, Dr Dawn Skelton, from UCL, Institute of Human Performance will be speaking on **Prevention of Falls Among Older People – A National Priority**. She will review the valuable role that exercise has to play in the maintenance of independence and in reducing falls and injuries in older people.

Attendance at the Festival is completely free to academics at the University of Leicester. And for those Members and Affiliates who are not working at Leicester, the Physiological Society has a limited number of free tickets. If you are interested in attending this workshop, please contact Maggie Leggett as soon as possible to reserve a place.

Natasha Moses
Maggie Leggett

The House of Lords Select Committee Hearing on the Use of Animals in Scientific Procedures

On the 22nd January 2002, Colin Blakemore, the President of the Physiological Society, gave evidence at the House of Lords Select Committee Hearing on the Use of Animals in Scientific Procedures.

Over the last few months many organisations have been called to give evidence to this Select Committee from both sides of the debate. Representatives from the RSPCA, UFAW, FRAME, UKLSC, RDS and the AMRC have all been called, along with senior representatives from the drug industry and universities.

Questions from the Lords were both general and searching. In his answers, Colin described the professional pride felt by scientists following the introduction of the Act in 1986, making the UK the world leader in animal experimentation legislation. He talked about the campaigns against the abuse of animals in various areas of human life, and the increased public concern about science and regulatory controls. He also described the regrettable and considerable ignorance about why and how animals are used by scientists.

Speaking for the academic community, Colin praised the legal changes made to help combat violent protests, and the Department of Health and other leading figures for speaking out in support of animal experimentation. However, there is still some uncertainty felt in the academic community about how effective these new laws would be. The Lords were obviously shocked by his descriptions of the serious personal attacks Colin himself has suffered.

The Lords were particularly interested in increasing dialogue between those opposed to animal experimentation and those in favour. Colin explained his role, with Les Ward, (from Advocates for Animals) in setting up the Boyd Group, and described some of that group's successes, such as unanimous agreement on banning the use of animals for cosmetics testing, and the publication of a useful booklet on the use of primates. Although this group may lack members from extreme anti-vivisection groups, FRAME, the RSPCA and Advocates for Animals are all members. The Lords were sufficiently impressed by this that a representative, Lord Taverne, attended the following meeting of the Boyd Group in February. Subsequent to this meeting a workshop has been set up by the House of Lords Select Committee, inviting representatives of the Boyd Group and other interested parties to discuss some of the issues on which the Committee feels it would like to make recommendations. Both the Lords and the Boyd Group recognise this as a significant step forward.

The discussion then moved to GM animals, and their effect on the overall number of animals used. Colin suggested that this is likely to lead to an increase, but that the potential benefits from this type of work could be huge. He also suggested, in response to a question from the Select Committee, that an absolute ban on the use of primates could not be recommended at the present time.

Bureaucracy was another subject discussed during the forum. Colin admitted that it had caused some impedance, and suggested introducing a 'fast track' approach that would take account of earlier reviews of the proposed project. In addition, he recommended involving inspectors at earlier stages of the application process.

The final question addressed whether, in the future, it would be possible to end all animal experimenta-

tion. Whilst agreeing this was a desirable goal, and commenting on the great advances made in the uses of alternatives, Colin voiced the opinion that this was unlikely to be feasible in the immediate future if we wanted medical science to continue to progress at the current rate.

I have attended a few of these hearings, and witnessed some gruelling interviews, and on this occasion it was a pleasure to hear the reasons why many of you continue to work on animals explained so eloquently by the President of the Society.

Maggie Leggett

Universities UK Publication – 50 years of UK University Research

Universities UK, the Committee of Vice Chancellors, is undertaking a particularly ambitious and exciting project to profile the success of UK university research. They intend to bring out a publication which will profile university research over the past 50 years and the impact this has had on the everyday lives of people in the UK.

It is being undertaken to link with the Queen's Golden Jubilee Celebrations in the summer. They intend to seek a great deal of media coverage, and to print and distribute over two million copies. This is, therefore, a unique opportunity to generate awareness and national pride in the success of university research in the UK.

Sadly the original criteria excluded the majority of physiological research, as any findings 'that might be considered to be sensitive, such as those that involve animal experiments etc' were prohibited. But thanks to one of our Members, Adrian Rees, who brought this matter to our attention we were able to contact UUK and point out how many important discoveries would be have to be omitted based on this condition.

Thankfully, Universities UK were very receptive to our arguments. A few days later, with the help of the External Relations Committee, we submitted a range of examples of research relying on animal experimentation including *In-vitro* fertilisation, the Krebs cycle, nervous conduction and muscular contraction.

This project has the potential to generate significant interest amongst the general public in university research. This will then provide an excellent platform from which to continue making the case for adequate funding for research. We are therefore very proud to be part of this initiative and look forward to seeing some of our submissions in print in a few months time.

Maggie Leggett

The Physiological Society

Membership of the Council 2002-2003

Call for Nominations

Members of the Society who qualify to vote are encouraged to stand for election to the Council.

The current governance structure allows for 20 Members of the Society to be nominated for, and elected to, the Council by the Membership. There will be several vacancies commencing from this year's AGM (11th September) for member-nominated trustees on the Council, and Members are therefore invited to put themselves or others forward for nomination. In the event of there being more candidates proposed than there are places, a postal ballot will be held.

Candidates for nomination must be:

- Ordinary Members of the Society
- Nominated by 5 other Members of the Society
- Not disqualified from serving as a Director of a Company or as a Trustee of a Charity

The Council will meet three times each year, usually in London. In addition to service on the Council itself, members can expect to serve on one or more Sub-Committees of the Society (for example, Education and Membership, External Relations, Meetings or International). Trusteeship is unpaid, but expenses for travel to meetings, and where necessary, overnight accommodation are reimbursed. Elections are held each year but Members of the Council can normally expect to serve for 4 years, although this can be extended if the Member is subsequently elected to serve on the Executive Committee. For more information about what service on the Council is likely to entail, prospective members should contact Sheila Greaves at sgreaves@physoc.org.

Nomination forms are downloadable from the Society's website www.physoc.org. or are available by email from sgreaves@physoc.org. If it is impracticable to obtain all signatures on one form, copies may be circulated to proposers and returned separately to the Society.

The closing date for receipt of nominations is Friday 14 June 2002

Forms should be returned to Sheila Greaves, The Physiological Society, PO Box 11319, London WC1V 6YB

Prize Lectures for 2003

Members are invited to propose individuals to deliver the Society's Prize Lectures for 2003. The Prize Lectures to be given in 2003 include:

The Annual Review Prize Lecture

The Annual Review Prize Lecture was initiated by the Society in 1968. There is a £500 prize, which consists of £250 for the award and £250 as an honorarium upon publication of the script in the *Journal of Physiology*.

The Bayliss Starling Lecture

The Bayliss Starling Lecture was initiated in 1960 when the then Committee

resolved that there should be a joint memorial to Bayliss and Starling, in the form of a triennial lectureship. These lectures are published in the *Journal of Physiology*.

The G L Brown Lecture

In 1975 the then Committee instituted a series of lectures in memory of Professor Sir Lindor Brown. The purpose of these lectures is to stimulate an interest in physiology. Heads of Departments are asked if they wish to invite the G L Brown Lecturer to their department as the lectures are not given during Scientific Meetings of the Society.

There is a £1000 prize, which consists of £750 for the award and £250 as an honorarium upon publication of the script in *Experimental Physiology*.

To nominate an individual for a Prize lectureship please write to Sheila Greaves by Monday 1 July 2002 with the following information:

- The name and address of the individual you would like to propose
- Why you would like to propose them – what it is about their field of research and achievements that you feel qualify them for this award.
- Details of a seconder (each nomination must be supported by two members of the Society) and their signature

Please send your nominations to Sheila Greaves either by email at sgreaves@physoc.org or by post at The Physiological Society, PO Box 11319, London WC1V 6YB

The Physiological Society

International Bursaries

The Society will offer a limited number of bursaries of up to £250 each for Young Physiologists from countries outside the UK and Ireland to attend domestic Scientific Meetings of The Physiological Society. Applications are open to non-Members and non-Affiliates, as well as to those who have joined the Society. Candidates will normally be expected to present an Oral or Poster Communication at the Scientific Meeting, and will be encouraged to join The Physiological Society if not already a Member. Applicants should be sponsored by the Head of their Department or Institute, or by their supervisor (if a PhD student), or a Member of The Physiological Society (if not a Member).

There is no deadline for applications, but they should be made not less than 10 weeks before the Scientific Meeting that the applicant wishes to attend. Three hard copies must be posted to the Society in order to be considered. (Faxed copies will be considered if a deadline is near, on the understanding that the hard copies will be posted as well.)

Applications should be made on forms available from Jamie Gould (Membership and Grants Administrator) at The Physiological Society office (The Physiological Society, PO Box 11319, London WC1V 6YB, UK; email: jgould@physoc.org). Forms are also available on the Society's website at http://www.physoc.org/international and on page 35 (opposite) of this magazine.

The Physiological Society

Intercalated BSc Bursaries

The Society has agreed to make an allocation (£20,000 for 2002 / 2003) for the support of medical, dental and veterinary students who wish to intercalate a BSc containing a strong element of physiology and including an experimental physiology research project.

Eligibility

British medical, dental and veterinary students studying in the British Isles, intercalating a BSc within the UK who have no government, LEA or other external support for the intercalated year(s).

Awards

Up to £2,000.

Applications

The deadlines are **June 30th** and **November 30th**. Applications should be submitted by the Head of Department of Physiology (or equivalent) in the intercalating host department, following an internal selection process by a properly constituted committee to ensure lack of bias. No more than two applications may be submitted from an institution.

Evaluation

Completed applications will be circulated to all members of the Physiological Society's Grants Sub-Committee, whose scoring will determine funding. When an institution submits more than one application, the Head of Physiology (or equivalent) will be asked to rank those applicants, although that information will count only as a reference point and will not be binding on the Sub-Committee. Assessment will take into account academic ability, research potential, and financial need, and the details of the research project proposed.

Application forms are available from The Administrator (BSc Bursaries), The Physiological Society, PO Box 11319, London WC1V 6YB, on page 37 of this magazine, or may be downloaded from the web.

Tel: (020) 7269 5710
Fax: (020) 7269 5720
Email: admin@physoc.org
Web site: http://www.physoc.org

The Physiological Society

INTERNATIONAL BURSARY SCHEME APPLICATION FORM

(PLEASE TYPE)

Name Age

Address

Postcode Nationality

Tel Email

Degrees (inc subjects and dates)

Post/status PhD year of study (1st, 2nd, 3rd etc)

Are you a member of the Physiological Society? Yes/No (delete)

If yes, give membership number

Meeting to be attended, including date and location

Title and authors of abstract to be presented

Oral communication ☐

Poster communication ☐

Invited speaker ☐

Please tick one box

Estimated cost breakdown (travel, accomodation)

Total sum requested £

Funds awarded/requested from other sources (give expected dates of notification)
Applicants are expected to have applied to their research sponsoring organisation (ie source of salary) if it awards travel grants, and any award from the Society will take this (and funds from any other sources) into account

List your last three principal publications, including titles

List any previous presentations at Phsiological Society meetings, including title (up to three)

Please indicate the specific relevance of the meeting to your current research or future career development

Please give the name and address of your Sponsor (either the Head of your Department / Institute, your Supervisor (if a PhD student) or a member of the Physiological Society. **Please ask your Sponsor to provide a brief letter of support and to mail or fax it with a signed copy of this form to the Society at the address below (marked "International Bursaries").**

Name

Address

Postcode Tel

Fax Email

I support this application and confirm that the statement regarding available resources is correct

(Signature of Sponsor) Dated

If you are awarded a grant, please tick the form of payment preferred:

Cheque to be collected at the meeting ☐ Payment into your bank account ☐

For bank account payments please complete the following (all information is confidential)

Bank/Building Society

Account Number Swift Code

Name of account holder

Full address of account holder

Bank's Full Street Address

After completion, please return THREE **TYPED COPIES** of this form and supporting documentation (including copies of the abstract detailed overleaf) to: The Administrator (International Bursaries), The Physiological Society, PO Box 11319, London WC1V 6YB. Fax: +44(0)20 7269 5720. Note: applications should be received **10 WEEKS** before. Faxed copies will be accepted near to this 10 week limit, but **only** on the understanding that three copies are also being posted.

The Physiological Society

APPLICATION FOR INTERCALATED BSc BURSARY

(PLEASE TYPE)

Applicant's details

Name | Date of Birth

Address

Postcode

Tel | Fax | Email

Desired Course of Study

Institution where intercalated course will take place (name and address)

Details of physiology element in course (must include experimental physiology project).
Please attach a one page summary of the experimental project, with title and supervisor

Funding bodies to whom application for fees, subsistence etc have already been made

Please supply additional information or comments concerning your efforts to obtain funding from another source (use continuation sheet if necessary)

Career Objectives

Reasons for wishing to intercalate a BSc, including any relevant background, accomplishments to date and career objectives (use continuation sheet if insufficient space)

Previous Studies and Relevant Work Experience

A Levels/Highers Subject Year Grade

University Degree Subject

Institution

Course subjects/grades

Year 1

Year 2

Year 3

Details of any special projects/outstanding achievements

Other relevant work or study prior to present course

Confidential Letters of Support

The application must be accompanied by letters in support from two referees. These will normally be the Head of Department or Dean of the Institution in which you wish to take an Intercalated BSc, and an academic tutor who knows your work and personal circumstances, including financial.

1 Name Position

Address

Tel

2 Name Position

Address

Tel

If you are awarded a grant, we would like to transfer the funds directly into your bank/building society account. Please complete. (All information is confidential)

Bank/Building Society Account Number

Name of account holder Sort Code

On completion, the first referee should return **SIX COPIES** of this form and of supporting documentation to The Administrator (BSc Bursaries), The Physiological Society, PO Box 11319, London WC1V 6YB.

Closing dates June 30th and November 30th.

NOVARTIS FOUNDATION BURSARY SCHEME

Bursaries are offered for Novartis Foundation symposia in 2002/3

No.253

MOLECULAR CLOCKS AND LIGHT SIGNALLING

(2) 3-5 September 2002

Closing date for applications: 1 June 2002

No.254

IMMUNO-INFORMATICS: BIOINFORMATIC STRATEGIES

for better understanding of immune function

(7) 8-10 October 2002

Closing date for applications: 1 July 2002

No.256

CANCER AND INFLAMMATION

(11) 12-14 November 2002

Closing date for applications: 1 August 2002

No.257

ANAPHYLAXIS

(24) 25-27 February 2003

Closing date for applications: 24 November 2002

Purpose

To enable young scientists to attend Novartis Foundation symposia (in London unless otherwise stated) and, immediately following the meeting, spend between four and twelve weeks in the department of one of the symposium participants.

Award

a) travel expenses to symposium and host laboratory *and* b) board and lodging for the duration of the bursary

Qualifications

Applicants (of any nationality) must be aged between 23-35 years on the closing date for application.
It is essential that they be actively engaged in research on the topic covered by their chosen symposium.
They should not already have accepted an invitation to participate in that symposium.

Applications

Addressed to:

Bursary Scheme Administrator
The Novartis Foundation
41 Portland Place
London W1B 1BN
UK

Tel: +44 (0)20 7636 9456

Fax: +44 (0)20 7436 2840

Email: bursary@novartisfound.org.uk

including the following information:

- Full name, address and date of birth
- Title of symposium
- Qualifications and short resumé of university education
- Career history, inc. full list of publications
- Full details of current research
- Aims of future career
- Names and addresses of two referees

Further information

For further information about the bursary scheme in general and the topics covered by the symposia, contact the Bursary Scheme Administrator at the above address or visit:
http://www.novartisfound.org.uk/bursary.htm

Noticeboard

No notice is carried for more than three successive editions. Notices are starred so that readers can see at a glance whether this is the first (one star) or final (three stars) appearance of the notice. Notices for the Autumn 2002 edition should reach the **Administration Office by 14 May 2002**.

ELECTRONIC SUBMISSION TO THE JOURNAL OF PHYSIOLOGY

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

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

YOUNG PHYSIOLOGIST'S SYMPOSIA 2002

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

YOUNG PHYSIOLOGIST'S SYMPOSIA 2002

Advance Notices
more information will be disseminated via email

University of Bristol
24 June 2002
'Sore Points and Hot Topics, the Physiology of Inflammation'

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

University of Leeds
8-9 September 2002
All abstracts welcome

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

CAREERS CONFERENCES

Organised in conjunction with other UKLSC Societies, these are suitable for undergraduates and postgraduates. There will be talks on a variety of careers, from patent law to science journalism and working in industry, and an opportunity to have your CV reviewed by a specialist. More information will be sent to departments in September. This year they will be held at:

University of Sheffield
2 November 2002

University of Glasgow
16 November 2002

King's College, London
30 November 2002

MOLECULAR TECHNIQUES FOR LIFE SCIENCES

Glasgow Caledonian University

2-6 September 2002 and 27-31 January 2003

This is a hands-on laboratory based course to introduce participants to techniques used in molecular biology investigations by a sequential experimental programme and intercalated lectures to transform tissue to sequence. Details can be accessed from our website www.sbbs.gcal.ac.uk/ short courses or by contacting Adrian R Pierotti at the following address:

School of Biological & Biomedical Sciences
Caledonian University
Glasgow G4 0BA
Scotland

Phone: +44 (0)141 331 3241
Fax: +44 (0)141 331 3208

http://sbbs.gcal.ac.uk/research/staff_profiles/Adrian_Pierotti.html

**

MICROELECTRODE TECHNIQUES FOR CELL PHYSIOLOGY

19th Workshop 4-18 September 2002

Laboratory of the Marine Biological Association of the UK, Citadel Hill, Plymouth, PL1 2PB

Information for applicants

- The workshop provides intensive practical experience of a number of microelectrode, patch clamp and optical techniques applied to single cells. It is intended for postgraduate students, post doctoral workers or established scientists wishing to apply these techniques in their research.
- The following basic techniques are offered: Two electrode voltage clamp, Patch clamp, Single electrode voltage-clamp, Dye injection, Ion-sensitive microelectrodes, Fluorescent indicators.
- There are 16 places. Participants work in pairs and have the opportunity to do three 3-day experiments in the two weeks. In addition, lectures and practical sessions on electronics, data acquisition and computer analysis, and microscopy will be given. Daily lectures given by teachers and visiting lecturers cover the basic techniques taught and certain specialised topics. A copy of the Plymouth Microelectrode Handbook will be provided.
- Accommodation (for 14 nights – arrive & depart on Wednesday) is close to the laboratory and includes breakfast. Lunch is provided in the lab each day and an allowance is given for an evening meal.
- The course fee of £1100 includes accommodation, meals and tuition. Participants are responsible for their own travel arrangements.

The closing date for applications is 30 April 2002 A meeting to assess applications will occur during May and all applicants will be notified of the outcome.

How to apply

There is no application form.

1 Please give a concise description of your research, your reasons for wishing to attend and your experience of techniques taught on the work-shop. List in order of priority four techniques you would like to learn.

2 Provide a brief CV (2 sides maximum) and list of publications.

3 The application must be accompanied by a letter of recommendation from an academic referee, preferably PhD supervisor or Head of Laboratory. This letter should indicate how your career, the laboratory in which you work and the area of research that you intend to pursue will benefit from your participation in the workshop.

4 What is your likely source of funding?

Funding

Applicants with MRC or BBSRC Studentships – Simply state you have a studentship in your application. Do not apply to the Research Council directly.

Dale and Rushton Funds of the Physiological Society – help with funding is usually available for young physiologists working in the UK. If you wish to apply please indicate in your application to the workshop. There is no need to apply directly to the Dale and Rushton funds before workshop applications are assessed.

Bursaries – The workshop can provide some half bursaries – if you think you will have difficulty finding the full fee please indicate in your application.

Applications should be sent to:

David Ogden,
Microelectrode Techniques, NIMR,
The Ridgeway, London NW7 1AA, UK

email: dogden@nimr.mrc.ac.uk

Information on internet:
www.nimr.mrc.ac.uk/Events/microelectrode.htm

**

British Society for Cardiovascular Research meeting

THE DEVELOPING HEART: BIOLOGY AND PROTECTION

6-7 September 2002
University of Bristol, UK

e-mail: m.s.suleiman@bristol.ac.uk

*