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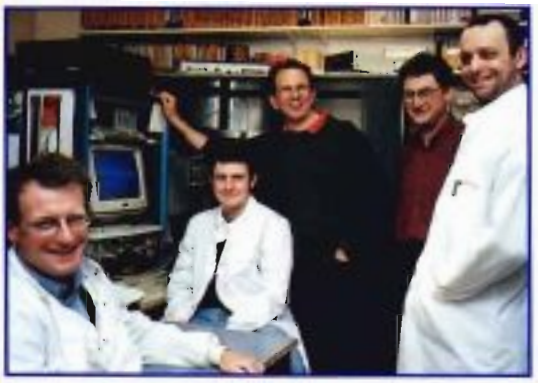
Newcastle & UCL Meetings

Features on :

Muscle Disease

Gene Regulation

Summer 1999
No 35



(l-r) John Sayer, Gavin Stewart, Michael Gray, Nick Simmons and Mike Glanville

Sandra Daley and Kate Askew (3rd year project students) with Colin Brown at the confocal microscope

Anya Hurlbert (left) with her research group

Adrian Rees and Jenny Dean (in auditory psychophysics lab)

(l-r) Mark Larman, Patrick Harrison and Jonathan Brennan fishing for sea urchins (Michael Whitaker's laboratory)

Photography courtesy of Martin Rosenberg

Front cover photograph: Courtesy of The University of Newcastle

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ACTION POINTS

Affiliate Travel Grant Scheme: The next two deadlines for receipt of applications are 31 July and 30 September 1999.

Postgraduate Support Fund: The deadline for receipt of applications is 31 July 1999.

Change of Address: Please can Members inform the Administration Office of any changes of address, telephone or fax numbers.

Email Addresses: The Society is making increasing use of email addresses. Please can Members inform the Administration Office of new email addresses, or changes to existing ones. If your email does not appear in the Grey Book it is unlikely that we have it. Changes can be emailed to admin@physoc.org.

Glasgow Meeting: Abstracts should be submitted to the Meetings Secretary between 14 and 24 June 1999.

Chile Meeting: Abstracts should be submitted to the Meetings Secretary's Office between 9 to 19 August 1999.

Magazine: Letters and articles for inclusion in the next issue should reach the Editor by 27 August 1999. Advertisements and Notices should reach the Administration Office by 20 September 1999 whilst items for the Special Interest Group Forum should reach the Meetings Secretary's Office by 1 September 1999 and items for Committee News should reach the Committee Secretary's Office by 1 September 1999.

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GUIDELINES FOR CONTRIBUTORS

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

Format of articles

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

Length of articles

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

Submission of articles

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

Deadlines for submission

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

Illustrations

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

Author photographs

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

References

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

Suggestions for articles

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

Magazine Online

PHYSIOLOGY AT NEWCASTLE

The past few years, in particular, have seen Physiological Sciences in Newcastle on an up. In contrast to many physiology departments around the country, Newcastle has managed to resist the growing impetus for mergers, so maintaining a focussed strength for the discipline. The external perception of the quality of our research has improved markedly in the last ten years, culminating in our 5A grade in the 1996 research assessment exercise. Recently, we have heard unofficially that we have achieved the maximum 24 points in our teaching quality assessment and that our teaching has been praised for its breadth and innovation. It is thus very appropriate that we are hosting research symposia based around two areas of research strength in the Department and a teaching symposium on the uses of web-based teaching. We have a strong tradition in Newcastle of offering a broad-based Physiology degree and of using our research to inform our teaching. Everyone in the Department is proud to see this philosophy endorsed by external assessors and rightly so, as there are very few departments across the country in any discipline who have achieved this degree of excellence in both teaching and research.

Newcastle has always had a presence in the area of cell signalling. Some will remember the very successful Physiological Society Symposium on Calcium Signalling Mechanisms we put on here three years ago. We have invested further and recruited Tim Cheek from Cambridge, Keith Jones from UCL and Alex McDougall from the Station Zoologique, Villefranche. Jim Gillespie has taken a chair in the Department of Surgery here in Newcastle, but remains an associate member of the Department. The **Cell Signalling Group**'s (Tim Cheek , Keith Jones, Alex McDougall,Michael Whitaker) main research interests lie in calcium signalling during secretion and in the cell division cycle during early embryonic development in sea urchin, ascidian, mouse and *Drosophilia* embryos.

Entrance to Medical School
Photograph courtesy of Martin Roseberg

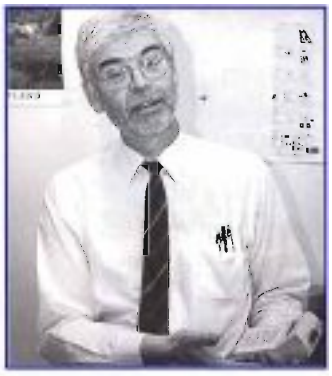
We have also invested in molecular cell biology of epithelia by appointing David Thwaites to a lectureship. David trained here, so we are very pleased that he has recently been awarded a five year MRC Career Establishment Award. The **Epithelial Research Group** (Adrian Allen, Barry Argent, Colin Brown, Ann Clark, Mike Gray, Barry Hirst, Jeff Pearson, Nick Simmons, David Thwaites) is known for its work on the function and regulation of ion channels, membrane transporters and on mucus and epithelial barrier properties. The group exploits the tools of molecular biology to address questions about the molecular nature of epithelial Cl- channels and transporters for organic solutes and the molecular regulation of nutrient transporters, particularly in the gut and kidney. We are pleased that these aspects of the research are to be strengthened further by the recruitment of Andi Werner from the Max-Planck Institute Dortmund to a Readership in Molecular Biology; we

look forward to his arrival in September.

Tim Griffiths, a neurologist, has joined us as a Wellcome Clinical Fellow. He retains links with the brain-imaging group at Queen's Square in London. His arrival has catalysed some outstanding PET and fMRI studies that have identified the areas of the brain engaged in higher order processing of auditory information from moving sound objects. The approach is based on the very fruitful combination of subjects with identified neurological deficits and state-of-the-art auditory psychophysics.

Anya Hurlbert (right), with subject in visual-auditory experiment.
Photograph courtesy of Martin Rosenberg

The **Neuroscience Research Group** (Gary Green, Anya Hurlbert, Adrian Rees, David Sanders) is interested in the higher order processing of both visual and auditory information using approaches that range from pure pyychophysics, through fMRI, PET and the new magneto-encephalographic (MEG) imaging to single cell recording and mathematical modelling of a neurone's transfer function.



Jim Reed
Photograph courtesy of Martin Rosenberg

Newcastle has for some time been a centre of **diving** research (Jim Reed). This has continued with support from the HSE for a Centre of Excellence in lung function and diving research. There is also a developing interest in subjective and objective measures of breathlessness, as part of a programme of **exercise** research.It is a tribute to the breadth of Physiology as a discipline that the Department can accommodate research that spans breathlessness and brain imaging, cloning of transporters and cell division, gut physiology and gametes and that data from the Department appears in journals as divergent as Development, Cell and Nature Neuroscience, as well as in Nature and the journal of Physiology, of course.

Laura Bastenfield (3rd year student) with her "edible" model of the organ of Corti.
Photograph courtesy of Martin Rosenberg

The Department is committed to providing high quality teaching to students in physiology (QAA 24), as well as others studying for medicine (QAA 24), dentistry (QAA 23) and the biomedical sciences. Our popular honours degree in Physiological Sciences covers the broad base of physiology over 2 years. David Sanders, Chairman of the Board of Studies in Physiology writes about teaching in the adjacent article. I will mention only a recent innovation, highlighted in the QAA report: the establishment of study groups in the second and third honours years. Students work in small groups (usually 4) to research a task and report back the outcome. These groups develop the inquisitive skills of students, provide a regular focus for nurturing scientific discussion and allow team-working and time-management skills to be acquired.

Physiologists in Newcastle contribute to the wider promotion of physiology, in particular by active participation in the varied functions of the Physiological Society. The Department currently

provides three main committee members, and editor of Journal of Physiology, two editors of Experimantal Physiology, Chairman of the External Affairs Sub-committee, a member of the Education Sub-committee and the convenor of the Sensory Functions Special Interest Group. In addition to this full scientific meeting of the society, the younger members of the department are hosting a Young Physiologists' symposium later in the year (9&10 September, 1999).

Michael Whitaker (Head of Department of Physiological Sciences)
Photograph courtesy of Martin Rosenberg

The Department owes its present successes to a shared commitment to excellence by all its members. Nonetheless, it cannot be entirely coincidental that the improvements over the last ten years have coincided with Adrian Allen's tenure of the Headship. He stepped down just over two years ago; this is the first Society meeting since then, so it is appropriate to acknowledge his achievements on behalf of the Department. He is now Director of Biomedical Sciences at faculty level. It is also amusing to note that until his arrival in the Department, just over 20 years ago, Adrian was a biochemist !

A recent Science Alive event in the Department.

Michael Whitaker
University of Newcastle

PHYSIOLOGY TEACHING AT NEWCASTLE

We were recently awarded 24 points in the Department's Quality Assurance Assessment and despite the comment from an immunologist colleague that this was merely a bureaucratic success, we are delighted to be working in a teaching 24 and a research rated 5A team.

There is a long tradition in Newcastle of staff seeking to balance teaching and research responsibilities and quality management and teaching innovation have long been emphasized here though we certainly don't claim to be unique. We have had staff/student committees for 25 years and we were the first department in the University to have a local network of computers which were used for teaching. The present teaching system for the undergraduate degree in Physiology depends very heavily on all the academic staff of the department and, of course, they are all contributors to the research rating as well. Research provides a major input to teaching, informing the teaching and giving the students the opportunity to experience frontiers of science research. The curriculum is broadly based and all the honours level modules, spread over two years of the degree programme, have teaching staff who are research active in those areas. The students start the degree with good academic records having an average science A level score of 24 points (BBB) and about 70% graduate with a first or 2:1 degree.

Until recently, lectures formed the basis of the teaching. However, we were becoming concerned that students were not thinking, or even learning, as much

as they could or should. We have introduced study-groups to overcome this and they have two important roles.

Firstly, to replace some lectures with research tasks to be undertaken by the 4 students in the group with checks to ensure that they have completed the task successfully. This is honours-level problem-based teaching. Tasks range from researching the paracrine control of pancreatic exocrine secretion to designing experiments to investigate breath holding. Secondly, study groups are used to encourage the students to share the wider reading and by feeding back the information they have collected they are rehearsing the ideas and the facts contained in those papers.

Sixth formers performing egg and blood pressure measurements as part of the Science Alive day hosted by the Department.

All in all, this approach has had the obvious benefit that students are learning material as they go along during term and that they are talking science on a regular basis. It is now in its second year and although we have made rapid progress in finding a system that works, we are still working to improve the efficiency of the process in terms of staff time. The department has the benefit of being located in a modern building but it was designed 20 years ago and we are short of space. The provision of equipment in teaching labs is a continual budgetary nightmare with which all colleagues will be familiar. However we have labs which are well equipped and last summer we replaced the 30 computers used for data collection in experiments and for word processing with Pentium based machines that can also now be used for web-based teaching.

Stuart Cooper & James Coates (3rd year project students), increasing their dead space.
Photograph courtesy of Martin Rosenberg

"I am an outer hair cell" (3rd year students).
Photograph courtesy of Martin Rosenberg

The Department also teaches 2 cohorts of medical students (440 students), 1 cohort of dental students (75) and delivers a first year science course to 260 students. The honours programme has about 45 students per year for 2 years. This teaching provision equates to a student-staff ratio of about 16:1 which takes us full circle to the point that staff – technicians, secretaries and academics – are the most important resource in producing a good degree programme. Our teaching for medical and dental students is in an integrated environment, crossing traditional subject-based boundaries, with an emphasis on early clinical experience. Such an approach provides a stimulating environment for students , while fostering cross-departmental/discipline interactions. All our teaching is supported by excellent support facilities, including a Charter-mark library and Faculty Computing Centre, directed by a physiologist, Geoff Hammond; a spin off of the latter is the teaching symposium associated with the meeting.

David J Sanders
University of Newcastle

PHYSIOLOGY AT UCL

The Department of Physiology is centred on the Gower Street site in Bloomsbury and is distributed in two major buildings - the Medical Sciences Building with its impressive portico and the imposing Rockefeller Building. These are linked by the famous tunnel under Gower Street. Physiology is also accommodated in several smaller Institutes on the Bloomsbury-Middlesex Hospital Campus - for example in the Hatter Institute (Cardiology) and the Institute of Urology. However its largest sub-division is on the Royal Free Campus of the new Royal Free and University College School of Medicine of UCL: what a mouthful! This school, which was formed in August 1998 also incorporates major post-graduate medical institutes - those of Ophthalmology, Orthopaedics (Stanmore), Neurology and Child Health together with the Eastman Dental School.

UCL Main Building

Undergraduate teaching for medical students in Physiology is taught on both the Gower Street site and Royal Free Campus but from 2000 it will be concentrated in the Cruciform Building (the old University College Hospital), with a new curriculum designed to accommodate the better of the fads and fancies of the Medical Educationalists. It will take its first students (330) in September 2000 . Science teaching is predominantly in Gower Street but third year honours projects, special study modules for the medical course, etc. will be taught throughout the enlarged Medical School. This new structure also supports an enormous diversity of research interest of the Department of Physiology. We have maintained, and even expanded our core interests in cell physiology and cellular neuroscience, principally on Gower Street, as the hub of our activity, these other centres mean that human and systems physiology form a major focus of our interests and contributions.

The Meeting, from 20th - 22nd April, provided a good opportunity for judging the diversity, and depth, of our research interests. The symposia reflected many of these interests. Michael Hausser and Angus Silver put together an exciting session on central synaptic transmission; from vesicles to networks. This touched on interests held in the department on the fundamental mechanisms of secretion and cell signaling (see Shamshad Cockcroft, Bastien Gomperts, Peter Tatham, Geraint Thomas, Anna Koffer) to the study of neuronal interactions (David Attwell, Peter Mobbs, Alex Thomson, Frances Edwards, James Halliwell). Jonathan Ashmore and Mike Duchen arranged a symposium dealing with imaging from molecules to man, again very appropriate for a department that has wide interests in the

Mike Spyer

development of new optical and other imaging techniques. Jonathan has engineered an MRC collaborative group in this area and major initiatives to develop confocal microscopy have been funded by The Wellcome Trust (Mike Duchen, Steve Bolsover) and in 2-photon microscopy by the BBSRC (Chris Richards). The role of neurosteroids was the focus of a symposium organised by Jonathan Fry, and the growing interest in purines in CNS function (Frances Edwards, Mike Spyer) was covered by a symposium organised by Frances Edwards and Sue Robertson. This took place on the Royal Free Campus where the Autonomic Neuroscience Institute (Mike Spyer, Dave Jordan, Geoff Burnstock and others) have major interests in autonomic function. Mike Gilbey organized a symposium on rhythmic activity in the nervous system, and Phil Harrison organised an exciting day reviewing human motor control. These form only a part of our portfolio of 'active' science, and numerous members of the Department - we have 36 HEFCE-funded staff members - have been ignored in this survey but their work was represented in demonstrations, communications and posters.

Gwenaelle Geleoc at the microscope
Photograph courtesy of Janet Grylls

The meeting was a challenge with so many different activities going on. Jonathan Ashmore did an excellent job in integrating the variety of activities with enormous support from the technical and secretarial staff. For me it was a poignant moment as I retire from the Headship to become Dean of the Royal Free Campus this autumn to be succeeded by Peter Mobbs and so it was my last occasion as Host. Twenty years as a Departmental Head is more than enough for my colleagues - and for me. This is not a time for reminiscences but rather of wishing the Department well in the future and looking forward to further meetings of the Society.

Mike Spyer
UCL

UCL Main Building

EDITOR ON THE MOVE...

Professor Bill Winlow has moved and is now at the University of Central Lancashire.
Full address details can be found towards the front of the magazine.

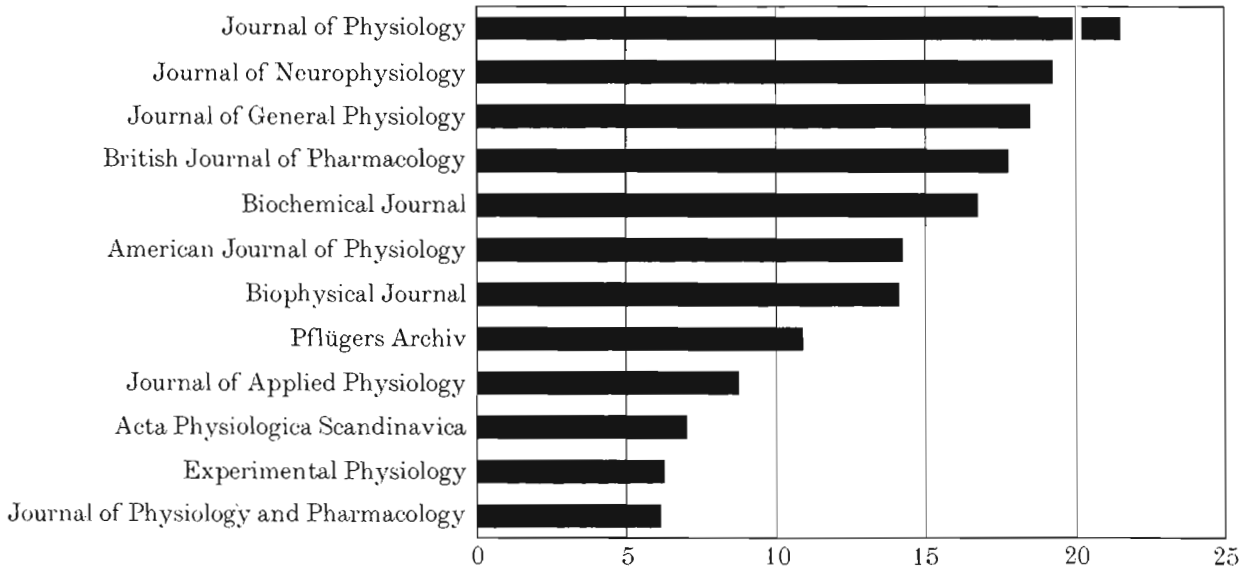
Dear Editor

Alex Verkhratsky's letter in the Spring 1999 issue of the magazine draws attention to the problems caused by paying too much attention to the impact factors of journals. Indeed there are many problems associated with the use of impact factors (Seglen, 1997). However, since significant notice is taken of them, it is important that the figures are accurate. The Institute of Scientific Information (ISI) has confirmed that an unfortunate oversight led to a miscalculation of the 1997 two year impact factor for The Journal,published in the Science Citation Index Journal Citation Reports.The corrected two year impact factor of 3.76 is consistent with the role of The Journal of Physiology as the key journal for papers reporting high quality original science with a rapid influence on physiology. Impact factors do not give any information regarding the longevity of papers. A better indication of this is in the cited half-life of an article. The long cited half-life (9.7 years) of articles published in The Journal of Physiology shows that the influence of the papers is sustained. These two strengths are reflected in the five year impact factor of 21.47 given in the ISI Journal Expected Citation Rates.

Seglen, P. O. (1997). British Medical Journal 314, 498-502.

David Eisner (Chairman)&
Barry Hirst (Secretary)
(For the Editorial Board of The Journal of Physiology)

Seglen, P. O. (1997). *British Medical Journal* **314**, 498–502.



New Working Party to press for 4-year biosciences PhD programmes with increased stipends

Following its highly successful symposium on Postgraduate Training in the Life Sciences held last September, UKLSC organised a Working Dinner in January to discuss how to take forward the consensus that emerged for increased stipends and 4-year PhD programmes with project rotations in the first year. Representatives from the Wellcome Trust, BBSRC, MRC, Royal Society, UK Council for Graduate Education, CVCP, and large and small pharmaceutical companies, attended the Dinner.

Those present fully supported the earlier recommendations for change, and agreed that it had become more difficult to find excellent graduates to fill available PhD studentships in the life sciences. If the UK was to maintain its current preeminence in the biosciences, and if the biosciences were to fulfil government expectations of providing future benefits to the economy and improvements in the quality of life, then it was essential to provide more incentive for the best graduates to pursue a career in biomedical research. An increase in stipend to match that currently offered by the Wellcome Trust was a key requirement. The addition of a common first year, with rotations through prospective laboratories, was considered to be equally important, to give the first year students enough information to make a rational choice of project and supervisor. The first year would also broaden the students' experience and provide a useful stepping-off point for those who realised that they were not suited to research. Dr Patricia Chisholm (Wellcome Trust) described the high quality of students applying for the Trust's very competitive, fully funded, 4-year PhD courses as "absolutely staggering", and the same point was made by Martin Raff about the 4-year MRC PhD course that has been running at UCL.

The meeting agreed to establish a Working Party under the chairmanship of Prof Sir Brian Follett (VC of Warwick University). The Working Party will include both academic and industrial members, and its remit will be to draw up proposals to present to the OST for the introduction of 4-year PhD programmes with increased stipends in September 2000. Since it is clear that the government will not be convinced by hearsay argument, the Working Party will employ a researcher to obtain statistics on the impact of a higher stipend and a 4-year programme on the quality of applicants, and, if possible, on the research success of PhD graduates. The Working Party will also try to determine whether universities are producing an appropriate number of PhDs in the life sciences.

Mike Withnall &
Martin Raff

REGULATION OF SIGNAL TRANSDUCTION AND GENE EXPRESSION BY REDUCED OXYGEN

In this article David Millhorn discusses recent developments in hypoxia-induced gene regulation with respect to signal transduction pathways and protein-DNA interactions regulating transcription.

Gene regulation is a complex biological process that results from molecular interactions among nuclear protein factors (transcription factors) and DNA control sequences. These protein-DNA interactions often occur as the result of an extracellular stimulus that is transmitted to the nucleus by a specific signal transduction pathway(s). Although numerous stimuli have been identified which regulate gene expression, perhaps none is more intriguing than reduced oxygen (hypoxia). Hypoxia-induced gene expression has been implicated in a number of physiological processes, including erythropoiesis, carotid body chemoreceptor function, and angiogenesis, all of which enhance the delivery of oxygen to tissue. Genes involved in mediating each of these important processes are normally activated by long-term (hours to days) rather than acute (seconds to minutes) episodes of hypoxia. However, this does not rule-out the possibility that genes can be regulated very quickly by reduced oxygen. For example, our laboratory measured increased transcription of the *tyrosine hydroxylase* (TH), gene within 15-30 minutes following the onset of hypoxia in pheochromocytoma (PC12) cells (**1**).

Most of the investigations of hypoxia-induced gene regulation have focussed on either the signal transduction pathways or the protein-DNA interactions that regulate transcription. Here I shall briefly describe recent developments in these areas. A more detailed discussion of hypoxia-induced gene regulation can be found elsewhere (**2**). An important distinction that should be made when studying signal transduction is whether or not the cells of interest depolarize during hypoxia. Figure 1 summarizes most of the known hypoxia-regulated signal transduction and gene regulatory mechanisms in the excitable oxygen-sensitive PC12 cell line. PC12 cells depolarize during hypoxia due to inhibition of an oxygen-sensitive potassium channel, which we have identified as the Kv1.2 channel (**3**).

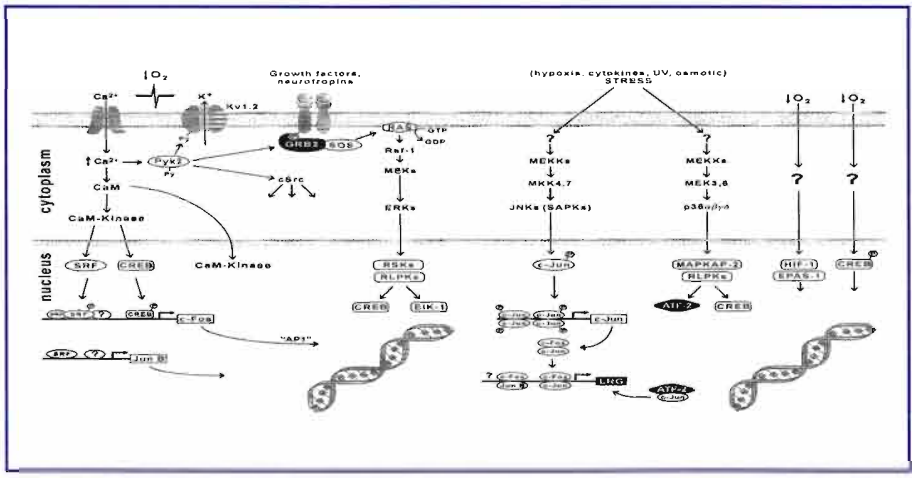


Figure 1. *Major signal transduction pathways and gene regulatory mechanisms that are regulated by reduced oxygen in PC12 cells.*

Depolarization activates voltage-dependent calcium channels leading to translocation of calcium from the extracellular space, which in turn can regulate gene expression via several known calcium-dependent pathways. This is certainly the case in PC12 cells where the hypoxia-induced expression of the immediate-early genes (IEG), *c-fos* and *junB,* and certain late response genes (LRG) such as tyrosine hydroxylase is prevented by removal of calcium from the extracellular milieu or by chelation of intracellular free calcium (**4**). On-going work in our laboratory suggests that calmodulin-dependent protein kinases (CaM-K) are involved in the calcium-dependent regulation of some hypoxia-responsive genes. In non-excitable cells, translocation of extracellular calcium is lost as a mechanism for gene regulation. However, induced-release of calcium from intracellular storage organelles could be involved.

It is also important to recognize that hypoxia is a metabolic stress which can limit cellular activity. This raises an important question. How do oxygen-sensing cells maintain high levels of activity during chronic hypoxia? The answer to this question is unclear, however it seems likely that oxygen-sensing cells take on a special phenotype that protects them against the harmful effects of hypoxia. Thus, it is entirely possible that *de novo* gene expression mediates hypoxia tolerance as well as specific functions (e.g. erythropoiesis, angiogenesis, chemoreceptor function, etc.) during hypoxia. We recently initiated a series of studies to identify the signal transduction mechanisms and genes that confer the hypoxia tolerant phenotype in PC12 cells. We focussed our studies on the three parallel mitogen/stress-activated protein kinase pathways, which include the mitogen-activated protein kinase (MAPK), c-jun N-terminal kinase (JNK), and the p38 (p38, p38β, p38δ and p38γ) kinase pathways. The JNK and p38 kinase pathways have been implicated in the responses to various stressful stimuli such as ultraviolet irradiation and osmotic stress. We found that the p38 and p38γ kinase pathways are activated by hypoxia, and that activation of these enzymes is thought to activate nuclear transcription factors. We have also measured an increase in MAPK (p42/p44) enzyme activity during hypoxia in PC12 cells, and the involvement of this pathway in regulating transcription of a reporter gene that contains a hypoxia-regulated enhancer (HRE). Thus, signal transduction pathways that have historically been associated with either growth or stress are also regulated by reduced oxygen in PC12 cells. Although we know very little about the genes that are regulated by these pathways or the role of these genes in regulating the cellular response to hypoxia, it is possible that some are involved in conferring a hypoxia tolerant phenotype. Certainly, this is an area that deserves more investigation.

A primary function of signal transduction pathways is to activate protein factors in the nucleus that are involved in regulation of transcription. There has been considerable interest in identifying transcription factors that regulate hypoxia responsive genes. A major breakthrough was the discovery of a transcriptional protein complex called Hypoxia-Inducible Factor-1 (HIF-1), which was first shown to be essential for hypoxia-induced transcription of the erythropoietin (Epo) gene in HEP3B cells (**5**). HIF-1 is a basic helix-loop-helix (bHLH) PAS domain DNA binding protein that forms a heterodimer with aryl hydrocarbon nuclear receptor

translocator (ARNT). There is growing evidence that HIF-1 is also involved in regulation of genes other than Epo during hypoxia. Another exciting development was the discovery of other bHLH-PAS proteins such as endothelial PAS protein (EPAS-1) that regulate the transcriptional response to hypoxia of certain genes (e.g. VEGF)(**6**). The signal transduction pathways that regulate the bHLH-PAS transcription factors remain unclear. There is also evidence that other transcription factors (e.g. AP1, CREB, and SRF) might also be involved in regulating gene expression during hypoxia. In addition, we recently discovered a novel kinase pathway that is activated by hypoxia and phosphorylates the cAMP response element binding protein (CREB), a primary transcription factor for a wide variety of genes (**7**). Thus, activation of transcription might occur via different signal transduction and gene regulatory mechanisms in different tissues and cell types (e.g. excitable vs. non-excitable).

Oxygen is a unique stimulus that readily diffuses throughout the cell. Thus, hypoxia may regulate gene expression by a variety of different mechanisms in different cell types. Major challenges for future research include: 1) identification of oxygen sensory mechanisms, 2) further identification and characterization of oxygen-regulated signal transduction pathways, 3) identification of additional genes that are regulated by hypoxia, and 4) understanding the role that these genes play in regulating the response to hypoxia. Such information will provide new insights into hypoxia-regulated physiological and pathological processes.

The author's research is supported by grants from the National Institutes of Health (HL-33831, HL-59945, HL-07571) and the US Army.

David Millhorn
University of Cincinnati

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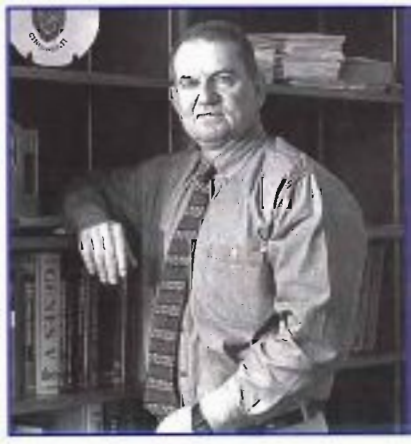

David Millhorn

Genes, Proteins and Muscle Disease

The muscular dystrophies were described during the 19th Century. Here John Harris reviews the genetic abnormalities underlying the diseases and current therapeutic strategies.

History

Dystrophia muscularis progressiva was a term first used by the German neurologist/neuropathologist Erb in 1891 to define a group of inherited progressive degenerative diseases of muscle. The term is non-specific in the sense that "muscular dystrophy" describes any one of a large number of diseases that are usually differentiated on the basis of the selectivity of affected muscles, the pattern of inheritance, the age of onset and the rate of progression of wasting and weakness.

The most severe form of the disease is the X-linked form first described in 1836 by Conte and Gioja. This disease, affecting young boys who become severely disabled by the age of 8-10 years, was soon shown to be a primary disease of muscle by Meryon (1852), Duchenne (1868) and Gowers (1879) . The disease, known as Duchenne muscular dystrophy, affects approximately 1:3;500 live male births. Much rarer forms of muscular dystrophy were recorded during the early to middle 19th century with clinical phenotypes that differed to varying degrees from that of Duchenne muscular dystrophy. The diagnosis of primary muscle diseases became an art form, requiring experience and a dedicated attention to detail, and as recently as 1994 Gardner-Medwin and Walton wrote that "the classification of the muscle diseases consists in listing those disorders which conform to the operational definition of muscular dystrophy and which seem to be separate entities on genetic, clinical and pathological grounds". Using these clinical criteria more than twenty diseases of muscle have been formally recognised.

Given their relative rarity (most general practitioners, for example, will never see a case of muscular dystrophy in their working lives) the capacity for mis-diagnosis is considerable. Even establishing patterns of inheritance, a seemingly simple exercise, is often difficult because of small families, widely spaced generations and the instability of family relationships.

As well as being often difficult to diagnose, the muscular dystrophies are extraordinarily difficult to treat. The quality of life has been improved by well informed nursing, physiotherapy and occupational therapy, and access to appropriate orthopaedic surgery and ventilatory support have similarly played a major role in adding to the comfort of the patients. But the degenerative process cannot be reversed or even slowed down.

Genes and Proteins

Against this rather bleak history, the impact of advances in our understanding of the molecular genetics of the diseases, and the recognition of the genes and gene products involved has been enormous. In 1979, Lindenbaum *et al* located the gene involved in the expression of Duchenne muscular dystrophy to the short-arm of the X-chromosome. The gene was identified in Kunkel's laboratory in Boston and the gene product, dystrophin was isolated by Hoffman *et al* in 1987. The identification of the protein product led almost immediately to the routine use of dystrophin – specific antibodies for the definative diagnosis of Duchenne muscular dystrophy. It also led to the recognition that a benign form of the disease, known as Becker muscular dystrophy was also due to an abnormality on the dystrophin gene: in the severe Duchenne form, the abnormality is usually a deletion or point mutation that disrupts the reading frame but in the benign form, the reading frame is maintained and the gene product, though abnormal in some way, remains semi-functional.

Dystrophin is a large cytoskeletal protein of >400KD. It is located immediately beneath the plasma membrane of skeletal muscle fibres. It comprises an N-terminal region that binds to f-actin, a rod-like domain, a cysteine rich region and a carboxy terminal. Dystrophin is now known to be linked to a complex of transmembrane and sub-sarcolemmal proteins that link, in turn to the extracellular matrix of the muscle fibre. The precise organisation of this complex is not fully understood, and the linking structures and binding domains of the relevant proteins has yet to be determined, but a contemporary cartoon is shown in figure 1.

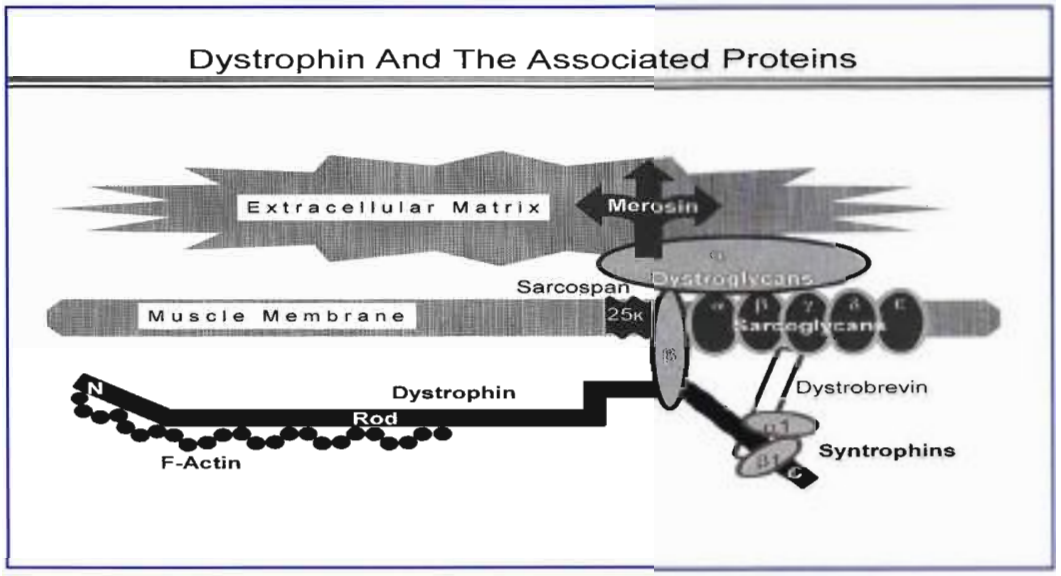

Figure 1. *Cartoon showing the possible relationships between dystrophin, actin, the complex of proteins making up the dystroglycan/ sarcoglycan complex and the extracellular matrix. Courtesy of Dr L V B Anderson, School of Neurosciences and Psychiatry, University of Newcastle.*

Few anticipated the clinical consequences that would follow the recognition of this complex of cytoskeletal, sub-sarcolemmical and transmembrane proteins. The genes encoding many of the relevant proteins have been identified and abnormalities in the genes and their protein products have been shown to be responsible for the expression of various autosomal forms of the muscular dystrophies. Table 1 summarises the currently available information on the relationship between gene, protein and disease.

One result of the extraordinary developments of the last decade has been a transformation of the diagnostic process from one based exclusively on clinical phenotype and pattern of inheritance to one based on a combination of clinical assessment, molecular genetics and protein expression. The more accurate diagnosis now available for so many diseases of muscle has not simply allowed the formal diagnosis of disease in a number of patients for whom diagnosis was difficult, but prognosis is more accurate and, most importantly, genetic counselling is much more precise.

There are also profound implications for treatment. One feature of the muscles of almost all patients with Duchenne muscular dystrophy is that they contain a small but variable number of muscle fibres which express some dystrophin. These so-called "revertant" fibres seem to have undergone a second mutation that has restored the reading frame. One therapeutic strategy, therefore, is to find a way of encouraging that process in affected muscles. A second strategy is based on the finding that an autosomal dystrophin homologue, utrophin, is transiently expressed in foetal muscle but is normally only retained at the neuromuscular junction.

If the utrophin gene can be upregulated, utrophin could, conceivably, take the place of dystrophin as the major cytoskeletal component of the complex of proteins. Preliminary work on animals with similar diseases caused by the lack of functional dystrophin suggests that such a strategy might alleviate the degeneration of muscle fibres.

The third strategy is gene-therapy; that is the transfer of a normal copy of the dystrophin gene, either directly or indirectly, into dystrophic muscle. All of these strategies are complicated and difficult, involving the solution of technical problems on one hand and the control of expression of translocated genes and the localisation of gene products on the other.

One problem that has to be faced when devising a therapeutic strategy is that despite our growing understanding of the molecular and genetic bases of muscle disease, the physiological function of dystrophin and its complex of related proteins remains unknown. Various possibilities have been explored. Many have suggested that dystrophin acts to stabilise the muscle fibre membrane; others favour the regulation or stabilisation of Ca^{2+} channels in the sarcolemma. The data supporting such suggestions cannot be considered definitive. The challenge to the physiologist is worthy of more attention, because no therapeutic strategy can be properly assessed if the appropriate functional studies cannot even be defined. With approximately a dozen proteins to study, integrated groups of physiologists and biochemists could play a major role in the study of this fascinating group of diseases.

John Harris
Universityof Newcastle

Professor John Harris is Action Research Professor of Experimental Neurology in the School of Neurosciences and Psychiatry, Medical School, University of Newcastle upon Tyne.

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Form of Muscular Dystrophy	Inheritance	Gene	Protein
DUCHENNE	X-linked	Xp21	DYSTROPHIN
BECKER	X-linked	Xp21	DYSTROPHIN
LIMB GIRDLE 2E	Autosomal	4q 12	*B* SARCOGLYCAN
LIMB GIRDLE 2F	Autosomal	5q 33-34	o SARCOGLYCAN
LIMB GIRDLE 2D	Autosomal	17q 12-21	∝ SARCOGLYCAN
LIMB GIRDLE 2C	Autosomal	13q 12	*y* SARCOGLYCAN
CONGENITAL	Autosomal	6q 22-23	MEROSIN

Table 1. *The relationship between some of the primary myopathies, conforming to the working definition of muscular dystrophy, pattern of inheritance, gene and gene product. All of these diseases relate to abnormalities in the "Dystrophin complex" (see Fig 1). More will certainly be found. Many other diseases classified as muscular dystrophies are caused by abnormalities remote from this complex (see Neuromuscular Disorders, 1991, 1, 1-3).*

Communication and Neuroscience at Keele: An Institution!

In common with many other Universities, Keele has decided to realign its smaller departments to form new larger Schools. This has resulted in the Dept of Communication and Neuroscience being merged with the nearby larger Department of Biological Sciences, to form the School of Life Sciences, which has also been joined by a protein crystallography group from Physics. But the particular mission of Communication and Neuroscience is to be protected by keeping the existing staff and their laboratories together in their current building. This unit will be renamed the MacKay Institute of Communication and Neuroscience after its founder, the late Professor Donald MacKay. Research in the Institute will continue to focus on the three areas originally established by Donald - hearing, speech and vision. And Communication and Neuroscience staff have already set up two courses that reflect their research interests, an undergraduate principal course in Neuroscience and an EPSRC-funded Master's course in Machine Vision and Neurocomputing. These will add to the portfolio in Life Sciences which also includes undergraduate courses in Biochemistry, Biology and Biomedical Science and a Master's course in Parasitology that is run by a consortium of north-west universities.

Carole Hackney

The new Head of School is Professor Carole Hackney, the previous head of Communication and Neuroscience. Carole was recently awarded a personal chair in auditory neuroscience, and has been a member of the Physiological Society for a number of years. Other Physiological Society members are being recruited too. For instance, Dr Paul Kolston is transferring his Royal Society fellowship from Bristol to work with the Keele auditory group and has been offered a lectureship when his current funding ends.

Staff in Communication and Neuroscience have been collaborating for many years with staff from Biological Sciences, on both the research and teaching fronts. But a major new equipment grant from the Wellcome Trust to fund a multiphoton laser scanning system that will be used in projects spanning from apoptosis in the thymus and pancreas though to calcium imaging in cochlear hair cells has already illustrated the benefits of working together more closely. The new Head of School and Keele University itself, however, are keen to maintain the unique character of the unit established by Donald MacKay, so hopefully Communication and Neuroscience will remain alive and well at Keele for many years!

Carole Hackney
University of Keele

The Journal of Physiology

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Which are the key papers published in The Journal of Physiology in each decade ?
Vote now for a chance to celebrate the millenium.

All suggestions will be pooled, and the winner will be the person whose list coincides most closely with the 12 most popular references (Editorial Board decision final !).

Prizes: A Magnum of Champagne to the winner

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The first 50 entrants will receive a JP Party bag !

Send your 12 suggestions – one for each decade, from the 1880s – via the electronic form available at http://physiology.cup .cam.ac.uk/Jphysiol/Competition
or to The Journal of Physiology Publications Office.

Closing date for submission is 30 July 1999.

Report on the Physiological Society Undergraduate Symposium

During last semester, Sheffield University's Department of Biomedical Science hosted its first Undergraduate Teaching Symposium. This was exclusively supported by the Physiological Society and was held in the Octagon Centre at Sheffield. The theme of the Symposium was "Cell and Molecular Aspects of Physiology" and Sheffield was delighted to invite contributions from Bob Burgoyne of Liverpool, Rod Dimaline and Tim Chek of Liverpool and Newcastle respectively. Several lectures were presented by members of the academic staff at Sheffield: Alan North, Mark Dunne, Helen Skaer and Stan White. The subject Cell and Molecular Aspects of Physiology was chosen since it represents an important and topical area for physiologists i.e. the integration of genetic and molecular information with holistic science. The speakers therefore covered aspects of cell signalling and exocytosis, ion channel structure-function and disease, gene expression in GI endocrine cells and the development and function of the kidney. Discussion sessions were moderated by invited guests and we are very grateful to Chris Peers and Malcolm Hunter from Biomedical Sciences at Leeds University and Peter Brown from Physiological Sciences at Manchester University for their time and considerable efforts during the day. Finally, the day attracted the largest audience for an Undergraduate Symposium supported by the Society. A total of over 400 students were present at the meeting. In addition to home students there was a very strong regional presence in evidence with more than 270 students from the Universities of Newcastle, Leeds, Liverpool, Wolverhampton, Manchester, Bradford, Keele and Nottingham making the journey to Sheffield.

Speakers, moderators and visiting academics.

Abstracts presented at the meeting can be downloaded from:
http://www.shef.ac.uk/uni/academic/A-C/biomsc/
The students attending the meeting were asked to complete an exit questionnaire. One hundred and thirty nine students replied. 93% approved of the "value of the Workshop" with 85% stating that the Workshop stimulated their interest in the subject matter. 97% of the respondents thought that the "academic content of the presented materials" was good or satisfactory, and 93% agreed that the subject matter was in fact appropriate to their course-work. The choice of lecturers was considered appropriate as 93% of students commented favourably on the "approachability of the lecturers", 98.5% of respondents thought that the "presentation of lecturers" was satisfactory or above, and 96% indicated that the "use of visual aids" was good or satisfactory. Finally the site of the Workshop ("lecture accomodation") was also deemed good or satisfactory by 94% of the respondents.

Undergraduates receiving literature from Scarlett Buckley

Some of the comments received from the students were as follows:-

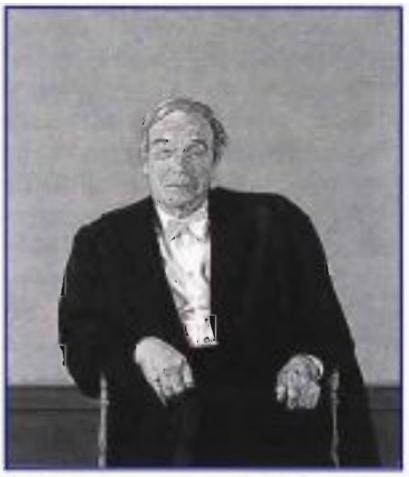
- "In general, excellent workshop with a good range of topics. The majority of talks were given at an appropriate level".
- "Chocolates with the tea would have been nice!"
- "Free beer rather than coffee!"
- "The workshop proved very useful. The speakers I found most interesting were those who highlighted research in their laboratories – specifically that work undertaken by PhD students (at a time when my peers and I are contemplating this path)."

I'd like to take this opportunity to thank all those involved with the formal point of the day, and the students who attended this Symposium.

Mark Dunne
University of Sheffield

Professor Sir Alan Hodgkin OM KBE MA ScD FRS 1914-1998

Alan Hodgkin was distinguished for his contributions to the understanding of nerve conduction, the excitation of muscle, and phototransduction in the retina. With his colleagues Bernard Katz and Andrew Huxley, he established the ionic basis of the action potential, revolutionising neuroscience and laying the foundations for subsequent work, now burgeoning more than ever, on ion channels. In 1963, at the age of 49, he won the Nobel Prize for Physiology and Medicine with Andrew Huxley and John Eccles. He was a Fellow of the Royal Society at the age of 40, and held its Foulerton Research Chair from 1952 to 1969. In 1970 he succeeded F J W Roughton to the John Humphrey Plummer Chair of Biophysics in the University of Cambridge. He was President of the Royal Society from 1970 to 1975, its Croonian Lecturer in 1957, and winner of its Royal Medal in 1958 and its Copley Medal in 1965. He was Master of Trinity College from 1978 to 1984, President of the Marine Biological Association from 1966 to 1976, and Chancellor of the University of Leicester from 1971 to 1984. He served on the Committee of The Physiological Society from 1949 to 1953 and again as Foreign Secretary from 1961 to 1967. He gave the Annual Review Lecture in the Society's Centenary year (1976) and became an Honorary Member in 1979. He was made KBE in 1972, and a Member of the Order of Merit in 1973, an Order in which he joined his cousin by marriage, Dorothy Crowfoot Hodgkin, and was later to be joined by his collaborator and life-long friend Andrew Huxley, the three making up an eighth of the total membership.



Bryan Organ's portrait of Sir Alan Hodgkin OM as Chancellor of the University of Leicester.
Photograph courtesy of the University of Leicester

Alan Hodgkin was born on 5 February 1914 near Banbury, Oxfordshire, the oldest of three brothers. His family was Quaker, whose strong traditions in medicine included 'Uncle Hodgkin' after whom Hodgkin's Disease is named. His father, a friend of Keith Lucas, originator of the All-or-None Law, died in 1918 on a mission to investigate conditions among refugees in Armenia. Alan Hodgkin's autobiography tells us that being sent away to the Downs School, Colwall, near Malvern, in his ninth year was not a happy experience, and subsequent entry to Gresham's School, Holt, in Norfolk, found him in the bottom class. But he worked his way up to win a Scholarship to Trinity College, Cambridge, in Botany, Zoology, and Chemistry. His future Director of Studies, the zoologist Carl Pantin, persuaded him to use the time between school and university to learn as much mathematics, physics, and German as possible. Though he was largely self-taught in mathematics and physics, his technical innovation in methods of electrophysiological recording and his elegance and quickness with mathematical arguments must owe something to Pantin's advice. These qualities were to become hallmarks of his future scientific papers, which were rigorous in their theoretical basis, as was the clarity – simplicity even – and directness in the writing. German was learned during an extended visit to Frankfurt, where experience of Nazism removed the absolutist pacifism of his Quaker background.

At Cambridge, Alan Hodgkin became quickly introduced into the Natural Science Club, a 'somewhat elitist group' that included among its members many scientists who would gain distinction. He was also later introduced by Victor Rothschild and the physiologist Grey Walter into the Apostles – the Cambridge Conversazione Society – a group of far greater exclusivity. It was evidently a bit of a toss-up whether he read physiology or zoology in his third year at Part II. Perhaps sneaking into a Physiological Society meeting in May 1934 helped, where he heard a 'splendid debate on humoral transmission with Henry Dale, G L Brown

and Feldberg on one side and Jack Eccles on the other'. But physiology also won out partly as a result of F J W Roughton's advice: 'if you want to find out anything really new you must join us in Physiology'. This advice sounds rather arrogantly phrased today. But find out new things he did.

Even as an undergraduate, Alan Hodgkin had started experiments studying nerve conduction. These experiments, showing that excitability is raised ahead of the propagating impulse, began to establish the local circuit theory of nervous conduction. His expertise in nerve however led to the nightmare of finding his Part II Tripos papers lacking any questions on this subject. Evidently the examiners thought their inclusion would be unfair to other candidates. A thesis on nerve conduction led to election as a Fellow of Trinity College in 1936 and, through A V Hill's introduction of his work to Gasser, to the invitation to spend a year at the Rockefeller Institute in New York. This year (1937–38) was of great importance. Gasser's laboratory 'helped turn (him) from an amateur into a professional scientist'. A visit to K S Cole in Woods Hole introduced him to the squid giant axon and would later introduce him to the voltage clamp. And he met the family of Peyton Rous whose daughter, Marion de Kay – Marni – was to become his wife in 1944.

Work on squid axon started in Plymouth just before the outbreak of war. With Andrew Huxley, he succeeded in making the first intracellular recording of an action potential. This recording overthrew the received opinion that resting selectivity to potassium ions was simply lost during an action potential, since the voltage overshot zero by several tens of mV. The result was written up as a note in *Nature*, but exploitation of the sodium hypothesis which began to emerge had to be abandoned until the latter part of the next decade.

During the war Alan Hodgkin worked briefly in medical physics, with Bryan Matthews, and later in the group developing airborne short wavelength (centimetre) radar. His work was directed primarily towards effective means of aircraft interception (AI) and naturally involved flight trials of equipment. This work was not without danger, since the circuitry was likely to flash over at altitude during the 15,000 V μs pulse required to get a decent range. Further the adapted aircraft were not always identified as friendly. Such an error resulted in the death in 1942 of AE Downing (who with G W Edwards from GEC and Alan Hodgkin made up the team undertaking flight trials) and his pilot when an adapted Beaufighter was shot down by Spitfires, ordered to intercept an unidentified aircraft. The work was of great importance to the survival of our country during a period of great peril, directly enabling the destruction of many enemy aircraft.

The end of the war permitted the return to Cambridge and to basic science. This was not necessarily the easiest transition to make. Alan Hodgkin's autobiography records a letter from Marni Hodgkin to her parents describing her husband as 'like a dolphin that has suddenly been released into the open sea. He plunges and gambols and cavorts in pure research after so long'. This next decade from 1945 would revolutionise neuroscience.

With W A H Rushton, cable theory was developed for application to nervous conduction. With Bernard Katz the sodium hypothesis, now testable, was firmly established by showing that the action potential changed in size and rate of depolarisation as predicted when Na^+ was replaced in the extracellular fluid. Goldman's constant field theory was also put into its useable, and still widely used form. With Andrew Huxley, the ionic movements that occurred during an action potential (only 10,000 K^+ ions lost per mm^2) were measured for the first time.

Above all, the voltage clamp was exploited with stunning success with both Katz and Huxley. The experimental results that gave the 1952 papers were collected in little more than a month in the summer of 1949. The rapidity was permitted because the hypothesis had been thought about pretty hard. The initial idea was that Na^+ would enter through a carrier-mediated mechanism. This carrier would be negatively charged so that it would sit at the outside of the membrane at negative membrane potentials. Depolarisation would

be needed to let the carrier transport Na^+ in; the transfer would be inactivated at longer times by a reaction between the carrier and some axoplasmic constituent. This carrier was also thought to bind Ca^{2+} at the outside, which immobilised it. The effects of Ca^{2+} on excitability would later be established in collaboration with Bernard Frankenhaeuser.

Alan Hodgkin & Andrew Huxley in Plymouth. It is believed that the photograph was taken in 1939 at the time of the first intracellular recording from the giant squid axon.

The carrier idea did not last long. Current would be caused by movement of the carrier, yet this current would have to be small compared with ionic current. Thus the unitary event would have to be the opening of an 'active patch' through which many Na^+ ions could move. This concept was already close to that of an ion channel and the 'gating currents' that were predicted would later be discovered by Armstrong and Bezanilla in the United States and by Keynes and Rojas in the UK. Later measurements with Richard Keynes of unidirectional fluxes and of their ratio would establish potassium permeability sites as pores, and indeed as pores occupied by several K^+ ions at a time.

The wonderfully elegant mathematical descriptions of the permeability changes to Na^+ and K^+ – the Hodgkin–Huxley formulation, m^3h for Na^+, n^4 for K^+ – have survived amazingly intact. It scarcely came as a surprise when potassium ion channels were later shown to be tetramers of pore-forming subunits. Further, recent evidence from W Catterall's laboratory (and others) suggests that in Na^+-channels, only three of the voltage-sensing S4 domains ($S4^{I,II,III}$) regulate activation, while the fourth ($S4^{IV}$) regulates inactivation. This is remarkably close to m^3h. Famously, the calculation of the propagating action potential was made by Andrew Huxley using a hand cranked calculator, owing to the lack of availability of the Cambridge University Computer. During this period too, Alan Hodgkin and W J Nastuk developed the discovery of Ling and Gerrard that fine glass microelectrodes could be inserted through the membrane of a cell, such as a skeletal muscle fibre. They hit on the idea of filling pipettes with 3M KCl and introduced a cathode follower with a driven shield, both developments that allowed action potentials to be recorded without distortion. In this technical innovation, as in the development of voltage clamping apparatus, he and his colleagues were supported by his instrument maker R H Cook. The paper describing the work on muscle, unlike the great majority of his others, was published in the *Journal of Comparative and Cellular Physiology*, owing to a 15-month wait experienced with the *Journal of Physiology*. So much electrophysiology that followed used this method. It was immediately picked up by Silvio Weidmann to record from cardiac muscle, and Alan Hodgkin extended cable theory to deal with conduction through intercalated disks. Currently, patch clamp is a particularly elegant combination of the voltage clamp of Hodgkin, Huxley and Katz and the micropipette of Nastuk and Hodgkin.

Work now turned to studies with Richard Keynes and later with Peter Caldwell and Trevor Shaw of active transport of ions by squid axon developing principles of sodium pump action in maintaining the ionic gradients whose storage of energy is essential for excitability. With Peter Baker and Trevor Shaw, the perfused giant axon was developed and was used to show that action potentials did not require metabolic energy for their generation or for their recovery. Effects of changes of the intracellular milieu on excitability were investigated with Knox Chandler and Hans Meves. All of these experiments put the final objections to the sodium hypothesis to rout, and Alan Hodgkin considered this development of the perfused axon in 1962 to be a decisive factor in the award of the Nobel Prize the following year. Ca^{2+} permeability of axons was established with Baker and Ridgway. Ca^{2+} was shown to enter partly through Na^+ channels and partly through voltage-gated Ca^{2+} channels, whose presence in axon was thereby demonstrated for the first time. The sodium–calcium exchange of axon was discovered with Mordie Blaustein, Peter Baker and Rick Steinhardt.

The microelectrode technique was beautifully exploited with Paul Horowicz in

studies of dissected single skeletal muscle fibres – a fiendishly difficult dissection. These studies showed how both K^+ and Cl^- permeated the resting membrane of skeletal muscle and how K^+ permeability was higher when the driving force on K^+ was inward - the now classical ($V-E_K$) dependence of inward rectifiers. The probable T-tubular location of inward rectifiers was established through beautiful experiments involving rapid K^+ concentration changes. Studies of excitation–contraction coupling began with measurements of potassium contractures and were continued with voltage clamp studies with W K Chandler and R H Adrian. With these colleagues he also established the ionic basis of the action potential of skeletal muscle and the beginnings of diversity of potassium permeability mechanisms. His last experiments on muscle were conducted with Shigehiro Nakajima, a rigorous extension of cable theory and careful measurement of sarcoplasmic resistivity.

Work on squid axon was arduous. At Plymouth, squid were captured by trawler during the day, and dissected and worked on during the evening and night. The combination of absence from home – the spouses of those working on squid were known as 'squidows' – analysis by day and experiment by night was exhausting. Hodgkin recalled himself and Frankenhaueser being mistaken for refugees by a Plymouth shopkeeper, who was worried enough at their exhausted state to contact the Director of the MBA and request they be properly fed. In 1962 Hodgkin had collaborated with M G F Fuortes in studies of *Limulus* eye, explaining how the gain of the eye was altered through its synaptic connections. In addition an extended visit to Cambridge by Denis Baylor, who brought the technique of intracellular recording from retina, permitted Alan Hodgkin to turn his attention to this system. Nonetheless the change of field must have made demands, because it occurred at a time when he had become President of the Royal Society, a position that carried its own responsibilities. In the period from 1970 to 1988 Alan Hodgkin brought the same reforming rigour and insight to phototransduction that he had brought to bear on nerve conduction. As well as Denis Baylor, his colleagues at this time included Trevor Lamb, Peter Detwiler, Peter McNaughton, P M O'Bryan and K-W Yau. His last paper in this series – a detailed kinetic analysis of the interplay between cGMP and the inhibitory effects of Ca^{2+} in salamander rods – was published in 1988 with Brian Nunn, whose death two months after its completion caused deep regret.

Alan Hodgkin's primary contributions were as a remarkable experimentalist able to find elegant ways of testing clear hypotheses. However he was also a very effective, assiduous scientific administrator. His tenure of the Presidency of the Royal Society occurred at a difficult time. The report in 1971 by his long-time friend Lord Rothschild – heading the Downing Street 'think-tank' – into the funding of scientific research caused considerable concern for the future of basic science. The Green Paper, *The Organisation and Management of Government Research and Development*, proposed a scheme of customer (government department) and contractor (the scientist) and the substantial transfer of funds from the Research Councils to other government departments, such as Health, Industry, Environment, and Energy. Hodgkin was particularly concerned for the future of the Natural Environment Research Council, then still in relative infancy. He did much to maintain science funding through high level negotations, on one occasion not letting pretty severe influenza deflect him. In the end the transfers were not as large as originally proposed. His preoccupation with this issue can be seen in his Anniversary Addresses to the Royal Society of 1972 and 1975. Thinking the most innovative science as 'not well suited to the specific contract', in 1972 he defended basic science with a quotation from Francis Bacon: 'The real and legitimate Goal of the Sciences is the endowment of human life with new Inventions and Riches.'

'Thus had anyone meditated on balistic machines and Battering Rams, as they were used by the Ancients, whatever application he might have exerted, and though he might have consumed a whole life in the pursuit yet he would never have hit upon the Invention of Flaming Engines, acting by means of Gunpowder; nor would any person who had made woolen Manufactories and Cotton the subject of his observation and reflection, have ever discovered thereby the nature of the Silkworm and Silk.'

He also initiated a development fund to secure the then somewhat shaky finances of the Royal Society, which had recently moved to new premises in Carlton House Terrace. Since the economic conditions in the UK could not be viewed optimistically at the time, this was a particularly difficult period to initiate such a policy. Yet the security was achieved. He also created a scientific dialogue with China, leading a delegation and going ahead with the visit in spite of last minute withdrawal of Chinese permission, at a time when the Cultural Revolution was a very recent event. As Master of Trinity he 'helped a little' with the development of Trinity Science Park in Cambridge. I suspect he did not find his duties as Chancellor of the University of Leicester always the easiest. He found the platitudes expected by some in the Chancellor's address difficult if not probably downright dishonest and he did not indulge in them. Behind the scenes he would be full of wise advice, and would take pleasure in the University's strengths in biology and physics.

Alan Hodgkin was an outstanding teacher. His lectures on nerve conduction in Cambridge were remakable for their clarity. In the 1960s, at the time when he had just won the Nobel Prize, he still taught in third-year practical classes – the only Professor so to teach us. He would help make experiments work and would take great pains to explain the principles. Explaining cable theory and running out of space, he would drop to his knees in the chalkdust to make use of the last bit of the blackboard. Although he was remarkably well networked through family and through friendship to an intellectual elite, there was a lack of any sense of position. He did not wish (as some do) to seem a great man, yet he undoubtedly was so. And the more so for his unfailing modesty and courtesy, especially towards undergraduates, and within The Physiological Society to younger scientists. Elsewhere he could be more exacting.

He had a debunking sense of humour and often wore a look of incompletely suppressed amusement at some foible. Evidently the trick of not quite suppressing laughter was learned during Quaker meetings in childhood. It is typical that he would recall in his autobiography the physicist J J Thompson's opening a conversation with W B Yeats with the sentence 'Been writing much poetry lately, Mr Keats?'. (At least the area of endeavour was right.) Or that his vote of thanks to J C Eccles for his lecture at the Dale Centenary Symposium should consist of the one delightfully ambiguous sentence: 'I have just one thing to say – you're all right, Jack'. Or indeed that he would share the audience's amusement at finding himself giving his Nobel Prize lecture in Stockholm in 1963 with a 'Reserved' sign stuck electrostatically (appropriately) to the seat of his trousers. He would later recall the incident with the aphorism "Nothing is more sure-fire than the bishop on the banana peel".

Alan Hodgkin was widely travelled, had a strong sense of wonder at the natural world and was deeply cultured. He was, in the words of a message from Chilean scientists to the Society at the time of his death, 'a scientist for all seasons'. Certainly he was a man against whom other scientists come, by some, to be measured. His long marriage to Marni, the daughter herself of a Nobel laureate, brought four children and was remarkably supportive during the long autumns of squid seasons, during his Presidency of the Royal Society and his Mastership of Trinity. And also during his long struggle with arthritis. Two things in life were of the greatest importance to him, and he put them in proper order in a letter written at the time of his 70th birthday: 'For 90% of the time science can be an intensely frustrating business, but the occasional breaks have brought me more happiness than anything else outside love and marriage'.

Peter Stanfield
University of Leicester

Sir Alan Hodgkin was:

Elected Ordinary Member	1938
Elected Honorary Member	1979
Member of The Physiological Society Committee	1949-1953
Foreign Secretary	1961-1967

Dr MJ Keating MB PhD 1940-1998

Michael Keating, who died on 14 Dec 1998 at the early age of 58, did pioneering work on the role of activity in determining the specificity of neural connections in the vertebrate brain.

After qualifying in Medicine at the London Hospital, Keating was appointed assistant lecturer in the Department of Physiology at the University of Edinburgh, where in 1966 he began work on a PhD in the research group headed by RMGaze.

Keating (right) and Gaze: Visual field mapping at Mill Hill.
Photograph courtesy of Simon Grant.

Keating was interested in studying how the two eyes form maps of the visual world in the primary visual centres of the brain. The prevailing view at the time was that molecular labels with complementary affinities are attached to retinal cells and their targets early in development, and that the orderly mapping of nerve connections between eyes and brain were a product of these matching chemoaffinities. In Gaze's group this idea was being investigated electophysiologically by mapping the visual representations from each eye to the optic tectum in frogs whose retinae had been experimentally manipulated at embryonic stages when these molecules were believed to be generated. The frog retino-tectal system has two components; a direct projection to the tectum from the contralateral retina and an indirect projection originating from the ipsilateral retina. Earlier results had shown that when one eye was embryonically altered, the direct maps formed by such eyes were reorganized in a way that could be explained by chemoaffinity theory; in addition, however, the map formed by the other, unaltered eye was also reorganized, a finding difficult to account for by any variant of the chemoaffinity idea. Keating realized that a critical outcome of this unexplained reorganization was to bring the maps from the two eyes into visual correspondence. He presented this analysis as a demonstration to the Edinburgh meeting of the Physiological Society in July 1968 and, in a double-poster of densely-worded prose, condensed into an only slighter shorter Abstract, suggested a radical alternative to the prevailing view: nerve connections, he proposed, were being established at points "simultaneously receiving a similar pattern of spatiotemporal excitation from the same point in the visual field, through the [two eyes]". This was a profound insight which pre-dated much of our current understanding of activity-dependent synaptic plasticity. Keating went on in subsequent work with Gaze and others to demonstrate that neural activity resulting from early visual experience governed the spatial integration of binocular maps in the frog, establishing that elements of synaptic circuitry are susceptible to functional adaptation, even in the brains of relatively primitive animals previously assumed to be connectionally hard-wired.

Keating moved with Gaze to the National Institute for Medical Research in Mill Hill in 1970, becoming head of the Division of Neurophysiology in 1976. At Mill Hill, Keating turned his attention to another fundamental issue, asking why it is that some developing systems are especially influenced by early sensory experience while others are clearly not. To tackle this question, Keating decided to move into more complex mammalian systems, and to investigate developmental interactions between visual and auditory inputs to the superior colliculus. To this end, he set up an auditory physiology laboratory in which recordings could be obtained under free-field anechoic conditions. This new development was instrumental to the discovery that auditory

neurons in the deep layers of this nucleus have spatial receptive fields distributed to form a map of sound location and, subsequently, that bi-modal (visual and auditory) sensory experience is necessary for the formation of this auditory map, especially during a critical developmental period associated with major head growth.

It was during this time that Keating first began to suffer from cluster-headaches, a condition which eventually became so disabling that he gave up his position as Head of Division in 1985, and in 1991 took early retirement. Throughout this period of adversity the enthusiasm and powers of application which he habitually brought to his work remained undiminished.

It was commonly said of Mike Keating by those who knew him that he was one of the cleverest people they had ever met. He was also one of the funniest. He was an effortlessly lucid and entertaining talker, equally effective as conference speaker or conversationalist. He loved an intellectual scrap, whether scientific or political, and in coffee room debates his right wing politics and passionate Catholicism gave him plenty of scope for taking on - and for the most part disposing of - all comers. Writing, however, was a more arduous task, to be endured rather than enjoyed. His dilatory approach to writing up his work was legendary, causing American collaborators on two occasions to make special trips to the UK, virtually camping in his office until their manuscript in progress was completed.

Keating was a physiologist's physiologist. For him, the system was the thing. We can only speculate on what he might have achieved if ill health had not cut him down in mid career. His many friends in the Society mourn the loss of a gifted scientist, and a generous, witty and life-enhancing colleague.

Simon Grant & Chris Kennard
Imperial College School of Medicine

Tim Bliss
National Institute for Medical Research

GREY BOOK UPDATES

GREY BOOK CHANGES FOR THE NEW ISSUE NEED TO BE AT THE ADMINISTRATION OFFICE NO LATER THAN 14 th JULY 1999.

PLEASE UPDATE YOUR ADDRESS, TELEPHONE, FAX AND EMAIL.

Send changes to:
Charlotte Parry
The Physiological Society
PO Box 11319
LONDON
WC1E 7JF

Email: cparry@physoc.org

PLACENTAL & PERINATAL PHYSIOLOGY

Our meeting in Manchester in April was apparently enjoyed by all who attended. It was focused on a symposium entitled `Maternofetal Exchange: Current Status and Future Directions'. Invited speakers presented work on: regulation of trophoblast transporters (Sibley), transporter activity in placentas from growth restricted babies (Jansson), placental vitamin transport (Ganapathy), maternofetal exchange of fatty acids (Haggarty), placental glucose transport (Illsley), finishing off with a presentation by Kent Thornburg of a conceptual framework for future work on the mechanisms of maternofetal transfer of water, still woefully poorly understood. These invited lectures were interspersed with free communications. We would be particularly keen for feedback on whether attendees felt that this format was a success or not.

Posters were presented the next day: probably not ideal but the session was, nevertheless well attended and plenty of discussion was stimulated.
The symposium was attended by around 80 people and half of these came to the SIG dinner the same evening. This was an informal affair which, as is often the way, became even more informal as the evening went on and wine glasses emptied!

Following the discussion at the end of the symposium our plan is to have a designated session at the Meeting in Birmingham in December of this year, with an invited lecture. We will then meet again in Aberdeen in September 2000, in association with a symposium on `Fetoplacental Interactions'.

Abigail Fowden
Colin Sibley

EDUCATION

As you may be aware, Sue Ward has relinquished her role as convenor of the Education SIG to me. Before going any further, I would like to thank Sue for both getting this group up and running and for organizing the excellent meetings to date. On this note, I would also like to extend grateful thanks to Steven Barasi and John Patterson, the organizers of the Teaching Workshop held at the Cardiff Meeting.

The next symposium of the Education SIG is to be held at this meeting and its' title is "Using the Internet to Support Teaching". The group needs to look forward to the year 2000. As convenor of the group, I am willing to act as its' focus. However, I would welcome suggestions for both themes of futute meetings and their venue. Equally, I am also open to suggestions as to future directions the group shoul take, eg development of the SIG website, possible links with other organizations eg British Pharmacological Society. My contact details are in the Grey Book.

Enjoy the symposia, and I look forward to meeting and speaking to members of the group in Newcastle.

Ian Kay

Honorary Membership of The Physiological Society

Congratulations to Professor Gerhard Giebisch of Yale University School of Medicine and Professor Syogoro Nishi of Kurume University School of Medicine on their election to Honorary Membership of the Society.

GRANTS AVAILABLE FROM THE SOCIETY

Introduction

An important element of the Society's Charitable Expenditure (see the Annual Report) is the awarding of grants, broadly to support the career development and activities of individuals within the physiological sciences, and particularly those associated with the Society as students, Affiliates and Members. The Grants Sub-Committee, in consultation with the Committee of the Society, oversees the grant categories, adjusts the division of the funds, and from time to time considers new initiatives that reflect the grant needs of the physiological community. Details of the categories of grants, guidelines and forms are all available on the Society's Website, which should be consulted as the most up-to-date source of information. This article aims to clarify the functions of the different grants schemes, and the factors taken into account in deciding awards.

Affiliate Travel Grants

PhD students and young post-doctoral scientists are encouraged to become Affiliates of the Society, and to present their work-in-progress at scientific meetings of the Society in the first instance. Attendance and presentation at international meetings is also encouraged, and an Affiliate may apply for a 'one-off' Affiliate Travel Grant to present at an appropriate international meeting (Symposium, Conference or Workshop). Priority is given to post-doctoral scientists and final year PhD students with a record of presentations to the Society, to those giving oral presentations, and to those planning to combine the meeting with specific scientific discussions or visits.

Dale and Rushton Funds

These funds, now amalgamated, are mainly to support scientific visits by Members or Affiliates, for training courses, specific collaborative research, or presentation of work at international meetings. Travel within the UK is generally not supported. In exceptional cases, support for individuals involved in physiological research who are neither Members nor Affiliates will be considered, but a strong case must be made by a sponsoring Member of the Society. Affiliates who are eligible for an Affiliate Travel Grant are expected to apply for the latter in the first instance, and may not submit parallel applications for Affiliate Travel and Dale & Rushton funds for the same meeting.

Vacation Studentships

These are seen as an excellent way to attract undergraduate or newly graduated students into physiological research, and to help identify able experimentalists who may go on to a PhD or to clinical research. In considering applications, the Grants Sub-Committee scores for the quality, originality and practicability of the project, its training function, and the scientific promise of the student. Projects must be based in the laboratory of a Member of the Society.

MSc Bursaries

Taught MSc and MRes courses are increasingly seen as important in postgraduate training, particularly as 'conversion' courses, bridging the gap between scientific disciplines, or between theoretical and practical aspects of a field. However, in most cases, the students have to find their own fees and living costs, a major outlay. Organisers of MSc/MRes courses with a strong element of physiology and including a physiology research project, are invited to put forward applicants for two deadlines : end May for students starting the course in the following Sept/October, and end November for students already enrolled on a course. Awards are made on the basis of research promise and financial need.

Postgraduate support

It occasionally happens that through exceptional circumstances outside their control, a postgraduate student needs longer than anticipated to complete their PhD studies, and needs emergency funds for a few weeks' to months' work. The 'exceptional circumstances' could include severe illness of the student, death or unavoidable change of supervisor, or unforeseeable problems with experimental work. Awards are made on the basis of documented research ability of the postgraduate, and the nature of the special circumstances precipitating the hardship. Funds are not provided simply to extend a PhD project or to support hardship resulting from poor scientific or financial planning.

Intercalated BSc bursaries

There is concern that with the increasing pressure to streamline courses in medicine, dentistry and veterinary medicine, and the withdrawal of some schemes (e.g. MRC) that previously funded intercalated BScs, fewer students in these fields will apply for intercalated BSc courses. There would be serious knock-on effects in the quality of clinical and veterinary research, and for the tradition of physiological research and innovation in these fields. In a new scheme being launched in 1999, institutions offering intercalated BSc courses for medical, dental or veterinary students are invited to submit 1-2 student applications for Physiological Society bursary support, for up to £2,000 per award. The intercalated BSc should include a strong element of physiology, and an experimental research project on a physiological topic. Candidates must be put forward following a fair selection procedure by the host institution. Students automatically funded for the intercalating year by the local education authority, or already receiving other bursary support, are ineligible. Awards will be based on the scientific promise and career objectives of the student, the quality of the research project, and financial need.

Special funds for joint international meetings and IUPS

The Society has traditionally set aside around £30,000 per annum to provide block support for travel to international meetings that figure as important dates on our meetings' calendar. Previously, the funds accumulated over four years were used to send delegates to meetings of the International Union of Physiological Sciences (IUPS), but recently the funds have been partly used to support travel to more frequent joint meetings of the Society (e.g. Prague 1998, Pucon Chile 1999), with less emphasis on IUPS. In deciding awards, consideration is given to the contribution to the meeting (speaker, symposium organiser, oral or poster communication), and links with the host country (to encourage research exchange and collaboration). Joint meetings of the Society are seen as excellent opportunities to make the Society more international, and to encourage physiologists in other countries to join the Society.

Details of grants available from the Society are posted on our Website.

Joan Abbott

MEMBERSHIP MADE EASIER AND OTHER INNOVATIONS

Many years ago, considerable hurdles had to be surmounted in order to become a member of the Physiological Society. A large and aged ledger used to circulate at dinners between the port and speeches and Members could either support or black-ball a name by making an appropriate mark. When the positive votes exceeded a substantial, but seemingly indeterminate number, the lucky individual would be scrutinised by the Committee and then placed on a ballot paper for final approval at the next AGM or semi-AGM. It seemed it was easier to become a member of the MCC! The rules were subsequently relaxed, so that now the candidate is asked to demonstrate some professional interest in the physiological sciences and only six Members are required to sign a form, before a ballot paper is drawn up.

However the process is still rather cumbersome and time-consuming which gives the impression to many that gaining membership is still an exclusive, rather than inclusive procedure. Furthermore, because the physiological sciences are always evolving we should be looking to accept and retain Members from a wider constituency and make the whole process less daunting.

Consequently, it has been proposed that the rules for achieving membership are again altered.

The new proposals, however, require changing the Articles of Association. This can only be undertaken by Special Resolution put to the Membership vote, and will be passed if 75% of those Members voting, vote in favour. The Articles of Association govern the running of the Society and from these Articles arise the Standing Orders and Domestic Rules. The Domestic Rules set down the more specific details of the powers granted by the Articles and these too will need to be altered in line with the Articles. Changing the Domestic Rules requires a simple majority of over 50% of those Members voting to vote in favour. The Articles and Domestic Rules are printed in the Grey Book (pp 26-33 and 34-39 in the current version) and I'm sure that many of you regard them as essential bed-time reading. In this year's AGM papers are printed proposed changes to the existing Articles and the means whereby these changes can be put into effect through the Domestic Rules. However it is worthwhile making clear the consequences of such proposals:

* an application for Ordinary membership may be made by an individual on writing to the Administration Office of the Society. The application should be supported by three Members, or He ads of Physiology departments whether Members or not. Approval will come from the membership sub-committee and not the AGM.

* the ballot paper will therefore be abolished

* the semi-AGM will also be abolished as this was constituted solely for approval of new Members.

In addition it has been proposed that the category of Foreign Member be abolished and anyone either from the UK & Eire or from the rest of the world would apply to be an Ordinary Member. Allied to this it is proposed that the title Foreign Secretary be changed to International Secretary, this sounds less colonial and reflects the idea that he or she is charged to integrate the activities of the Physiological Society with activities in the rest of the world.

Given the importance of the above proposals, the Committee has decided that all Members entitled to vote should be given an opportunity to do so by holding a postal ballot for those Members who cannot attend and vote in person at the AGM.
Members are reminded that they only have one vote!

I'm sure that there will be a full discussion at the AGM in Newcastle but the Secretaries will try to answer any questions before then.

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 1999 edition (to be distributed on 6 August 1999) should reach the ***Administration Office by 18 June.***

The Maternal Brain: An International Meeting on Neurobiological and Neuroendocrine Adaptation and Disorders in Pregnancy and Postpartum.

Topics: Neuroendocrine adaptations: neurosteroids, lactational infertility, prolactin, plasticity of oxytocin neurones, and modulation of stress hormone responses.

Neurobiological systems: maternal behaviour, neuroimmune mechanisms, desensitisation to pain, puerperal psychosis, and regulation of apetite.

The presentations will consist of molecular through to clinical research. There will be plenary speakers, free communications and poster presentations.

For further details see Web site:-
http://www.phl.ed.ac.uk/~mbrain/ or contact Dr Richard Windle by email at: **maternal.brain@bristol.ac.uk** or at Dept of Anatomy, University of Bristol, Bristol, BS8 1TD. **

PULMONARY CIRCULATION VII
June 27-30, 1999. Prague, Czech Republic.

Immediately preceding the Second Congress of the Federation of European Physiological Societies/ International Union of Physiological Sciences (Prague, June 29- July 4, 1999).

Contact Vaclav Hampl, PhD, Associate Professor, Dept of Physiology, Charles University Second Medical School, Plzenska 130/221, 150 00 Prague 5, Czech Republic.
Tel: +4202 57210345
Fax: +4202 5721 0995

MAIN TOPICS

Mechanisms of oxygen sensing in the pulmonary vasculature
Pulmonary vascular connective tissue
Nitric oxide and other radicals in the pulmonary circulation
Long-term nitric oxide treatment
Adult respiratory distress syndrome
Pulmonary embolism update
Primary pulmonary hypertension
Lung transplant **

International Neurotoxicology Association, 7th Meeting
4 – 9 July 1999 ; University of Leicester, UK

Abstract deadline: 30 April 1999
Contact: INA-7 Secretariat: tel: +44 116 223 1485
Email: jm42@le.ac.uk
Website: http://home.att.et/~crofton99/ina/ *

YOU AN EXPERT WITNESS?

Readers will be only too aware that litigants are ever more willing to resort to courts to seek redress. However, like all problems, this presents opportunities for some professionals. Possible one of the most interesting is to become an expert witness.

Strictly speaking, an expert witness is an individual who possesses knowledge or experience beyond that expected of a layman and who makes that knowledge available to a court. As a result, the role carries a heavy burden of responsibility and ethical obligation: the opinion must not be biased by any personal, professional or financial interest, and must reflect the current developments in the field. The expert witness must obviously be knowledgeable, but should also be able to communicate clearly and be willing to moderate opinion in the light of new evidence.

The *UK Register of Expert Witnesses* is the first point of contact for any readers who feel they have the qualities needed for this demanding role. Your details can be listed in the printed *Register* and distributed to over 3,000 firms of solicitors throughout the UK. Once passed for inclusion a unique range of services becomes available to you, such as: access to factsheets in issues connected to your expert witness activities, a quarterly newsletter, a helpline and specially negotiated rates for PI insurance.

For more information contact Kate Porter at J S Publications, PO Box 505, Newmarket, Suffolk, CB8 7TF. Tel: 01638 561590 Fax 01638 560924, E-mail: **ukrew@jspubs.com** *

Symposium at the Newcastle Meeting (13-15 July 1999) The Gut: Diet & Health

G.J. Dockray (Liverpool, UK) will present the A.A. Harper lecture.

Transepithelial signalling: the role of enteroendocrine cells. K.M. Sanders (Reno, NV, USA)

The role of interstitial cells of Cajal in the generation of electrical rhythmicity and mediation of enteric neurotransmission. M. Kedinger (Strasbourg, France)

Cellular crosstalk and regulatory molecules involved in the gut development
and differentiation. F.H.Leibach (Augusta, GA, USA)

Intestinal peptide transporter(s): biochemistry and physiology. M. Palacin (Barcelona, Spain)

Cystinuria, Lysinuria and Cystinuria. D. Keppler (Heidelberg, Germany)

Conjugate export pumps of the multidrug resistance protein (MRP) family in liver, intestine, and kidney. S.P. Colgan (Boston, MA, USA)

Moleculer Mechanisms of Leukocyte - Epithelial Interactions. M.A. Clark (Newcastle, UK)

Intestinal M cells and pathogen invasion
Dr. D.T. Thwaites
Dept of Physiological Sciences,
University of Newcastle upon Tyne,
Newcastle upon Tyne NE2 4HH
Tel: +44 191 222 8559 (Office)
Tel: +44 191 222 7772 (Lab)
Fax: +44 191 222 6706 *

Biochemical Society Meetings
University of Keele,20-22 July 1999

Organisers: S.Hazelwood(Keele);C.Kielty (Manchester); D.Tuckwell (Manchester); S. Bidey (Manchester); P. Lowenstein (Manchester); C. Tate (Cambridge) R. Grisshammer (Cambridge)

The Morton Medal Lecture:
Professor Anthony Watts (Oxford)
The need for expression expertise in solid state NMR studies of membrane proteins - successes and wish lists.

Colloquia:
·Molecular Control of Apoptosis
·Gene Therapy: From Bench to Bedside
·Expression and Purification of Membrane Proteins
·Structure and function of A-domains

Information:
Full programme and registration form is available at: http://www.biochemsoc.org.uk/meetings/keele99/default.htm
Deadline for abstracts: 7 May 1999
Deadline for application: 21 June 1999
Registration fee: Members £25.00
Non-members £100.00 per day

Contact details:
For further information contact: The Meetings Office, Biochemical Society,
59 Portland Place, London W1N 3AJ, Tel: 0171 580 3481 Fax: 0171 637 7626
e-mail: *meetings@biochemsoc.org.uk*

Speakers include:
P. Aebischer (Lausanne) I. Anegon (Nantes France) H. Blasey (Serono), H. Brady (London) S. Buchanan (London), M. Castro (Manchester), Y. Chernajovsky (London), P. Clarke (Dundee), W. DeGrip (Nijmegen)
C. Dive (Manchester), J. Emsley (Leicester), S. Farrow (Glaxo), R. Flachmann (Heidelberg) R. Grisshammer (Cambridge), J. Groves (Bristol), A. Haines (Cobra Therapeutics), J. Ham (London), R. Hawkins (Manchester), V. Hedge (Keele), C. Higgins (London)
S. High (Manchester), N. Hogg (London), M. Hollingdale (Leeds), H. Kiefer (Stuttgart) D. Klatzmann (Paris), S. Kochanek (Cologne) D. Latchman (London) A. Lever (Cambridge), P. Lowenstein (Manchester), R. Mayne (Alabama), N. Millar (London), B. Miroux (CNRS Meudon-bellevue France), M. Needham (Zeneca), G. Packham (London) M. Paulsson (Cologne) S. Perkins (London), B. Poolman (Groningen) R. Possee (Oxford) P. Reeves (Cambridge USA) K. Samejima (Edinburgh) S. Samulski (N. Carolina) , L. Seymour (Birmingham) A. Shuttleworth (Manchester) G. Smith (Oxford) J. Stolz (Erlangen) C. Tate (Cambridge) , J. Trowesdale (Cambridge) D. Tuckwell (Manchester) J. Uney (Bristol) ,
A. Ward (Leeds), Professor Anthony Watts (Oxford), M.Whyte (Sheffield) L.Young (Birmingham) *

VISITING SCIENTISTS

Foreign visitors of the status of at least post-graduate student, working in laboratories of Members of the Society, may be made "Visiting Scientists" by the Society. The names of such persons, with the dates of their visits and a letter of support, should be sent to the Foreign Secretary, Professor D A Brown, Dept of Pharmacology, University College London, Gower Street, London WC1E 6BT. ***

1999 World Congress on Neurohypophysial Hormones

August 28 – September 2, 1999
Edinburgh, Scotland

Secretariat:
WCNH 1999, Alison J Douglas / Mike Ludwig, Department of Physiology, University Medical School, Teviot Place, Edinburgh EH8 9AG, UK

Phone: +44 (0) 131 650 3274 or 3275
Fax: +44 (0) 131 650 6527
Email: WCNH.1999@ed.ac.uk
Website: http://www.bms.ed.ac.uk/wcnh/

Scientific Organising Committee: Alison J Douglas, Mike Ludwig, Gareth Leng, John A Russell *

Unused Lloyd-Haldane/ Scholander Gas Analysis System required.

Professor Sue Ward (Centre for Exercise Science & Medicine, University of Glasgow) is anxious to locate an unused Lloyd-Haldane or Scholander gas analysis system for purchase or donation. If any colleagues can help, please could they contact Sue at .

TIMES THEY ARE A CHANGING...

In their heart of hearts, nobody really likes change, but change is sometimes a good thing !
In the Autumn issue of the magazine, Professor Maynard Case will discuss changes in governance of the Society, and why they are necessary.
At present we lag behind both the Pharmacological and the Biochemical Society in terms of organisation, so change is in the air, in the hope that we can produce an efficient organisation by the millenium.

50th HARDEN CONFERENCE; ANNEXINS

1-5 September 1999 , Wye College, Kent, UK
Conference Organiser: S. Moss (London)
Organising Committee: A. Brisson (Groningen), R. Donato (Perugia), V. Gerke (Muenster), A. Lewit-Bentley (Paris), F. Russo-Marie (Paris)
Harden Lecture: H. Haigler (California, USA), Annexin XII flips out on acid and inserts into membranes
Keynote Lectures: C. Creutz (Charlottesville, USA), Calcium-dependent, membrane-binding proteins: Annexins, copines, and tricalbins
R. Huber (Martinsreid, Germany), Versatility and conservation in the annexin family of proteins. J. Dedman (Cincinnati, USA), Annexins: The Search for Function
Titles of lectures are subject to change.
Speakers include: M-F. Bader (France), A. Brisson (Netherlands), R. Donato (Italy), J. Ernst (USA), M. Fernandez (Spain), R. Flower (UK), V. Gerke (Germany), J. Gruenberg (Switzerland), K. Hajjar (USA), S. Jäckle (Germany), A. Lewit-Bentley (France), S. Moss (UK), G. Nelsestuen (USA), A. Noegel (Germany), H. Pollard (USA), C. Reutelingsperger (Netherlands), F. Russo-Marie (France), B. Seaton (USA), K. Simons (Germany), J. Tait (USA), D. Waisman (Canada), J. Walker (UK), R. Wuthier (USA)
Information
The full programme and registration form is available at:
http://www.biochemsoc.org.uk/meetings/harden/default.htm
Deadline for application: 2 July 1999.
The meeting is limited to 150 participants.
Registration fee: £300.00 (ensuite), £280.50 (standard).Covers registration, accommodation and meals. There will be a limited number of bursaries for younger members of the Biochemical Society and other sponsoring societies.
The Harden conferences are residential research conferences held annually under the auspices of he Biochemical Society. Each conference covers a specialist topic and is aimed at the forefront of biological research.
The conferences are planned to be of an interdisciplinary nature, bringing together scientists from various backgrounds who have a common interest in, but different approaches to, the topic of the conference. To maintain a suitably high level of discussion and presentation at the conference, it is desirable that participants be experienced in the field covered; most of the participants will be expected to have postdoctoral or equivalent experience, although Ph.D. students will also be welcome. Each conference lasts four to five days, with planned scientific sessions morning and evening, and the afternoon left clear for informal scientific interchange and recreation. The planned scientific sessions feature speakers invited by the Conference Chairman and, in addition, time is left for discussion andcontributions by other participants.
For further information contact: The Meetings Office, Biochemical Society, 59 Portland Place, London W1N 3AJ
Tel: 0171 580 3481 Fax: 0171 637 7626
E-mail: meetings@biochemsoc.org.uk *

University of Glasgow Meeting September 15-17th 1999

The staff of the Division of Neuroscience and Biomedical Systems at Glasgow are beginning preparations for the meeting . The number of designated sessions and symposia have increased since the initial announcement in 1998.
Currently the meeting will run designated sessions of the following special interests groups:
Cellular Neurophysiology
Sommatosensory Control
Heart & Cardiac Muscle
Somatosensory Functions
Smooth muscle
Human Physiology.
There will also be a series of symposia associated with the designated sessions.
Sensory and motor integration in the spinal cord (full day)
Cardiac function in health and disease (half day)
Regulation of ion channels and Ca2+ in smooth muscle (half day)
Challenges to human thermoregulation (full day).
Abstract submission period 14-24th June
Look forward to seeing you there!
Godfrey Smith *

News on personal security precautions

The RDS has always advised members that, if they work with animals and may become a target for animal rights protesters, they should ensure that, as far as possible, their home address is not publicly listed.

Until recently, we had assumed that it was a legal requirement for your name to be on the electoral register, which is a public document. However, we are now informed by one member that the Electoral Registration Officer at his local authority has agreed to list him under a pseudonym.
We understand that this has been done before for other people who have a genuine need to keep their home address confidential.
It is now possible to buy (for under stlg20) a CD-ROM called the UK Info Disc, which contains all UK names and addresses on electoral registers in a searchable format. Local authorities are finalising electoral registers at the moment, so we would urge you to act rapidly if you wish to apply to use a pseudonym.
We suggest you telephone the Electoral Registration Officer at your local authority and explain that you are at risk from animal rights extremists, explain about the CD-ROM and ask if you can use a pseudonym for future elections.
If you need any further advice or information, please telephone the RDS Office on 0171-287-2818.

Joint Meeting with the Chilean Physiological Society - Pucon 13-16 November 1999

GRANT APPLICATION FORM

Surname (IN CAPITALS) _____ Title & Forenames _____

Work Address _____

_____

Date of Birth _____ Membership No _____

Work Tel No _____ Fax No _____

Appointment/ Status _____ Employer/ Funding Body _____

Funds are available towards the costs of physiologists wishing to attend the meeting and present their work. The sum available is not yet known, but it is hoped it will be £400 - 500. Applicants should also pursue other sources of funding.

Details of employment or status: *Please tick one box*

Member of UK/ Irish department of Physiology or related sciences:

graduate student	☐
postdoctoral worker	☐
academic staff member	☐
technical staff member	☐
visitor	☐
*NHS clinician not part of a Medical School	☐
*Member of MRC or other UK research institute, or equivalent	☐
*Other (please provide details)	☐

Relationship with the Society: *Please tick one box*

Member	☐
Affiliate	☐
Candidate for Membership	☐

INVITED SPEAKER

SYMPOSIUM ORGANISER

* NOTE: if you tick an asterisked box, please send a covering note explaining why you need assistance from the Society.

Title ofAbstract: _____

_____

Other sources of funds: give details of other bodies to which you have applied or intend to apply for funding, including the maximum possible award and the date of notification _____

_____

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

Signature of Head of Department confirming eligibility if not Member or Affiliate

Signed ..... Name.....

On completion of this form, please return to Assistant Administrator (Grants for Chile), The Physiological Society, PO Box 11319, London WC1E 7JF.

DEADLINE FOR RECEIPT OF COMPLETED FORMS FRIDAY 9 JULY 1999

Professor Steve Bolsover & Group; (l-r) Fabienne Archer, Rachel Ashworth, Ozbek Ibrahim, Jacob Millkan, Vinita Pandey & Nicola Parkinson

Michael Hausser & Soren Christensen

Simon Mitchell

Physiology Football Team 1999