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# The Physiological Society Magazine

*Imperial College Meeting*

*Features on :*

*Graded potential synapses*

*Ion channel expression & metastatic activity in cancer cells*

*Physiology in weightlessness*

*Patch-Clamp Technology*

**Spring 2000**
**No 38**

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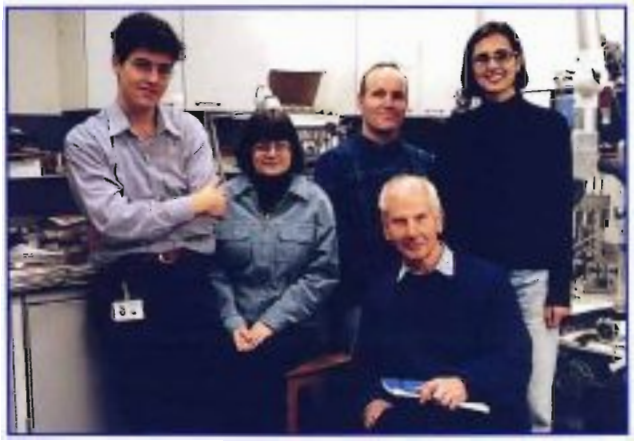
Marysia Mycielska, Marek Szatkowski & Stan Head

Alex Nowicky, Peter Ellaway, Steve Rawlinson & Nick Davey



Microcirculation Group ; Dario Montermini, Hilary Moffitt, Chris Neal, Ushma Savia & Charles Michel (seated)

Scott Fraser, Sumathi Sekaran, Angela Liu & Mustafa Djamgoz

Photography courtesy of Martin Rosenberg

Front cover photograph: Courtesy of Peter Simmons

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**Affiliate Travel Grant Scheme:** The next deadline for receipt of applications is 31 March 2000.

**Vacation Studentships :** The next deadline for receipt of applications is 30 April 2000.

**Change of Address:** Members should inform the Administration Office of any changes of address, telephone, fax or email addresses. Changes can be emailed to :- admin@physoc.org

**BudapestMeeting:** Abstracts should be submitted to the Meetings Secretary's Office by 10 March 2000.

**Magazine:** Letters and articles for inclusion in the next issue will have been collected by the time this goes to press. Contributions for the Autumn issue should reach the Editor by 12 May 2000. Advertisements and Notices and items for the Special Interest Group Forum, should reach the Administration Office by 2 June 2000 and items for Committee News should reach the Committee Secretary's Office by 2 June 2000. Please cite references on articles in the style of The Journal of Physiology.

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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 500 words to 2000 words.

### Submission of articles

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

### Deadlines for submission

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

### Illustrations

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

### Author photographs

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

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

### Suggestions for articles

These should be made either to the Editor, to the Editorial Assistant or to a member of the Magazine Editorial Group (see below).

### Magazine Online

The magazine is now available on our website.

# PHYSIOLOGY AT IMPERIAL COLLEGE

Although one of the founders of the Society, T.H.Huxley, was a professor at the Royal School of Mines, experimental physiology did not come to South Kensington until the twentieth century. In 1903, the University of London opened its Physiological Laboratory in the Imperial Institute at a site which is now at the heart of Imperial College. The first and only Director of the Laboratory was A.D.Waller, a man of private means, who relinquished his lectureship at St Mary's Hospital Medical School to take up the position without emoluments and receive the title of Professor. At St Mary's in 1887, Waller had laid the foundations of electrocardiography when he showed that the electrical activity of the heart could be recorded from a human subject using external electrodes. Within a few years of his arrival at South Kensington, he earned a place in the history of anaesthesia by determining for the first time the dose response relations of chloroform in a study which was to make it a much safer anaesthetic. Always an active member of the Society, Waller had arranged scientific meetings at St Mary's, at his substantial home in St John's Wood and in the laboratories at the Imperial Institute. The University of London closed the laboratory shortly after Waller's death in 1922, claiming that the space was urgently needed for administration.

Maria Catley & Peter Ellaway

Charles Michel

John Laycock

50 years passed by before the Society was to meet at South Kensington once again. In 1972 it came by invitation of Colin Caro, who had set up the Physiological Flow Studies Unit at Imperial College in the late 1960s. Since then there have been meetings at IC roughly once every 10 years, the most recent one being held in December 1991. Over the years the Physiological Flow Studies Unit grew and its interests broadened. In 1989, Imperial College established the Centre for Biological and Medical Systems and this evolved into a department in 1997. From the outset the Physiological Flow Studies Unit was a group within Biological and Medical Systems as several new lines of research developed. Research activity is still strong in the areas of the fluid and solid mechanics of tissues and organs (e.g. on blood flow and arterial disease, on the airflow in the respiratory tract and on the mechanics of connective tissues), but there is also now a major commitment to the development of Medical Imaging and Visualisation (Virtual Reality, MRI and Image guided surgery) along with the monitoring of cardio-respiratory activity in human subjects and thermoregulation in horses.

In the 1960s and 1970s physiological research was also occurring almost surreptitiously in other departments of the College. Members the Applied Optics Section in the Department of Physics shared a history of vision

research which spanned 100 years from the time of Sir William Abney. This interest was developed by the late Keith Ruddock into a strong group investigating the electrophysiology of the fish retina alongside the psychophysics of human vision. Together with a group of protein crystallographers, Keith moved into the Biophysics Section that was set up in the Physics Department in the 1970s. One of Keith's students (Mustafa Djamgoz) has continued to investigate the fish retina in the Biology Department. His work emphasised the remarkable cellular and synaptic plasticity of the fish retina and gradually expanded into other areas of cell physiology (see article in Science, News & Views section). Recently an Ion Channel Interest Group has been formed to serve as a forum for bringing together colleagues from the various corners of the College, including those in the departments of Biochemistry, Physics (Biophysics), Biology and various Divisions of the Medical School including the National Heart and Lung Institute.

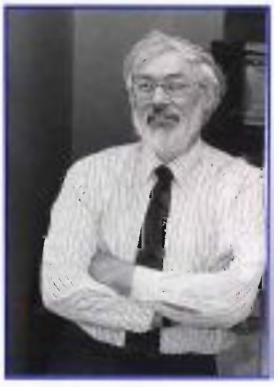
Mustafa Djamgoz

John Skinner & Sinead Morrissey

In 1988, St Mary's Hospital Medical School joined Imperial College to become its first medical school. Although the Department of Physiology and Biophysics at St Mary's retained its separate identity in Paddington for the next 10 years, links between the St Mary's departments and those at South Kensington started to strengthen. In August 1997, the merger of the Charing Cross and Westminster Medical School, the National Heart and Lung Institute and the Royal Postgraduate Medical School with the existing medical school at St Mary's led to the formation of the Imperial College School of Medicine. Thus the numbers of people within the College who were engaged in research in the Physiological Sciences was increased several fold by the stroke a pen. They were, however, scattered over several different sites in West London.

Richard Kitney

This separation of basic scientists in the medical schools from the science and engineering departments at South Kensington was partly ameliorated the following year by the opening of the Sir Alexander Fleming Building on the main IC campus. This building houses the Division of Biomedical Sciences and the Department of Biology. Whereas all members of the former preclinical departments at St Mary's moved to the new building in South Kensington, the Division of Neuroscience and Psychological Medicine was a more obvious home for many in the preclinical departments at Charing Cross. Many of the physiologists, anatomists, pharmacologists and biochemists from the Charing Cross and Westminster Medical School remained on the Charing Cross Hospital site and now form the principal base of this Neuroscience Division.



Steve Walter

Some of the physiologists, however, moved from the Charing Cross site to the new building in South Kensington to set

up research groups working on muscle energetics and renal physiology in the Division of Biomedical Sciences. Here they have colleagues working on blood rheology, the microcirculation and endothelial cell biology, innervation of muscle, electrophysiology of prostatic epithelia and, until very recently, oscillations in the firing of hippocampal neurones.

Integrative physiology is alive and well on the Charing Cross site, even though the divisional structure of the merged schools within Imperial College has removed visible signs of the subject. Physiological research under the umbrella of Neuroscience is being conducted into sensorimotor control (corticospinal control of movement, spinal cord injury, muscle spindles in motor control, eye movements, posture), neuroendocrinology (interactions between vasopressin and prolactin, glucocorticoids in the control of neuroendocrine function) and development and plasticity of neuromuscular systems. In the Cardiovascular and Respiratory Medicine Division on the Charing Cross site groups are working on mechano-electric feedback in the control of the cardiac cycle and the control of breathing in exercise, sleep and neurological disorders.

Paul Canfield

Many other groups concerned with applied cardiovascular and respiratory physiology are located in the National Heart and Lung Institute on the Brompton and Hammersmith sites. Also at the Hammersmith site, groups are investigating hypothalamic control of food intake and metabolism.

In addition to the opening of a new building and the major regrouping of academic staff into a new divisional structure, the School of Medicine (see www.med.ic.ac.uk) also introduced a new "vertically integrated course" so that physiology is no longer an identifiable subject in the "core curriculum" for medical students. Inevitably, however, there is a large physiological content to this new course, and members of the Society have played a major part in setting it on the road. Many of the special options in the course have a strong physiological flavour and, with growing links between the new divisions and the old departments, there is great potential for a further flowering of physiological science within the enlarged College. With the traditional strengths of the College in the Physical Sciences and Engineering, we are optimistic that this potential will soon be fulfilled, particularly as biological science has reached a stage when once again it has to become more quantitative.

Frank Harrison & Max Lab

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# HOW DO GRADED POTENTIAL SYNAPSES WORK? A VIEW FROM INSECT EYES.

*Peter Simmons uses the locust to investigate the complexities of graded synaptic transmission*

Transmission of graded potentials across synapses is an important mode of communication in nervous systems. It is the normal mode of communication in the early visual systems of most animals, including insects where these signals are particularly amenable to study. The use of graded potentials maximises the rate at which information can be carried in neurons, but the synapses that link different neurons are a major source of unreliability.

Many adult insects possess two different types of eyes: compound eyes and ocelli (Fig. 1). In compound eyes, information transmission is at a premium, because any loss degrades the insect's ability to see objects. Experimenters can chase signals from a photoreceptor to a second-order neuron by comparing responses to identical visual stimuli. Rob de Ruyter van Steveninck and Simon Laughlin [1] computed signal-to-noise ratios by repeatedly delivering the same sequence of randomly modulated light to a fly's eye. They showed that graded potentials in second-order neurons encode between 1,500 and 2,000 bits of information/second, about five times more than neurons that use trains of spikes. So, by avoiding the need to decode inter-spike interval into a signal level, information carrying capacity is greatly enhanced.

***FIGURE 1.*** *Head of the locust Schistocerca gregaria, showing compound eyes, which are striped in this species, and the single-lens ocelli (arrows). The insect uses its compound eyes to see and react to objects, whereas the ocelli collect light from wide areas and can help stabilise flight attitude by monitoring changes in the position of the visual horizon.*

But how well do synapses that carry graded potentials work? Their reliability could be limited by the stochastic manner in which quanta of neurotransmitter are released, and the photoreceptor output synapses introduce noise of around half a millivolt. The route of the signal when it leaves a second-order neuron is hard to follow directly in the compound eye, but is possible in the ocellar visual system where the small number of quite large neurons has enabled me to make recordings from pre- and postsynaptic neurons simultaneously. Second-order ocellar neurons excite some large, third-order neurons and also make lateral connections amongst each other, which are simpler to study. One type is inhibitory, and produces discrete postsynaptic potentials because it only normally transmits when the presynaptic neuron spikes. These spikes are smaller than the all-or-none impulses that propagate along long axons, and are variable in amplitude, so the graded nature of transmission across the synapse is clear. I can now include a measure of scatter into the operating curve for a synapse (Fig. 2; [2]). The absolute noise level is similar to that of the first synapse in the fly compound eye, although the range of postsynaptic potentials is much smaller.

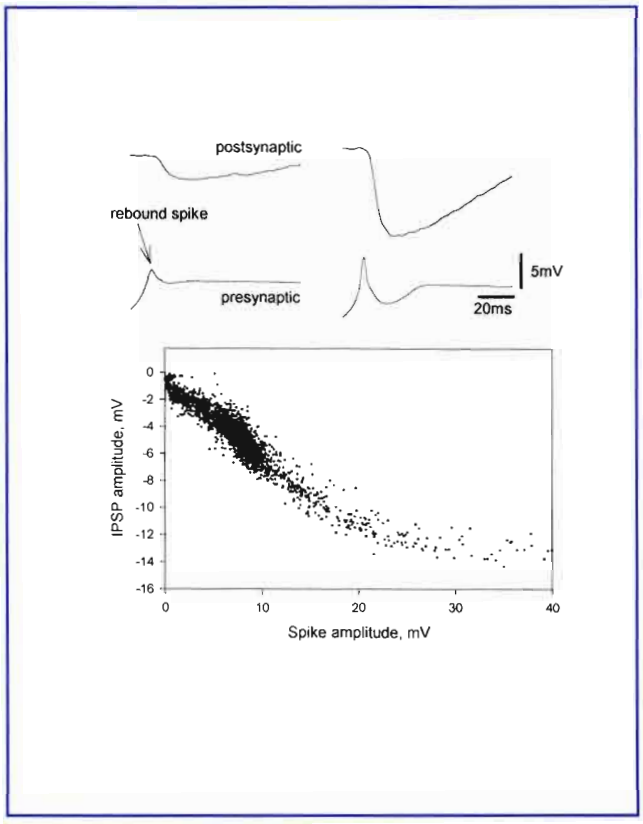


***FIGURE 2.*** *The transfer curve for an inhibitory synapse between two neurons in the ocellar pathway of the locust. Two intracellular recordings show rebound spikes of two amplitudes, together with the IPSPs each elicits in the postsynaptic neuron. The spikes are rebound events, each triggered when a pulse of injected hyperpolarising current ended. The graph includes just over 2,000 measurements of pre- and post-synaptic potential. For each value of presynaptic potential, the IPSP has a standard deviation of about 0.7mV, and most of this noise originates in the synapse.*

The noise in the synaptic transfer curve is constant throughout the operating range, which is relevant to understanding the way that different amplitudes of graded presynaptic potential regulate transmitter release. A simple link would be if potential affected the probability of quantal release in a global fashion, but the scatter in PSP amplitude would increase with the amplitude, assuming transmitter release is a Poisson process. In a communication to the Physiological Society [3], it has previously been noted that a global, Poisson process governing quantal release would involve abnormally high rates of vesicle discharge from compound eye photoreceptors. One way around this would be if each discrete synaptic bouton has a different threshold for release. Alternatively, the presynaptic potential might affect the availability of vesicles for release.

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# ION CHANNEL EXPRESSION AND METASTATIC ACTIVITY IN CANCER CELLS

*Mustafa Djamgoz discusses recent work on the possible role of ion channels in metastatic activity of prostate cancer cells.*

After more than twenty years of research on the cellular neurobiology of the vertebrate (mainly fish) retina, which is a wonderful system for learning about mechanisms of physiological plasticity and appreciating its power in terms of the system's functional output, we have become interested in pathophysiological change, in particular the process of *metastasis* in cancer. Essentially, metastasis is formation of secondary tumours by cells escaping from a primary tumour and is the main cause of death in most cancer patients. Metastasis is an extremely complex process beginning with cells 'breaking away' from the primary tumour, migrating through the basement membrane (facilitated by release of proteolytic enzymes), getting into circulation (blood or lymph), adhering to a secondary site (which may be tissue-specific), extravasating, proliferating etc. It is possible that dynamic gene expression also occurs during this cascade, as the migrating cells reach sequential milestones. In many respects, therefore, metastasis is probably no less complex than embryonic development. Nevertheless, metastasis can be considered as a series of basic cellular behaviours, including motility, invasion, secretion, adhesion and gene expression. Although such behaviours are generally well known to be controlled by ion channels, the possible role of ion channel activity in metastasis *per se* has not previously been investigated. Cancer cells are known to express ion channels, however. [In fact, ion channels have been studied extensively in cancerous cells due to the ease of culturing them.] Furthermore, electrodiagnosis of malignancy has been practised clinically, despite the underlying mechanisms remaining unknown (Cuzick et al.,1998).

The first, unique question that we addressed was whether voltage-gated ion channel expression varied between cells of different metastatic ability. Here, we turned initially to the Dunning system of rat prostate carcinoma, comprising a number of 'model' cell lines (derived from the same original tumour) of distinct metastatic character. We then extended the work to human cell lines and biopsy tissues. We have thus obtained a series of results which suggest that ion channels could indeed play an important role in cancer metastasis.

**Functional voltage-gated $Na^+$ channels are expressed selectively by strongly metastatic cells**

Whole-cell patch-clamp recordings showed that voltage-gated $Na^+$ channels (VGSCs) occur only in the strongly metastatic prostate cancer cell lines, in both rat (MAT-LyLu; Grimes et al.,1995) and human (PC-3; Laniado et al.,1997) (Fig. 1). In contrast, a large number of recordings from corresponding weakly metastatic (AT-2 and LNCaP) cells showed no VGSC activity. A more extensive study by Smith et al. (1998) on numerous rat and human prostate cancer cell lines, including some transfected with fragments of genomic DNA from metastases, showed that a positive correlation existed between VGSC expression and invasive potential (Fig. 2). All of the cell lines tested had voltage-gated $K^+$ currents, the density of which tended to be higher in the relatively weakly metastatic cells. Taken together, these results suggested that the

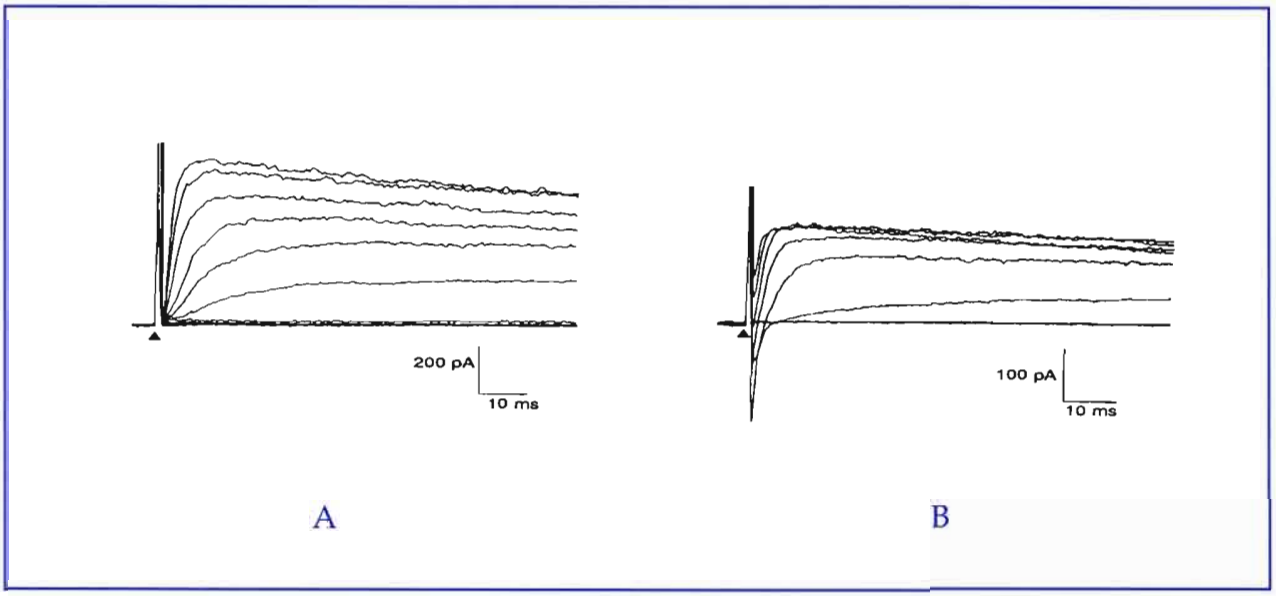


***Figure 1.*** *Typical voltage-activated whole-cell membrane currents recorded in an AT-2 (A) and a MAT-LyLu cell (B). The families of currents were elicited by depolarizing voltage pulses of 80 ms duration, applied in 10 mV increments from a holding potential of –90 mV. The onset of the voltage pulses, which lasted for the whole duration of the traces, is indicated by the arrow-head ▲). An inward, Na+ current was present only in the MAT-LyLu cells. Note the different current scales in A and B. Modified from Grimes et al. (1995).*

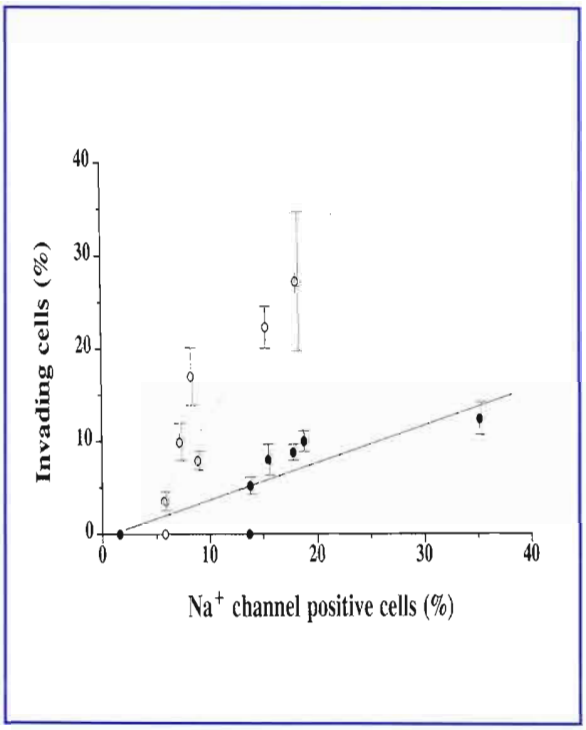


***Figure 2.*** *Positive correlations between the percentage of invading cells versus the percentage of VGSC-positive cells for various human (solid line) and rat Dunning (dotted line) cells (n=7 each). Linear regression analyses gave correlation coefficients of 0.83 (P<0.05) and 0.97 (P<0.01), respectively. Modified from Smith et al. (1998).*

membranes of the strongly metastatic cells would be much more electrically dynamic.

**Voltage-gated $Na^+$ channel activity can potentially enhance the metastatic process**

A series of *in vitro* assays were performed to test whether VGSC expression was an 'epiphenomenon' or whether it could contribute directly to the metastatic cascade. Suppression of VGSC activity with micromolar tetrodotoxin (TTX) produced a variety of effects on the MAT-LyLu cells, consistent with a role in metastasis. Thus, in the presence of TTX, cells' process length was reduced (Fraser et al.,1999) and directional lateral motility in 'wound' assays was inhibited (Fraser et al.,1998). In Matrigel assays, also, MAT-LyLu and PC-3 cells' invasive activity was reduced (Grimes et al.,1995; Laniado et al.,1997). Finally, we have found recently that TTX also suppresses MAT-LyLu cell's endocytic membrane activity, which would suggest that

that expression of VGSCs specifically in cells of high metastatic ability occurs in breast cancer as well (S.P. Fraser et al. - manuscript in preparation).

**A new concept in pathophysiology of metastatic disease?**

The work that we have done so far is consistent with VGSC expression and activity occurring as an integral part of the metastatic process in prostate cancer, and perhaps some other cancers as well. Thus, metastasis would appear to be a phenomenon of 'excitability', consistent with the abnormally hyperactive behaviour of metastasising cancer cells. Accordingly, cancer cells can acquire VGSCs or upregulate an existing basal level in order to become metastatic. Upregulation could occur in response to growth factors (GF's), some of which (e.g. nerve growth factor) are known to induce or upregulate VGSC expression in cells (Toledo-Aral et al.,1995). An interesting possibility is that VGSC upregulation occurs in response to a GF released by metastasising cells themselves thereby creating a positive feed-back effect involving: GF secretion ↖ VGSC induction/ upregulation ↖ further GF release ↖ more VGSCs etc., thereby greatly enhancing the efficacy of the metastatic cascade.

**Future perspectives**

From the evidence obtained, we propose that VGSCs are a novel target for diagnosis and inhibition of metastatic prostate cancer. However, many questions remain: What is the precise molecular nature of the 'culprit' VGSC and how is it regulated? What other roles (e.g. gene expression, protection against metabolic stress, cell death etc.) could VGSC activity play in metastasis? What is the role of other types of ion channel (e.g. $K^+$, $Ca^{2+}$, $Cl^-$) in prostate cancer? And what about other cancers?

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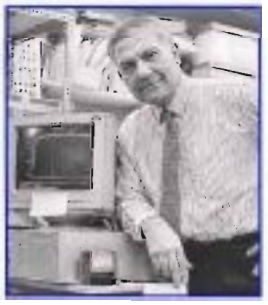

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VGSCs could also drive the cells' vesicular secretion. Since intra/extravasation and tissue invasion rely crucially upon release of proteolytic enzymes from metastasising cells, this could be an important role for the VGSCs. In contrast, TTX had no such effects on AT-2 or LNCaP cells, consistent with lack of expression of functional VGSCs in these cells. In summary, these observations are consistent with VGSC activity enhancing the metastatic process in several respects. Importantly, this could occur *in vivo,* since VGSC expression and pathological grading of epithelial structures in sections of human prostate biopsies are also strongly correlated, as *in vitro* (Stewart et al.,1999).

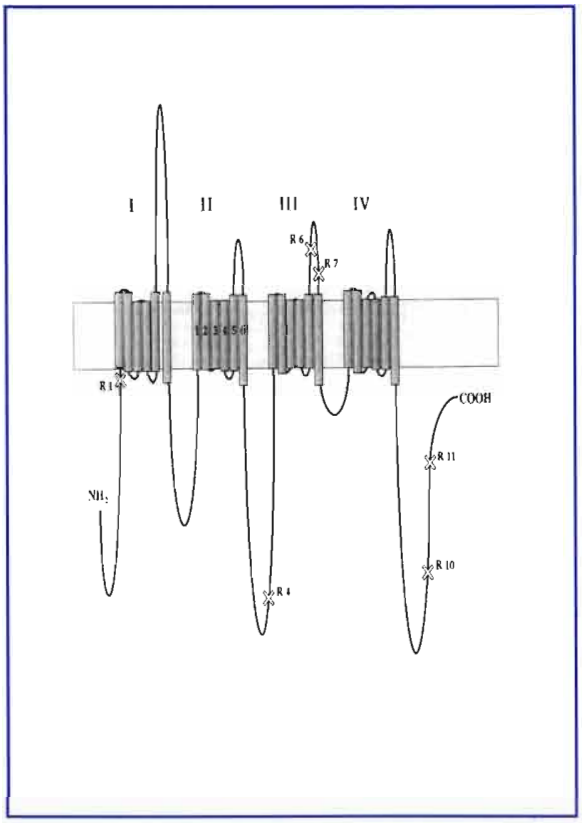


***Figure 3.*** *Schematic representation of the rSkM1 α-subunit found in the MAT-LyLu/AT-2 cells, drawn to approximate scale, with channel topology adopted from current VGSC models. The four domains, each containing six transmembrane segments, are numbered I to IV. Amino acid changing nucleotide differences (R1, R4, R6, R7, R10 and R11) detected are indicated by crosses. Modified from Diss et al. (1998).*

**Molecular nature of VGSC expression**

A combined electrophysiological and pharmacological study showed that the functional VGS current of the MAT-LyLu cells was of the TTX – sensitive neuronal type (Grimes & Djamgoz, 1998). A subsequent molecular biological study by Diss et al. (1998) identified adult skeletal (SkM) type mRNAs in MAT-LyLu and PC-3 cells (Fig. 3). However, this is unlikely to be wholly responsible for the VGS currents recorded in these cells, and further work is required to determine the molecular nature of other VGSC gene(s) expressed in rat and human prostate cancer cells. Interestingly, a basal level of VGSC expression was present in the AT-2/LNCaP cells, although these cells do not express functional VGSCs. It thus seems that prostate epithelial cells normally express a low level of VGSCα mRNA and that, when cells become metastatic, VGSC expression is greatly upregulated and enhances several aspects of the cells' activity critical to metastatic progression.

**VGSC expression in other types of cancer**

There is some evidence that VGSC expression also occurs in other cancers. In fact, it has been known for some time that small cell carcinoma of the lung is associated with neuronal properties (Blandino et al.,1995). Human glioblastoma cells were also found to have up-regulated VGSCs and to generate action potentials, unlike normal glia (Labrakakis et al.,1997). VGSC genes have been cloned from various carcinomas (e.g. Klugbauer et al.,1997). Finally, in a recent study, we have found

# PULLING G'S ABOARD THE VOMIT COMET: PHYSIOLOGY IN WEIGHTLESSNESS.

*"Parabolic flights were originally used by NASA to accustom astronauts to weightlessness prior to space missions. But they are also useful for physiologists." as Jonathan Cole reports.*

Several groups of researchers, including ourselves, have been investigating movement programming in a subject with no sensation of touch or joint/movement sensation below the neck. With the acquiescence and encouragement of the subject, Ian Waterman, we scientists have perturbed his ability to move, and/or receive information about the movement, in a variety of ways. Ian has been subjected to distorted or absent visual feedback, weights, magnetic stimulation, fatigue, variable resistance and, worst of all for him, mental arithmetic to distract him. All of these he has endured as we try to learn the limits of his unique abilities. But there has always been one further perturbation he himself wanted to try, and so this was why we wrote initially to Jim Lackner in Boston.

Professor Lackner's research interest is in movement, motion sickness and whole body spatial orientation. His lab is a wonderful underground treasure-trove, with more ways to make you sick, through body or room rotation, than one could have imagined. But he also experiments at NASA in Houston with their parabolic flight facility. This Boeing tanker, a KC135 similar to a 707, is perhaps better known as 'The Vomit Comet.' This was where Ian and I spent two weeks last year.

We met up with Jim, Paul DiZio and their team at Brandeis University, in Boston, for a week to do four experiments on reaching and knee bend movements. Once we had done the ground based work the kit was driven from Boston to Houston and reassembled on the plane. We had a more leisurely trip down, as Ian and I contemplated what we had let ourselves in for.

The 'KC' climbs to 32000 ft and then dives to 23000 ft. As it goes over the top there is 25s or so of weightlessness followed by a comparable time at 1.8g. On each 2 hour flight there are 40 parabolas in 4 runs of 10 - quite a ride.

We sat in the back for take off, though Ian, who could not move round during the flight, was in a fixed bucket seat

***Figure 1.*** *Three experiments in line aboard the KC135. On the left JC is reaching with his right index finger, in the centre the perceptions after knee bends are being reported and on the right IW is feeling awful, assisted by Jim Lackner (furthest away) and Paul DiZio. IW's task was to estimate steady flexion and extension movements of the elbow with the arm held in front of him. These he managed despite his nausea. Note the profusion of white plastic barf bags in our waist bands and chest pockets.*

throughout. Once airborne we all went to our positions, four experimental subjects and four running them (see Figure 1). There were two experiments on reaching under variable gravity, one on knee bends and one on estimating the length of a rod held in the outstretched and unseen hand. The aim of the experiment was to test movement trajectories and accuracy during the steady states of 0 and 2 g and during the rapid transitions between the two, when there was no awareness of the gravitational force. The positions of limb joints were recorded using an IR recorder

and two PCs bolted to the floor.
One experiment at a table involved reaching to set points. Another, which Ian did, involved flexion and extension of the elbow with eyes shut, estimating a 40 degree movement in the varying gravitational forces. During knee bends we had to describe what we felt: in 0 g the bends were felt to be less and slower, whilst in 2 g they felt faster and the floor seemed to rush up to meet one. Lastly Jim oversaw an experiment estimating how the length of an unseen rod altered in varying gravitational fields. For each experiment copious amounts of velcro were used to tether us to the floor or the table.
Though the results of the experiments are still being worked out and further experiments at NASA need to be done, one's perceptions give an idea of the results. As the plane closed in on the top of the parabola the first time, and we

*Figure 2. Jonathan Cole between reaching experiments.*

entered 0 g, it was like the biggest hump-back bridge you could imagine. My guts came into my throat... and stayed there! Things settled a little and I left my arm outstretched and it stayed there. I looked down at the table to make a reaching movement and it seemed so much farther away. I made a movement and, despite knowing what would happen, I could not prevent my arm going high and too far. I could not re-program the movement until I tried to do it and failed. But, most extraordinary of all, I looked at the others further down the plane and realised that they now appeared upside down, on the ceiling. More than that, I felt upside down as well. Then the plane shuddered a bit, the 25 s were up and 1.8 g was upon us. I felt amazingly heavy, my reaching movements were short and straight into the table. At least when I looked up we were all the right way up.

Doing knee bends in 2 g I felt as though I was going down so fast and deep: others even think the ground is rushing to meet them. In contrast, in 0 g I felt the bends so slow and slight, with the ground almost moving away as one bends towards it, despite my feet being secured to the floor. In judging the length of unseen rods in 2 g they seem to shorten as one flicks them up and down in the hand, (the arm is restrained at the wrist). In 0 g the rod seemed to lengthen. More than that, as I relaxed my arm itself seemed to lengthen as I flicked the rod up and down.

Initially I was very wary of the transitions, and nervous of feeling sick and vomiting. We all, after all, had 'barf' bags stuffed into our flights suits, and Ian and I had been told to have a light breakfast of bananas and clear fluids. But as I relaxed the nausea faded and I began to enjoy weightlessness, a feeling of great serenity and relaxation. So much so that I had a strong feeling that time itself had slowed down. I wondered if I was imaging this, but Jim Lackner has done some experiments on this and found that counted time does not alter, (though that is not the same as experienced time).

Jim had called the parabolic flight a demanding experiment environment, with some understatement. The plane is screaming up and down at 45 degrees to the horizontal, there is very little space and we are all trying to do experiments requiring great exactness whilst feeling sick, and, for many, vomiting. The previous day's flight had to be stopped for a while to clear up the floating vomit of

someone who had missed their barf bag. Despite all this Jim and the team ran four simultaneous studies, in a space the size of a small bathroom, all of which worked. Before we went up Jim and Paul had casually said they had never been sick. Fortunately, to maintain the honour of British Physiology, I did not have to use the barf bag either.

***Figure 3.*** *Jonathan Cole after the flight on the tarmac at Ellington Field with the KC135 behind. An official NASA "hero-shot".*

Two hours later we had touched down. Ian had unfortunately been sick, which fascinated Jim and Paul given Ian's condition. Ian's mixed feelings at having survived parabolic but at the cost of being sick were not helped by my own insufferable smugness at not barfing. I went up the next day as well, completing the experiments and floating in weightlessness. Both enormous fun as well as being good science. To experience weightlessness, even for forty 25 second periods, is fascinating. One astronaut and shuttle veteran had told me that he thought that all our experiences of the world were altered by gravity, whilst another used to feel homesick not for the world during her space flights, but for space on her return. To experience the relaxation and grace of weightlessness, even temporarily, is to understand.

*Jonathan Cole*
*Clinical Neurological Sciences*
*Southampton University and*
*Poole Hospital*

**Acknowledgements**

I am very grateful to the Wellcome Trust for a travel grant and to Professors Jim Lackner and Paul DiZio for local support and, of course, letting us pull some g's.

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# PRESENT AND FUTURE OF PATCH-CLAMP TECHNOLOGY

*Hubert Affolter presents another article in our occasional series from developers active in the field of physiological instrumentation.*

The patch-clamp technique was introduced by Erwin Neher and Berndt Sakmann (1976) for recording the currents in a small patch of membrane under voltage-clamp conditions. Since then a number of changes have occurred, most notably the development of the "gigaseal" by Neher. Various recording configurations allow intracellular recordings to be made with the same type of recording setup as used for patch recording from the cell surface or from cell-free membrane patches.

Over the years this technique was developed from an esoteric technique used by biophysicists to a well-accepted standard technique in the collection of analytic tools for physiologists. This technique has now penetrated many of the biological research fields, such as Neurobiology, Pharmacology, and Molecular Biology. A major contribution to the acceptance of the technique was the awarding of the Nobel prize to Neher and Sakmann. Another contribution was the improvement of the available hardware and software, making the patch-clamp technique more user- friendly and less intimidating.

HEKA Elektronik was the manufacturer of the first commercial amplifier, the EPC5, soon to be followed by the "classic" EPC7. The successor of the EPC7 is the computer-controlled EPC9. The EPC9 was, and still appears, a revolutionary design: it has no knobs or switches. The goal was to have the computer do any task which could be delegated to it, thus relieving the experimenter from repetitive tasks and giving him more time for his actual experiment. This approach also makes the experiment more predictable and reliable. The fundamental paradigm change was that the user can set the amplifier to follow the conditions required by the experiment, instead of the "classic" approach where the user has to adapt to the requirement of the amplifier.

**Patch-clamping today**

The researcher today has a broad selection of available solutions when setting up or extending a patch-clamp setup. He/she will have to judge and decide where his priorities will be, and which experimental conditions will rule his experimental setup.

There are basically four possible options:

**1.** There are low-cost solutions for student laboratories.
**2.** There are amplifiers optimized for the best biophysical signal. Thus, a selection of up to 30 physical knobs, switches, and dials permit the user to tune the amplifier to its best performance.
**3.** There are amplifiers optimized for lowest noise when measuring single channel events, but making compromises in the whole cell range.
**4.** There is the EPC9 which is optimized for whole cell patching, and has the best amplifier noise performance in that range. A unique feature with this amplifier is that it is fully integrated in an acquisition and analysis program.

Also, today the user is in the comfortable position of being able to select from various acquisition and analysis programs for patch-clamping. These packages cost from nothing to less than a postdoc's monthly salary. Some of the software solutions have been used for many years and will fulfill most of the requirements of the users.

Basically, the software packages fall in three groups:

**1.** Packages which are free for university researchers such as the "Strathclyde" program collection.
**2.** Axon's pClamp which is gradually shifting from DOS to Windows.
**3.** HEKA's PULSE+PULSEFIT which runs under Windows and MacOS. The major

difference of this program compared to the other two groups is that it pushes the idea of an integrated and integratable system.

Out of many discussions with researchers from the University, as well as the industrial environment, I can distill three different approaches:

**1.** I have very little money to spend. I am only interested in the price tag of the amplifier.
**2.** I buy what I already know, or what my neighbour has, or what I feel is the "standard".
**3.** Show me what your solution can do.

Contrary to what many people expect, the first approach is not easy, since the least expensive setup is not the sum of the least expensive parts and, in the end, may not be a cheap solution. If one compares the total costs of a solution from different vendors one may be surprised that an integrated system like the EPC9 (which is all the electronics needed for a patch-clamp setup) costs less than the sum of single components. This error, can be quite common in those universities where the purchase department buys equipment according to price bidding, and the researcher is then confronted with the result.

Today, one should also consider that more and more research is performed on interacting systems, such as trans-synaptic signaling, coupling of gap-junctions, or combining patch-clamping with imaging. Such experimental setups are so demanding that one desperately tries to automate as much as one can! Here an integrated system is a great advantage. To support automation, we added the possibility of allowing an external program to control PULSE and the EPC9. The user can now write his own "super" program, e.g. starting various protocols depending on cellular parameters or synchronizing to other hardware.
Another advantage, especially important in industrial research, is that a computer - controlled amplifier can make a complete protocol of all experimental parameters. Even years later, the data file will contain a full description of the experiment.

Researchers also have to judge what their future research will focus on. Patch-clamping is already applied as a screening tool, not only in pharmaceutical research, but in academic research as well, e.g. in searching for channel expression. Over the last years I have seen a revival of whole-cell patch-clamping at the expense of single channel work. I notice more and more work being done in current clamp mode, too.

**Patch-clamping tomorrow**

I have been asked what I guess the next few years will bring to the patch-clamping community.

First, I expect to see more and more demanding experimental setups. Here is an example of a complex experiment already routinely done today: monitor the cell current while measuring the intracellular Calcium concentration with an intracellular dye and stimulating the cell by releasing intracellular calcium from a caged compound by a laser flash.

Second, I predict an increasing degree of automation up to fully automatic patch-clamping systems. There are various ongoing developments on automating patch-clamping. I am confident that within one to two years there will be working systems. In the beginning they will be expensive, but some spin-off development will make the daily chores easier and the experimental work more reliable and productive. A good guess is that it will require smart software and hardware integration.

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## MICROVASCULAR AND ENDOTHELIAL PHYSIOLOGY

The Microvascular and Endothelial SIG got up bright and early for a 9 am start on the Monday morning of the Birmingham meeting, undeterred by subzero temperatures and British Rail. We heard 11 oral communications, two of which were illustrated and viewed eight posters. Because of timetabling problems, the poster session was not as well attended as we had hoped and with no poster approval system in place for this meeting, some presenters felt a little let down. On the other hand, our Designated Lecture, given by Professor Neil Granger was very well attended and his outlook for the next millenium enjoyed by all. The Pfizer Prize was not awarded this year, partly because of the very small number of submissions. This is a factor which I hope we can remedy for the next round.

The Imperial College meeting of the Physiological Society will be a busy one for all those interested in microvascular and endothelial physiology. We have a full day symposium on the 'Response of the Endothelium to Pressure and Shear and the Cardiovascular Consequences' organised by John Lever and Charles Michel under the joint auspices of the British Microcirculation Society, The Physiological Society and the IUPS Commission on Microcirculation. Speakers will include:

**Responses of the endothelium**

Mechanical properties of endothelial cells ; *Geert Schmidt-Schönbein*, University of California, San Diego

Mechanosensitive cation channels in rat aortic endothelium *in situ* ; *Stewart Sage*, University of Cambridge

The effect of shear on endothelial cell calcium ; *Fitzroy Curry*, University of California, Davis

Acute permeability changes due to pressure and shear ; *Charles Michel*, Imperial College, London

Shear stress induced expression of NO synthase and consequences on oxide production in the microcirculation ; *Ulrich Pohl*, Ludwig-Maximilians-Universitat, Munich

Effects of shear stress on signal transduction and gene expression in endothelial cells ; *Shu Chien*, University of California, San Diego

**Vascular consequences**

Altered permeability responses of porcine coronary microvessels: roles for flow and exercise ; *Virginia Huxley*, University of Missouri

Shear modulation of angiogenesis ; *Olga Hudlicka*, University of Birmingham

Localizing factors in atherosclerosis ; *Peter Weinberg*, University of Reading

Physical environmental factors modulating leukocyte interaction with the vessel wall ; *Gerard Nash*, University of Birmingham

The symposium will be held on Wednesday 12th April and will be preceded by the Spring Meeting of the British Microcirculation Society (11th April). There will also be a Designated session for the SIG during the Physiological Society meeting.

Later in the year the SIG will be meeting at King's (December 18 –20th, 2000), where Ron Jacob is organising a half-day symposium on 'Endothelial Cell Calcium Signalling'.

As my time as SIG co-ordinator is about to end I would like ask for nominations for my replacement. If you are interested in taking on the job, or know of someone who is, please contact me. There will be a short business meeting during the IC meeting to discuss this. I hope you will find time to attend.

*Geraldine Clough*
*University of Southampton*

## NEUROENDOCRINOLOGY

The last Neuroendocrine designated session was at the University College meeting of the Society on 19-22 April 1999. It was preceeded by a highly successful symposium on Neurosteroids, which was sponsored by this Group. The symposium was opened by Professor Baulieu speaking on "Neurosteroids: definition, bichemistry and some physio-pathological aspects". There were 10 further presentations, a number of which centred on the ovarian cycle and GABA A receptors. These topics were reflected in the areas covered by the communications and posters.

As already announced, the next designated session is at the Imperial College meeting on 12 – 14 April and is associated with the Pfizer round. Looking further ahead, there will be a half day symposium on sex differences in physiological function at the meeting in King's College on 18-20 December this year. This will centre on neuroendocrine and behavioural aspects and members of the Group are encouraged to submit abstracts on related subjects.

With the merger of UMDS and King's College, I have moved to the Guy's Campus where my address is:

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New Hunt's House
GKT School of Medicine
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May I take the opportunity of wishing everyone in the Group every success in the New Millennium.

*Mary L Forsling*
*GKT School of Medicine*

## SMOOTH MUSCLE

*Report on Symposium on "Regulation of Smooth Muscle Tone"*
*16th November 1999, Pucon Chile*
*Organised by Jeremy Ward & J. Pablo Huidobro-Toro*

Eight invited presenters spoke for 20-30 minutes on the last morning of the joint meeting. The organisers did a good job of keeping things moving along and to schedule, particularly by leading by examples with their own well timed presentations. Dr Huidobro-Toro started the symposium with a presentation on sympathetic co-transmission in human blood vessels. He admitted to being the same person as a Dr Toro-Huidobro, who presented an oral communication at the Muscle Physiology session, and to being surprised at the transposition in his name, since he had submitted the abstracts on discs! Following his presentation there was much discussion on why neuropeptide Y, which he had clearly shown to be acting as an integral sympathetic co-transmitter, should be co-released with ATP and noradrenaline, and why all three have post-synaptic actions and affect vascular tone. Not surprisingly the informed debate was inconclusive. Jeremy Ward then made a masterful PowerPoint presentation (it didn't crash, you could read his slides and it was tasteful) on hypoxic pulmonary vasoconstriction (HPV). In a controversial field he presented persuasive data that K+ channels inhibition and depolarization can't explain everything about HPV, and suggested than an increased Ca2+ sensitivity stimulated by an unidentified factor are important to the mechanism of HPV. Elisa Marusic then showed her data on the genomic and non-genomic effects of mineralocorticoids in vascular smooth muscle. Her presentation included data on Na+-K+-ATPase activity and the effects of adrenalectomy on its isoforms, as well as the effects of

aldosterone on vascular Na+-H+ exchanger. From her data she concluded with the interesting suggestion that there may be a common cytosolic receptor for both genomic and non-genomic actions of aldosterone. I then spoke about work from my group exploring SR and myosin light chain kinase importance to uterine contractions.

After the coffee break the genitourinary emphasis continued. The audience were taken through the trials and tribulations of trying to investigate putative mechanisms linking ischaemia to pre-term births. Around 25% of pre-term labours have evidence of ischaemia, as judged by the placenta. Having examined and discounted endothelium, platelet activity factor, and gap junctions, Dr Germain's laboratory is currently looking at free radical production in the deciduas. Professor Stefani presented fascinating data on control of calcium-activated K+ channels (KCa) in the myometrium. In particular he put forward evidence that regulation occurs at the transcription level and that proteins remaining in the Golgi and hence channel proteins do not reach the surface membrane and the number of KCa channels at the end of pregnancy is reduced. Functionally, this could lead to enhanced contraction, at the time when it is required. Dr Villaton's work on the oviduct was directed at examining its contractile activity – is it random or not? It appears that in the isthmus it is stochastic but, using impressive *in situ* video digital camera imaging, showed that the beating of cilia move the egg to the uterus, under the influence of oestradiol. Finally, but by no means least, the Committee Secretary treated us to the facts of life ... most of us will experience incontinence! Having gained our attention he then spoke about unstable bladders, where multiple contractions occur to a single stimulus and his evidence that ATP is the transmitter. In normal bladder an ecto ATPase destroys the released ATP, but this may be down-regulated in the unstable bladders.

Given that this was the last session of the conference and the morning after the dinner, I think the organisers could consider themselves well pleased with the size and enthusiasm of their audience and the all round impression that this had been a very worthwhile symposium.

*Susan Wray*
*University of Liverpool*

# THE 25TH CONGRESS OF THE TURKISH PHYSIOLOGICAL SOCIETY AND FOLLOWING THE EUPHRATES THROUGH EASTERN MESOPOTAMIA!

A significant and interesting event in physiology took place in the Ataturk Conference Centre at Firat [Euphrates] University in Elazig between the 6th and 10th of September 1999. In spite of the great tragedies inflicted on the Turkish people by the earthquake a few weeks previously the Turkish physiologists went ahead with their 25th Congress, showing the fortitude that is their hallmark. In fact this was the largest annual Congress in the history of the Society. This annual national Physiological Society meeting included contributions from invited participants from outside Turkey. The Congress attracted 250 oral, poster or workshop presentations delivered by participants representing most of the Physiology Departments within Turkey as well as from Azerbaijan, Brazil, England, Germany, Iran, Pakistan, Saudi Arabia, Scotland and the USA. Many of the invited international delegates had collaborations with members of the Turkish Physiological Society, and some had supervised Turkish Ph.D. students who had returned to Turkey to take up faculty positions in physiology or related subjects. It was very much apparent to the British physiologist visiting Turkey for the first time what outstanding intellectual achievements had been made by Turkish postgraduate students studying for higher degrees in the UK, tackling the complexities of research projects in addition to language and cultural variations.

The meeting was opened by the president of the Turkish Physiological Society, Professor Dr. Nimet Unay Gundogan. Her words of welcome were echoed by Professor Haluk Kelestimur, Professor Sirri Kilic (Dean of the Medical School at Firat University in Elazig), Professor Bekir Yildirim (Vice-Rector of Firat University) and the Province Governor, whose great support was appreciated by all the delegates. A well planned and full programme had been devised and the meeting varied in pace with a mixture of longer reviews and shorter presentations. There were special interest sessions in neuroscience, neuroendocrinology, reproductive physiology, gastro-intestinal physiology, neuro-physiology, metabolism, exercise and respiratory physiology, free radical research, haematology, cardio-vascular and renal physiology and molecular studies. These areas of physiology include traditional strengths within Turkish academia as well as areas of rapid research development. Presentations by Turkish and visiting physiologists covered a variety of aspects of these topics and excellent simultaneous translation overcame potential language barriers. The programme included a variety of stimulating

*Fig. 1. Turkish Physiological Congress posters in the sunshine on the shore of lake Hazar.*

workshops. Two particularly popular workshops covered practical aspects of HPLC and whole cell patch clamp recording and these were run by David Russell and Ahmet Ayar respectively. The weather was mostly fine and this was just as well because one of the afternoon poster sessions was held in the open air at a scenic spot by Lake Hazar (Fig. 1).

Reflecting the determination of Turkish physiologists to establish and sustain excellent facilities and research programs, two panels were set up to lead discussions. The first panel was on *publishing in biomedical sciences* and covered topics such as tips for submission of manuscripts to high profile journals, reviewing processes and difficulties in publishing from developing countries. The second panel was on *the future in physiological-biomedical sciences* and included subjects such as using laboratory animals in biomedical sciences, the importance of multidisciplinary studies, and biomedical sciences in Turkey. These panels involved six short presentations of less than 10 minutes made by both Turkish and visiting scientists and useful and constructive discussions followed the talks. Also evident were strong interests in curriculum development, and the consequences for the teaching of physiology of moving from medical school curricula based on 'passive' learning to 'active' learning.

The delegates at the Congress worked hard with a full programme of scientific presentations, and they also played hard with exceptionally generous social events and outstanding cultural visits. The amazing hospitality included visits to the ancient city and castle of Harput (with beautiful views over the city of Elazig), the Firat University Museum

*Fig. 2. Group of Turkish and foreign physiologists near the Keban Dam. From left to right: Haluk Kelestimur, David Russell, Tony Payne, Bayram Yilmaz, Ron Blaxendale, Stephan Steinlechner, Elaine Hull, Des Gilmore & John Russell.*

(that contained artifacts dating from prehistoric times, recovered from the banks of the Euphrates, to the present), exotic and unusual Turkish dinners, and a tour to the Keban Dam lake (Fig.2)! A visit to a fish farm evoked rapid and impressive exercise physiology from Tony Payne who narrowly escaped become fish food, as the boardwalk over the fish tanks lurched, creaked and cracked. There

*Fig. 3. Mount Nemrut bedecked with physiologists as the sun sets.*

were also opportunities to see traditional dancing such as the "candle in the river", as well as delegate participation in dancing to local folk music, an experience not too dissimilar to the pleasures of

ceilidhs at the Scottish meetings of our own society.

After the scientific meeting we left Elazig for an exceptional cultural trip of biblical proportions. Fortunately, we climbed most of the 2,200 metres of Mount Nemrut in white Ford Transit vans, and visited the peak at dusk and again at sunrise. Mount Nemrut lies at the edge of the Mesopotamian plain and at its summit is a pyramidal tumulus of loose stones 50 metres high and 150 metres in diameter at the base, constructed in the 1st century BC. King Antiochus Epiphanes I is believed to lie in a tomb beneath this structure but even more remarkable are the enormous stone figures, (some 10 metres high) of lions, eagles and gods situated on the eastern and western terraces. Unfortunately all the stone figures, which were originally seated on thrones (Fig. 3), have been decapitated by the ravages of time (Fig. 4). In spite of this, Mount Nemrut is a world class archaeological site.

*Fig. 4. Three members of the Elazig Organising Committee with the head of Zeus. From left to right Drs Bayram Yilmaz (Committee Secretary), Ahmet Ayar and Oguz Ozcelik.*

The closing ceremony included a prize giving, with awards being presented for a life time contribution to Turkish physiology, an outstanding young investigator, and prizes for posters (congratulations to the strong Glasgow contingent that picked up a joint first prize). All the delegates were grateful to Professor Haluk Kelestimur and his organizing committee for such warm hospitality and a pleasant and fruitful Congress of the Turkish Physiological Society. It was a great privilege for us to attend the Congress and make very good friends during such an interesting visit to Turkey. Next year the Turkish Physiological Society will be holding their Congress in Eskisehir.

*Ron Baxendale (Glasgow)*
*Colin Brown (Edinburgh)*
*Mary Forsling (Guy's, King's & St Thomas', London)*
*Des Gilmore (Glasgow)*
*Tony Payne (Glasgow)*
*David Russell (Glasgow)*
*John Russell (Edinburgh)*
*Rod Scott (Aberdeen)*
*Susan Ward (Glasgow)*
*Brian Whipp (St George's London) & Cathy Wilson (St. George's London).*












*Photography courtesy of Phil Harrison, David Marples, Melanie Rees and Jeremy Ward*

# YOUNG PHYSIOLOGIST SYMPOSIUM , NEWCASTLE 9-10 SEPTEMBER 1999

Between the 9 and 10 of September 1999 the population of Physiologists in Newcastle increased; the Young Physiologist Symposium had arrived !!

This was the first time the event was organised in Newcastle. Ten speakers were invited from all over the UK and together with five local contributors, a full schedule of talks was guaranteed.

*Some of the participants at the Young Physiologists Symposium*

The theme of this meeting; "Sensing, Signalling and Secreting" was an attempt to reflect the varied interests of our Physiology department.

After a buffet lunch, the symposium attendees congregated for the first talk session. Donald Ward from the University of Manchester told us about calcium homeostasis and extra-cellular calcium ($Ca^{2+}$) sensing receptors. Continuing with the theme, Mark Fowler, from the University of Leeds, described two distinct intracellular $Ca^{2+}$ stores in the frog's early distal tube. Local lad Omar Aziz told us of the role of intracellular $Ca^{2+}$ in type II Pneumocytes physiology. On a different subject, Vicki Strugala, also from our department, described the effects of dietary fibre on the colonic mucus layer.

After a tea break, Holly Bridge from

*A scientific discussion in the museum between Donald Ward and Liwei Wang.*

Oxford discussed the possibility that neurons in V1 might detect surface slant. Owen Thomas, also from Oxford, told us about the response of binocular neurons in V2 to relative and absolute disparities. This was followed by Niall McLoughlin from UCL, describing the relationship between orientation preference, ocular dominance and retinotopy in the visual cortex of the macaque. Closing this session John Curtis, from the Medical School in Edinburgh, described possible roles for 'prions' in the healthy brain.

At the end of this second session, participants readied themselves for the social high point of the meeting: a much commended buffet dinner was served in the Hancock Museum, which was hosting an exhibition of movie props. What will thirty Physiologists do among Aliens , Darth-Vader and Austin Powers? Well, have many animated scientific discussions!!

*Young physiologist Mark Fowler and an unidentified attendant at the meeting.*

Next morning's session started with Harriet Allen, from Nottingham, explaining how our visual system is capable of discriminating complex

patterns of movements followed by Jane Aspell, from Newcastle, discussing the interaction of visual and auditory information. Sally Thornton, also from Newcastle, explained how neural processing of dynamic and static auditory stimuli might occur in the primary auditory pathway. Jorge Armory, from UCL, told us of new methods being used to investigate how the brain learns to fear.

Following a lively lunch, we congregated for our last talk session. Liwei Wang, from Cardiff University, discussed the possible roles of pICln, a protein that might be involved in the regulation of swelling activated chloride currents which tied in nicely with Ian Millar's, University of Sheffield, cautionary tale of volume regulation in epithelial cells. The closing talk was given by Victoria Nixon, now at Newcastle, on work she did in Sheffield on capacitation and zona induction of hamster spermatozoa.

After the talks finished, and while the other attendees enjoyed afternoon tea, we had the difficult task of deciding which was the best talk. All speakers had spent time and effort in the preparation of their presentations and showed a good understanding of their subject matter and time management (only two speakers exceeded the 20 minute time limit). From the first talk onwards, an active and interested participation of the audience was reflected in the many questions asked, all of them well handled by the speakers. In the end we decided to award the prize, generously contributed by the Physiological Society, to Harriet Allen, for her talk entitled 'Discriminating complex patterns of visual movement'. This was in recognition not only of the quality of the research presented, but also of her good use of visual props that helped to make a difficult topic understandable to mixed audience

*Your friendly organisers Stefan Boese and Marina Bloj.*

Our announcement of the prize brought the symposium officially to a close but many discussions continued in the North Terrace (our local pub). Attendees at the symposium, which not only included the speakers and members from our own Physiology Department, but also from neighbouring Psychology and Neuroanatomy, emphasised how they had enjoyed the opportunity to listen to worthy talks in a relaxed environment that promoted questions and discussions. Everybody agreed that it had been a good opportunity to gain insight into areas of Physiology that did not directly relate to their own research, something that we can not always do in more specialised meetings.

We hope that this will become a bi-annual event, but for the time being we would just like thank the Physiological Society and the Department of Physiological Sciences at Newcastle University for their encouragement and financial support in organising this meeting.

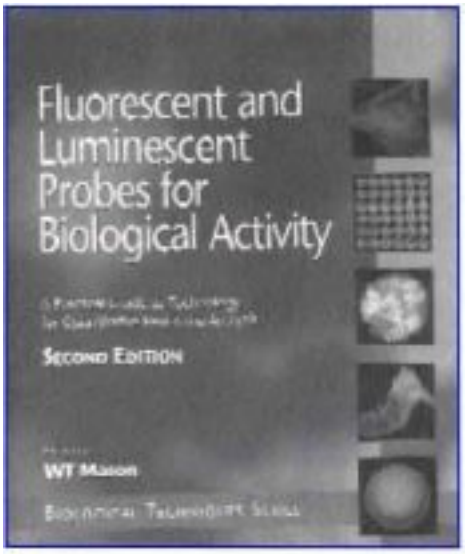
*Marina Bloj and Stefan Boese*
*University of Newcastle*

## COMPARATIVE PHYSIOLOGY

The 1000th meeting of the Society, and the last of the millennium, was an auspicious occasion to relaunch this SIG which was marked by a symposium on cardiorespiratory integration. Gerhard Heldmaier described the strategies used by our smaller cousins to overcome the rigours of winter, an appropriate topic given the temperature of the lecture theatres at the meeting. German ingenuity was evident in the elegant way in which he managed telemetric recordings from animals of just a few grammes to document the extreme bradycardia (down to just 4 bpm) and episodic ventilation associated with hibernation, and the dramatic tachycardia and hyperventilation during arousal. Tobias Wang had a shorter trip, across campus, to tell us about the mysteries of cardiac shunts in amphibians and reptiles. His thoughtful analysis of the functional consequences highlighted how the homeocentric view of life on this planet has led us to underestimate the utility of this supposedly inefficient method of cardiac output redistribution, showing that it is in fact tightly regulated according to metabolic demand. Stefan Nilson dug himself out of the impressive snow drifts blanketing Sweden at the time to lead us through the evolution of cardiovascular control in fishes ending with, appropriately, the novel modifications to the basic teleostean pattern found in the coldest active vertebrates, the fishes of Antarctica. The most arresting talk, it has to be said, was given by Craig Franklin who made the heroic trek from Oz to present the first data from what promises to be a classic program of evolutionary biology, examining the cardiovascular and respiratory physiology of related species living in close proximity but in quite distinct habitats. The image of the meeting for me was the sight of him waxing lyrically about a full colour, close-up view of a turtle's bottom! In case the thought 'he should get out more' crossed your mind I should point out that the subject was captured at the cost of tick and leech infestation, and the attention of a man-eating crocodile, from the Australian outback. I'm sure you'll agree, though, that the topic of rectal ventilation is a great conversation - stopper. The designated oral and poster sessions attracted a number of wide-ranging contributions including the effects of hypercapnia on toads and eels, bradykinin in lungfish, adrenaline in icefish, hypothermia in geese and, all the way from Italy, nitric oxide in anurans and fish.

Given the level of enthusiasm shown by the contributors, and those who were unable to make it this time, it was decided to make this an annual event. The next designated session of the Comparative SIG will therefore be held at the King's College, London meeting, 18-20th December 2000. I hope to see you there, and welcome suggestions for themes or speakers that would be appropriate for future meetings. The email list for the SIG needs updating, so if you want your name added or deleted (or know of someone who does) please let me know. I will send periodic mailings to keep the comparative physiology community informed of other relevant meetings, so please let me have any information that you think may be of general interest. Finally, may I wish you a happy and productive New Year.

*Stuart Egginton*
*Dept of Physiology*
*University of Birmingham*




Price: £ 49.95
ISBN: 0124478360

**Fluorescent and Luminescent Probes for Biological Activity *(2nd Edition)***:
A Practical Guide to Technology for Quantitative Real-Time Analysis, Ed. W. T. Mason, Academic Press, London, (1999).

This is the latest addition to this series of handbooks on the use of new methods in
biological research. The second edition provides an update on the previous version (published in 1991) by encompassing the advances made during the last decade in a whole range of topics involving the use of optical probes in biomedical experiments. The 46 chapters (including 19 new ones) represent substantial new material written by over 100 well recognised experts in the field. The material is well organised in 11 sections focused at specific areas of interest.

The contents range from a basic grounding in fluorescence techniques with a fairly extensive consideration of the theoretical and practical principles of fluorescence microscopy and also the potential pitfalls and problems likely to be encountered at the experimental level. This is followed by approximately 12 chapters of information on confocal microscopy, including multi-photon systems and Raman spectroscopy. A special consideration has been given to the technology behind the development and use of CCD cameras for digital imaging. The development and application of such technologies is described in relation to detection of specific proteins, DNA, and other molecules in gels as well as a comprehensive coverage of probes for ions, receptors, cellular organelles and processes such as gene expression.

The abundance of theoretical, technical and practical information contained in this handbook justifies the cost and makes it an excellent up to date guide for experimenters at all levels.

*Munir Hussain*
*University of Liverpool*

## Public Relations and Education Sub Committee

This Sub Committee has been formed from a division of the old Education and Information Sub Committee. It has responsibility for schools, media, public in general and web editing, and is chaired by Mike Gray.

The new Sub Committee has had quite a busy 12 months, including coordinating 5 sixth-form workshops (two day events where sixth formers visit a university and find out what physiology is all about and what it is like to study at university), 2 teachers workshops (where teachers come into a university to update their physiological knowledge and try out practicals that they can use in school), and representation at the Association for Science Education (ASE) meetings in Reading and Leeds.

More is planned for the year 2000. Prem Kumar is organising five sixth form workshops, Thelma Lovick is coordinating 3 teachers' workshops and update physiology courses for 'A' level students are in the pipeline. Louise Robson has been working on materials for young school children, and Jim McGarrick is planning to update The Society website on the educational side. The Sub Committee also plans to attend the British Association for the Advancement of Science meeting in September (London).

### *Can you help?*

In order for all these educational initiatives to be put in place and advertised successfully, we need a larger mailing list of schools. If you know biology teachers please could you email their name and school address to Maggie Leggett at: mleggett@physiology.demon.co.uk .
Your help is much appreciated.

*Maggie Leggett*

## Biochemical Society meetings which will take place in 2000

Contact for all meetings as follows:
Tel: +44 (0) 20 7580 3481,
Fax: +44 (0)20 7637 7626
http://www.biochemistry.org/meetings.htm
e-mail: meetings@biochemistry.org

**11-13 April 2000**
Structural Biology Meeting
Biochemical Society Conference, University of Leeds
Registration deadline 1 March 2000
Poster abstracts deadline 14 January 2000

**16-20 July 2000**
Beyond the Genome
18th International Congress of Biochemistry and Molecular Biology,
Understanding and exploiting molecules and cells in the third millennium,
International Convention Centre, Birmingham, UK.
Full details on
http://www.iubmb2000.org
email: info@iubmb2000.org

**13-15 July 2000**
Gene Action and Cellular Function in Parasitic Protozoa
Chancellor's Conference Centre, Manchester University
Registration deadline: 2 June 2000
Poster abstracts deadline: 14 April 2000

**21 July 2000**
Innate Immunity
GlaxoWellcome, Stevenage, Hertfordshire, UK.
Registration deadline: 9 June 2000
Poster abstracts deadline: 14 April 2000

**30 Jul - 2 Aug 2000**
Fatty Acid Desaturases: Form Function and Future
51st Harden Conference, Wye College, Kent, UK,
Registration deadline: 7 April 2000
Poster abstracts deadline: 2 June 2000

**18-22 Sept 2000**
Signalling in Plants
52nd Harden Conference, Wye College, Kent, UK
Registration deadline: 29 May 2000
Poster abstracts deadline: 21 July 2000

**18-21 Dec 2000**
Biochemical Society Conference
University of Sussex
Registration deadline: 1 November 2000
Poster abstracts deadline: 25 September 2000

## Peter J. Parker – New Chair of the Editorial Board for Biochemical Journal

The Biochemical Society is pleased to announce the appointment of Professor Peter J. Parker as the new Chairman of the Editorial Board of the *Biochemical Journal*. This appointment comes at a time of exciting online developments in the journal from complete electronic submission of papers to free access to the online archive.

Peter Parker (ICRF Laboratories, London, UK) is a past member of the *Biochemical Journal* Editorial Board and Editorial Committee, and has also served on the Editorial Board of *Journal of Biological Chemistry*. He is currently head of the ICRF phosphorylation laboratory and honorary Professor at UCL.

Professor Tony Turner (Chairman of Portland Press Board) said "We are sure that Peter Parker will continue to improve the quality, impact and accessibility of the *Biochemical Journal*."

"Peter Parker will command enormous respect, and he is just the man to lead the *Biochemical Journal* into the challenges of the next Millennium" said Professor Ken Siddle (outgoing Editorial Board Chairman).

The *Biochemical Journal* is published by Portland Press Ltd, the not-for-profit publishing subsidiary of The Biochemical Society.

**Information**

Further information about the *Biochemical Journal* contact:
Adam Marshall
Portland Press Ltd
59 Portland Place
London W1N 3AJ
Tel: +44 (0)20 7580 5530
Fax: +44 (0)20 7323 1136
http://www.portlandpress.com

**Journal web site:**

Biochemical Journal
www.BiochemJ.org
ISSN: 0264-6021
Volume 345-352 (24 issues)
£1110.00/US$1950.00

**Peter J. Parker**

Further information about Peter Parker can be found at the ICRF web site:

www.icnet.uk/research/prospectus/parkerp.html

## DEATHS

**The Society regrets to announce the deaths of Dr R A Burn-Murdoch (Member 1983) of St Thomas' and Professor W Jacobson (Member 1948) of Cambridge.**

**Obituaries will appear in the next issue of the *Magazine*.**

## APOLOGIES

"Regarding Anthony Clare's BBC interview with Jonathan Miller mentioned in the last magazine, Peter Stanfield has pointed out that the Adrian whom Miller was referring to was in fact E.D Adrian (then already Lord Adrian), not Richard, who subsequently inherited the title. Our correspondent admits that he was not aware there was more than one Adrian, hence the error. Apologies!"

## WHERE ARE THEY NOW ?

William Sharpey FRS has been accorded the soubriquet of "father of modern physiology in England", an achievement which was recognised by the founders of the Society when they elected him an Honorary Member at the third meeting on the 5th May 1876.

His friends and colleagues at University College London and elsewhere subscribed for a portrait bust to be made by William Hamo Thornycroft (1850-1925), the first commission for a young sculptor who went on to have a distinguished career, creating, among many others, statues of W.E.Gladstone, General Gordon and Oliver Cromwell.

The bust of Sharpey, in Sicilian marble, was completed in 1872 and exhibited at the Royal Academy before being presented to University College. The sculptor also made a reduced size model for plaster casts of which 112 were produced. It is likely that the plaster bust at University College Hospital is one of these but where are the others ? They might be in offices, libraries or broom cupboards around the world, perhaps unrecognised. I should very much like to hear from anybody who has located one.

Alan Sykes
Walthwaite How, Chapel Stile, Ambleside, Cumbria LA22 9JG, Tel.(01539)4 37241
alansykes@walthwaite.freeserve.co.uk

## THE LIFE SCIENCES DIRECTORY

Whilst browsing the home pages of several UK-based life sciences oriented learned societies I noticed that they had combined to produce the "Life Sciences Directory". To do this they appeared to have actually co-operated !
This publication lists the names and addresses of the members of the participating societies. It is also produced in hard copy and will be distributed to the members of the collaborating societies. It is a very practical aid to scientific communication and its appearance has to be welcomed.

It was with real disappointment that I discovered that the membership of the Physiological Society had been omitted.

I would like to enquire if the Physiological Society was invited to participate ? If so, what were the arguments that convinced the Committee not to participate ? Will the Committee be prepared to reconsider its decision when the members have been able to inspect the product ? I am certain that information on the membership of the Physiological Society would enhance the value of the Directory to Life Scientists of all persuasions.

If any member of the Physiological Society has reservations about the practical use of such a volume, I recommend that they speak to one of the thousand, or so, UK based members of societies affiliated to FASEB. The FASEB Directory of members must be one of the most useful publications they have on their bookshelves.

Brian Beechey
University of Liverpool

[Editor's note: Brian is right to raise the issue of combined membership lists. Yes, the Society was invited to take part in the combined Life Sciences Directory, but practical difficulties prevented us from taking part in the first issue. For the future: what do our members think about combined listings like these ? How would they feel about having their names and addresses published on a publicly accessible website ? Write or email and let me know what you think.]

*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 Summer 2000 edition (to be distributed on 14 April 2000) should reach the* ***Administration Office by 7 January.***

## XXXIV INTERNATIONAL CONGRESS OF PHYSIOLOGICAL SCIENCES

From Molecule to Malady
Christchurch, New Zealand, 26-31 August, 2001
For further information please visit out website:
**http://www.iups2001.org.nz*****

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## INTERNATIONAL SOCIETY FOR AUTONOMIC NEUROSCIENCE
## Millennium Congress, London, UK. 17-21 July 2000

**Major Topics:**
Development of the Autonomic Nervous System, Neuroimmunology
Recovery of Autonomic Nervous System Function After Spinal Injury
Sensations and Afferents
Developing Concepts in Ganglionic Integration, Techniques for Studying the Autonomic Nervous System
Novel Aspects of Neurotransmitters and Modulators, Purines and the Autonomic Nervous System: From Controversy to Clinic.
**Workshops / Debate / Satellites**
**Free posters / Oral presentations**

**Information:**
2nd ISAN Congress Secretariat
Congress House
65 West Drive
Cheam, Sutton, Surrey
SM2 7NB, UK.
***
Tel: +44 (0)208 661 0877
Fax: +44 (0)208 661 9036
E-mail: info@conforg.com
http://www.physiol.ucl.ac.uk/isan2000/

## TRANSPORTERS 2000 MEETING - COSTA BRAVA, SPAIN

At the end of the Summer 2000, September 10-15, you are cordially invited to attend the Transporters 2000 Meeting, which will be held on the Costa Brava (near Barcelona, Spain). Transporters 2000 is an international meeting covering Molecular Biology, Biochemistry, Cell Biology, Physiology and Physiopathology of membrane transporters. This meeting represents the first in a series to be held in Europe every second year. This proposal came after the series of meetings with the same thematic coverage initiated in the FASEB Summer Research Conference of 1997, and continued for 1999 and so on. The idea is to merge both series of meetings to organise one of them every year: once in North America, once in Europe.

**Topics**
Structure-function of transporters
Transporter trafficking, Regulation of transport function, Drug transporters
Nucleoside transporters, Cationic amino acid transporters, Glutamate transporters
Amines and GABA transporters
Peptide transporters

**Scientific Committee**

| | |
|---|---|
| Steve Baldwin | (University of Leeds) |
| Richard Boyd | (University of Oxford) |
| Hannelore Daniel | (University of Giessen) |
| Gian Gazzola | (Universita di Parma) |
| Cecilio Gimenez | (CBM-UAM) |
| Baruch Kanner | (Hebrew University) |
| Michael Kavanaugh | (OHSU) |
| Carol McLeod | (UCSD) |
| Heini Murer | (University of Zurich) |

**Local Organising Committee**
(Universitat de Barcelona)
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Antonio Felipe Javier Casado
Anna Guma Marta Camps
Perla Kaliman Joan Betran
Manuel Palacin: Co-organiser
Marcal Pastor-Anglada: Co-organiser

**Further information on the scientific programme, details for registration and poster presentations will be updated at the web page:**
http://www.nutrition.tum.de/insci/phys/transporters2000.htm

**Scientific Secretariat**
Transporters 2000
Departament de Bioquimica I Biologia Molecular, Facultat de Biologia
Universitat de Barcelona
Avda Diagonal 645
Barcelona 08028. SPAIN
Tel: (0034) 93 402 15 43
Fax: (0034) 93 402 15 59
Email: t2000@sun.bq.ub.es
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## FORUM OF EUROPEAN NEUROSCIENCE (FENS 2000) Brighton, 24-28 June 2000

The next forum meeting is being held in Brighton UK, hosted by the British Neuroscience Association on behalf of FENS. There will be nine plenary lectures, over 50 symposia representing all aspects of neuroscience in four broad themes

- molecular and cellular neuroscience
- behaviour and cognition
- systems neuroscience
- clinical neuroscience

There will also be broadly-themed poster sessions, satellite symposia and technical workshops as well as a large trade exhibition. All abstracts will be refereed and published in *European Journal of Neuroscience.*

The Physiological Society is represented on the National Committee for this meeting and it is likely that we will be sponsoring a number of symposia. We hope that many members will attend this meeting which is an ideal opportunity to highlight your research to a Europe-wide neuroscience audience.

**About Brighton - a city by the sea**
Brighton is a vibrant and cosmopolitan seaside resort with many restaurants, pubs and leisure facilities, as well as Regency architecture and a Royal Palace! Brighton has excellent transport links being 50 minutes by train from London. It has train and road links to Gatwick Airport (40 minutes) and is close to many channel ports. It is an excellent place to hold a summer scientific meeting especially as both FENS 2000 venues are on the seafront!

**Registration**
There will be reduced registration for Physiological Society members. Student registration is especially subsidised.

**More information**
registration, accommodation, social programme and general information contact Intermarket (Tel 01273 325315 Fax: 01273 323882 Email; Intermkt@pavilion.co.uk)
scientific programme, trade exhibition and sponsorship opportunities contact British Neuroscience Association (Tel 0151 794 5449 /Fax 0151 794 5517 Email bna@liv.ac.uk).
*Conf. Website - http//www.fens2000.org*

Over 4,000 people attended the last Forum of European Neuroscience (Berlin 1998) so please come along and enjoy the largest gathering of neuroscientists ever in the UK!

**The Scientific Programme**
***Invited Plenary Lecturers:***
HENRY MARKRAM Rehovot, Israel
STEVEN REPPERT Boston,USA
NANCY ROTHWELL Manchester, UK
SETH GRANT Edinburgh, UK
MARC TESSIER-LAVIGNE San Francisco, USA
FLORIAN HOLSBOER Munchen, Germany
ROGER TSIEN San Diego, USA
MARC JEANNEROD Lyon, France
REINHARD JAHN Gottingen, Germany

***Symposia:***
*Cellular and Molecular Neuroscience*
*Systems Neuroscience*
*Behaviour and Cognition*
*Clinical Neuroscience*

***Workshops will include:***
Targeting gene expression in the CNS using novel vectors
Gene and cell-based therapies for neurological disorders
Cell cycle-related mechanisms and neurodegeneration
Use of transgenic and KO mice in understanding affective disorders
Teaching neuroscience
New insights into function and plasticity from optical studies
Stereology for neuroscientists
Drosophila: Neural cell fate selection and neuron-glia switch
***

**5th INTERNATIONAL MUSCLE SYMPOSIUM**
**May 19-21, 2000, VIENNA, AUSTRIA**

Local Organising Committee
Manfred Frey, MD, Chairman
Pietro Giovanoli, MD, Secretary

**Scientific Committee**
Bruce Carlson, MD, PhD, (USA)
Ann Arbor (USA) John Faulkner, PhD,
Gerhard Freilinger, MD, Vienna (Austria)
Manfred Frey, MD, Vienna (Austria)
Helmut Gruber, MD, Vienna (Austria)
Ralph Manktelow, MD, Toronto (Canada)
Viktor E Meyer, MD, Zurich (Switzerland)

**Congress Venue**
Allgemeines Krankenhaus Wien
Horsaalzentrum Ebene 7, Horsaal 3
Wahringer Gurtel 18-20, A-1090 Vienna
Tel: (only during the Symposium)
+43 1 40400 1191

**Congress Secretariat**
Pietro Giovanoli, MD
Division of Plastic & Reconstructive Surgery, Department of Surgery
University of Vienna, Medical School
Wahringer Gurtel 18-20 A-1090 Vienna
Tel: +43 1 40400 6986
Fax: +43 1 40400 6988
Email: pietro.giovanoli@akh-wien.ac.at

**Scientific Program – Topics**
Basic and experimental research on muscle transplantation
Factors with influence on nerve and/or muscle regeneration, Muscle transposition or muscle transplantation ?
Morphology and choice of muscle transplants, Neurotization of the muscle
Neuromuscular reconstructions in the face, Functional muscle transplantation in extremities, Reconstruction of sphincter muscle function
Functional electrostimulation of muscles
Documentation of muscular function and evaluation of functional results
New indications for functional muscle transplantation , Free papers

**For further information log onto and click on the 5th International Muscle Symposium 2000 and follow the instructions provided.**
**www.akh-wien.ac.at/plastburg** ***

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**J Physiol ; 1950 - 1999 inclusive is available as a gift.**
**If interested please contact:-**
**edward.vaughanwilliams@hertford.ox.ac.uk**
**

**********

**NEUROLOGY FOR NEUROSCIENTISTS VI, Magdalen College, Oxford, U.K.**
**March 27-28th 2000**

A 2 day conference for neuroscientists on the basic science questions that clinical neurologists face and how neurological diseases can illuminate neural function.

This year's themes will include the basal ganglia, pain and epilepsy.

Subsidised by the Guarantors of Brain, the registration fee of £25 will cover all accommodation and symposium expenses.

For further info. send short cv (in event of oversubscription) to:
Prof. J B Clark.
Neurochemistry, National Hospital, Queen Sq. LONDON, WC1N 3BG.
Tel. 0207 837 3611 X 4201
email: nneurosc @ion.ucl.ac.uk
http://www.ion.ucl.ac.uk/neurochemistry/n4n.html).**

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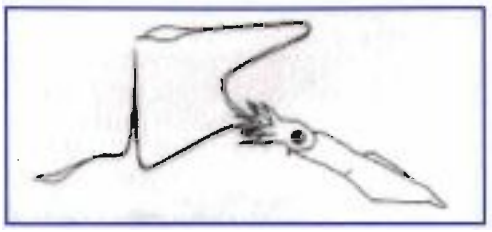
# MICROELECTRODE TECHNIQUES FOR CELL PHYSIOLOGY

**17th Workshop 6-20 September 2000**

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



## Information for applicants

* The workshop provides intensive practical experience of a number of microelectrode, patch clamp and optical techniques applied to single cells. It is intended for postgraduate students, post doctoral workers or established scientists wishing to apply these techniques in their research.

* The following basic techniques are offered: Two electrode voltage clamp, Patch clamp,Single electrode voltage-clamp, Dye injection, Ion-sensitive microelectrodes, Fluorescent indicators.

* There are 16 places. Participants work in pairs and have the opportunity to do three 3-day experiments in the two weeks. In addition, lectures and practical sessions on electronics, data acquisition and computer analysis, and microscopy will be given. Daily lectures given by teachers and visiting lecturers cover the basic techniques taught and certain spacialised topics. A copy of the Plymouth Microelectrode Handbook will be provided.

* Accommodation (for 14 nights - arrive & depart on Wednesday) is close to the laboratory and includes breakfast. Lunch is provided in the lab each day and an allowance is given for an evening meal.

* The course fee of £1100 includes accommodation, meals and tuition. Participants are responsible for their own travel arrangements.

**THE CLOSING DATE FOR APPLICATIONS IS 30 APRIL 2000 ;** A meeting to assess applications will occur during May and all applicants will be notified of the outcome.

## How to apply:

There is no application form.

1. Please give a concise description of your research, your reasons for wishing to attend and your experience of techniques taught on the workshop. List in order of priority four techniques you would like to learn.
2. Provide a brief CV (2 sides maximum) and list of publications.
3. The application must be accompanied by a letter of recommendation from an academic referee, preferably PhD supervisor or Head of Laboratory. This letter should indicate how your career, the laboratory in which you work and the area of research that you intend to pursue will benefit from your participation in the workshop.
4. What is your likely source of funding ?

## Funding

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

**Dale and Rushton Funds of the Physiological Society** - help with funding (up to £500) is usually available for young physiologists working in the UK. If you wish to apply please indicate in your application to the workshop. There is no need to apply directly to the Dale and Rushton funds before workshop applications are assessed.

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

## Applications should be sent to:-

David Ogden, Microelectrode Techniques, NIMR, The Ridgeway, London NW7 1AA, U.K.
email: **dogden@nimr.mrc.ac.uk**
Information on internet:
**www.nimr.mrc.ac.uk/events/microelectrode.htm**

**The Physiological Society**

# MOLECULAR TECHNIQUES WORKSHOP

## September 2000

## First, provisional notice

A 2 week workshop for the training of physiologists in molecular biological techniques is to be run at the Institute of Biomedical and Life Sciences at the University of Glasgow from 4th September – 15th September 2000. The workshop, which is organised under the auspices of the Physiological Society and the Wellcome Trust, will be based on practical experimental procedures (including the handling of DNA and RNA, sub-cloning, restriction enzyme digests, the use of antisense technology, RT-PCR, and site-directed mutagenesis) and will be appropriate for physiologists who are reading for a PhD or are at the post-doctoral level with little or no prior experience of molecular techniques. The number of students on the course will be limited to 16. Students should intend to follow a career in the physiological sciences.

Applications for a place on the course will be treated competitively and should include the following information:

* A hard (paper) copy of your curriculum vitae including your name, address, daytime telephone number, age, nationality and educational background (particularly any experience of molecular biological techniques).
* The nature of your current work (PhD/post-doctoral project).
* A brief account (fewer than 500 words) of how attendance at the workshop would benefit your current project and your subsequent career
* A letter of recommendation from a Society member to whom you are known.

Preliminary enquiries should be made to the Committee Secretary's Office at The Physiological Society, PO. Box 11319, LONDON WC1E 7JF
Email:
sgreaves@physiology.demon.co.uk
The closing date is 19 May 2000.

Further details concerning the course itself and possibilities for assistance towards subsistence will be sent to successful candidates. A charge of £250 will be made to cover the cost of accommodation, although a limited number of bursaries will be made available.

# Studies in Physiology

Physiological Society 25% members' discount

Portland Press

**The Studies in Physiology series (published on behalf of the Physiological Society) provides concise introductions to developments in complex areas of physiology for a wide audience.**

## Physiological Determinants of Exercise Tolerance in Humans

NEW

*Edited by* BJ Whipp, St George's Hospital Medical School and AJ Sargeant, Manchester Metropolitan University, UK

1 85578 026 7 Paperback October 1999 192 pages £22.00 Members' price £16.50

This book is designed to confront the challenges of identifying the causes of exercise intolerance, i.e. what causes an individual to be unable to sustain a particular work rate sufficiently long enough for the successful completion of the task.

The strength of this book lies in its integrative approach. That is, there is a logical progression from considerations of individual organ system responses to their interaction in constraining or limiting exercise tolerance, and how this may be influenced by physical training.

In this context, the book considers the following issues: skeletal muscle mechanics; the control of intramuscular energetics and tissue gas exchange; circulatory and cardiovascular system function and pulmonary limitations.

## Cardiovascular Regulation

*Edited by* D Jordan, Royal Free Hospital Medical School, and JM Marshall, University of Birmingham Medical School, UK

1 85578 024 0 Paperback 1995 170 pages £22.00 Members' price £16.50

*Cardiovascular Regulation* provides an up-to-date account of our current understanding of the control of the cardiovascular system which is not covered by existing student textbooks. Both students and lecturers of cardiovascular and exercise physiology, and medicine, dentistry and biomedical science will find this book informative and easy to read. Each chapter has numerous summary boxes and also 'Essential Reading' suggestions for additional reading for undergraduates and 'Further Reading' suggestions to cover the subject to postgraduate level.

## Neural Control of Skilled Human Movements

*Edited by* FWJ Cody, University of Manchester, UK

1 85578 081 X Paperback 1995 120 pages £22.00 Members' price £16.50

This textbook focuses on skilled movements in man, while drawing upon vital evidence obtained in other species. Attention is mainly directed at movements of the hand and arm, which have been studied most fully. The production of speech sounds is considered as another important example of skilled movement. Concise up-dates of current understanding of the roles of the main motor centres — cerebral cortex, basal ganglia, cerebellum and spinal cord — in skilled movement and its clinical impairments, are provided by a group of neuroscientists renowned for their research expertise and enthusiasm for teaching.

*Neural Control of Skilled Human Movement* is informative and easy to read. It will be of particular interest to science (neuroscience and physiology) undergraduates with a basic grounding in neurobiology and their teachers. In addition, the book contains much valuable source material for students of medicine, psychology, dentistry, physiotherapy, speech therapy and related health sciences.

## The Pathophysiology of the Gut and Airways
### An Introduction

*Edited by* PLR Andrews and JG Widdicombe, St. George's Hospital Medical School, London, UK

1 85578 022 4 Paperback 1993 150 pages £22.00 Members' price £16.50

This book examines the pathophysiological basis of a number of relatively common clinical problems of the gut and airways. These two systems share many similar physiological features which are reflected in the pathophysiological basis of the diseases and disorders reviewed.

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†Please add US$5.95 for first book, US$0.35 for each additional book

BTL/1099/A

# THE JOURNAL OF PHYSIOLOGY

## SYMPOSIUM

# Mitochondria in cell life and cell death

**Tuesday, 18th April 2000**
**San Diego, CA, USA**

### Keynote Lecture

**Douglas R. Green**
(San Diego)
- *Role of mitochondria in apoptotic cell death*

### Speakers include:

**Daniel Ricquier**
(Meudon)
- *Uncoupling proteins - from mitochondria to the physiology of energy balance?*

**Salvador Moncada**
(London)
- *Mitochondria and nitric oxide in health and disease*

**Brian O'Rourke**
(Baltimore)
- *Pathophysiological and protective roles of ion channels in the inner mitochondrial membrane*

**Claes Wollheim**
(Geneva)
- *Role of mitochondrial signal generation in glucose-stimulated insulin secretion*

**Rosario Rizzuto**
(Ferrara)
- *Mitochondrial calcium uptake and cell signaling*

**Michael R. Duchen**
(London)
- *Mitochondrial calcium uptake - from calcium signaling to cell death*

**Gyorgy Hajnoczky**
(Philadelphia)
- *Mitochondria, calcium signaling and cell death*

**Martin Crompton**
(London)
- *The mitochondrial permeability transition pore*

**Pierluigi Nicotera**
(Konstanz)
- *Mitochondria and neurodegeneration*

### Future symposia

**Spinal cord function and rehabilitation**
**Saturday 4 November 2000**
Society for Neuroscience 30th Annual Meeting,
New Orleans, LA, USA

**Epithelial fluid transport**
**August 2001**
IUPS, Christchurch, New Zealand

Registration is via the ***Experimental Biology 2000*** site at
http://www.faseb.org/meetings/eb2000/index.html *or* for further information go to
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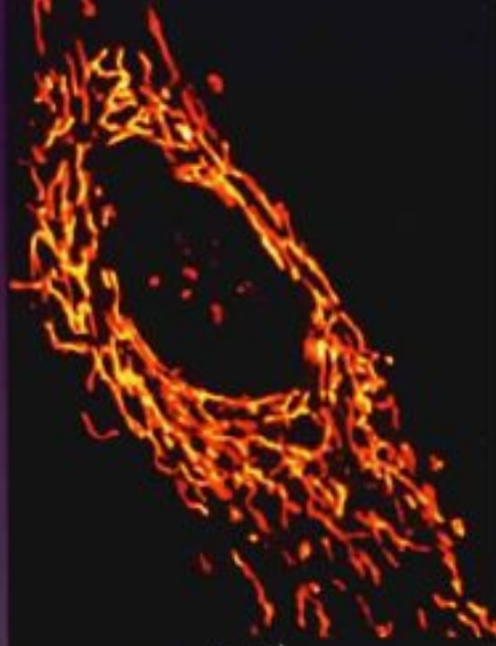
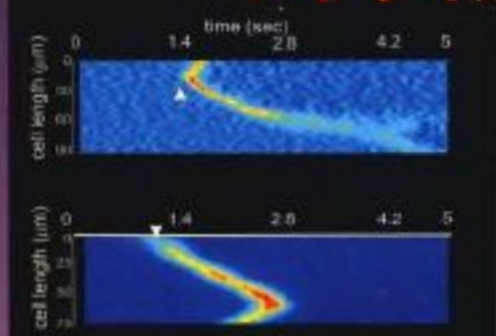
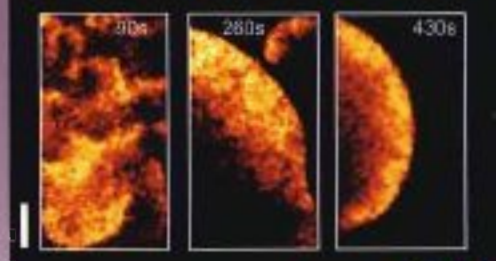
Email: JPSymposium@physoc.org

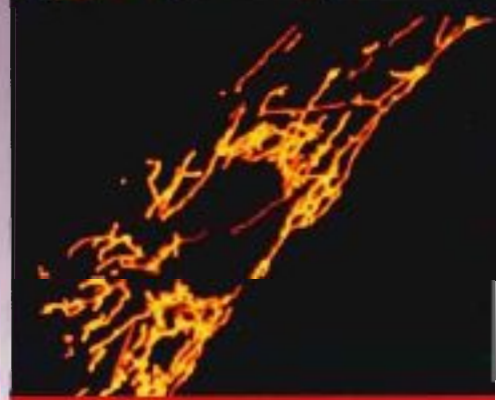










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