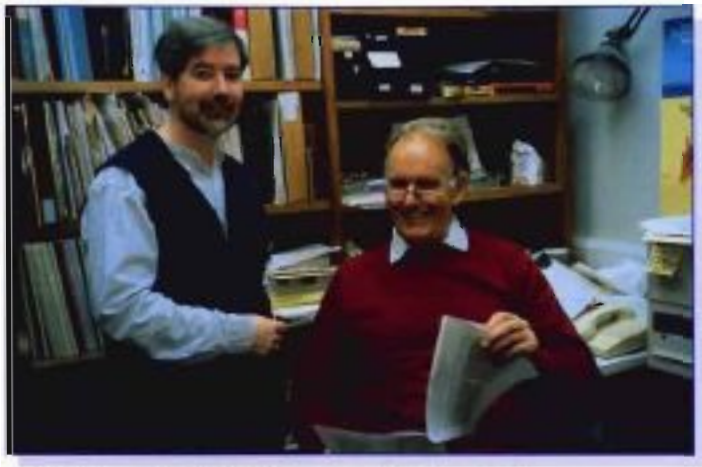
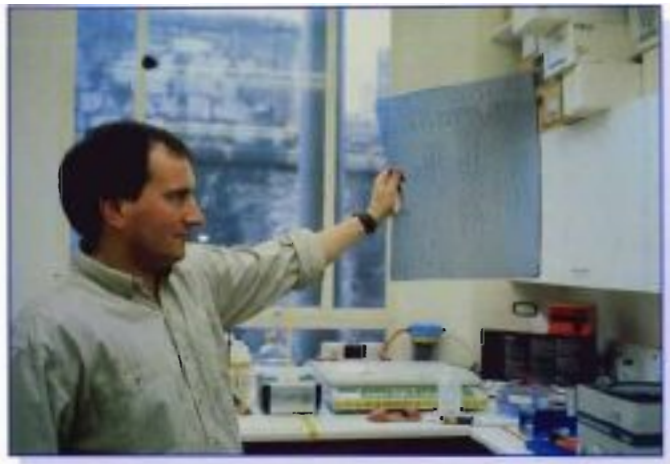
The Physiological Society Magazine

Summer 1997
No 27



(L-R) Professor Roddy Williamson and Dr Quentin Bone



Dr Richard Kirby (with gel of gaba-receptor sequence)

Pecten maximus

Dr Brian Milligan (in aquarium)

(L-R) Sir John Gray, Sir Eric Denton and Dr JV (Vic) Howarth

Photography by Martin Rosenberg and center picture by Professor Roddy Williamson

Front cover: Eledone cirrhosa, Courtesy of Professor Roddy Williamson.

Contents

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Action Points

- Affiliate Travel Grant Scheme: The next two deadlines for receipt of applications are 31 May and 31 July 1997.
- Annual General Meeting Agenda: Any Member wishing to raise items for discussion at the AGM (which will take place on 3 September at Bristol) is asked to send details to the Committee Secretary by 1 May 1997.
- Bristol Meeting: Abstracts should be submitted to the Meetings Secretary between 19 May and 30 May 1997.
- Committee Nominations: Nominations for membership of the Society's Committee may be made by five Members, with the agreement in writing of the nominee, and should be sent to the Committee Secretary by 1 June 1998.
- Email Addresses: The Society is making increasing use of email addresses. Please can Members inform the Administration Office of new email addresses, or changes to existing ones. Changes can be emailed to admin@physoc.org
- Experimental Physiology: Rapid Communications for the July 1997 issue of Experimental Physiology should reach the Distributing Editor's Office in Newcastle by 5 May 1997. Rapid Communications for the September 1997 issue should reach the DE's Office by 4 July.
- IUPS Congress, St Petersburg: The deadline for full hotel and dormitory payments to be received by the Congress Secretariat in Helsinki is 30 April 1997. There will be no refunds for any payments after this date.
- Magazine: Letters and articles for inclusion in the next issue should reach the Editor by 26 May 1997. Advertisements and Notices should reach the Administration Office by 9 June 1997 whilst items for Committee News should reach the Committee Secretary's Office by 9 June and items for the Special Interest Group Forum should reach the Meetings Secretary's Office by 9 June.
- Membership Proposals: Candidates for election as new Members at the 1997 Annual General Meeting should ensure that their proposal papers reach the Administration Office by 20 June 1997.
- Suspension of grants: Please note that as from 1 January 1997, until further notice, the following grants will no longer be available - Eastern European and Third World Visitor Fund, MSc Bursaries, New Lecturers Support Scheme, Postgraduate Support Fund.
- UMDS (St Thomas') Meeting: Abstracts should be submitted to the Meetings Secretary between 28 July and 7 August 1997.

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GUIDELINES FOR CONTRIBUTORS

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

Format of articles

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

Length of articles

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

Submission of articles

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

Deadlines for submission

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

Illustrations

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

Author photographs

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

References

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

Suggestions for articles

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

Magazine Editorial Group

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

PHYSIOLOGY IN PLYMOUTH - THE PAST AND THE PRESENT

THE PAST

The 'Cavernous Laboratory' welcomes visitors

The Marine Biological Association (MBA) was founded in 1884 at a meeting chaired by Thomas Henry Huxely (Royal Society President and soon to be the Association's first President) and attended by many of the original members of the newly formed Physiological Society. Presumably through the influence of the latter, the Association's mission was not only a broad study of the emerging field of Marine Biology but in particular, the study of the physiology of marine animals'. By 1888 the Laboratory had been built on Plymouth Hoe and the staff of two were already welcoming the first of a long stream of visiting researchers.

Even in those early days it was recognized that one of the main aims of the Laboratory would be to provide facilities for visitors, whatever their interest in the sea or its organisms; indeed, the 'cavernous laboratory', as the first floor accommodation was often called, could sometimes be so full with visitors, such as CA MacMunn, GP Bidder, and ET Brown, that the permanent staff were relegated to the basement. In 1896 the laboratory acquired its first boat, the 60ft long Busy Bee, and in the same year W Garstang began running teaching courses, the forerunner of the famous Plymouth Easter Classes, then attended by J Barcroft (later Sir Joseph Barcroft) and HH Dale (later Sir Henry Dale), and which continue today in the form of the Cell Physiology Workshop organized by D Ogden and C Brownlee.

Electric power introduced

A new building and a Department of General Physiology were added to the Laboratory in 1919 and, on the advice of the noted physiologists AV Hill and WM Bayliss, electric power was included in the specification to supplement the existing gas lighting. CFA Pantin was soon appointed as staff physiologist, and Hill, Bayliss and LT Hogben became regular visitors. When Pantin moved to Cambridge in 1929, he was replaced by CM Yonge, who was in turn succeeded by LE Bayliss when he took up the chair of Physiology in Bristol.

The first neurophysiological research

It was Otto Lowenstein however, working with the staff physiologist Alec Sand, who initiated the first neurophysiological work in Plymouth, an area of research that was soon to take on international significance. For, about this time JZ Young, another Plymouth visitor, re-discovered the squid giant axon, and this beautiful preparation was soon exploited by AL Hodgkin and AF Huxley in their Nobel Prize winning work on the mechanism of nervous transmission. The giant axon quickly became a mini industry in Plymouth, and Hodgkin and Huxley were followed by a regular clutch of winter visitors, such as PF Baker, WK Chandler, R Fettiplace, DA Haydon, D Hill, RD Keynes, and R Miledi, as well as occupying staff physiologists such as H Meves, TI Shaw, and JI Gillespie.

Of course Physiological research was not confined to the squid giant axon, for staff and visitors worked on numerous areas and preparations: for example, the nerve heat work of JV Howarth, the control of buoyancy by EJ Denton, work on the synapse by B Katz and AC Crawford, radioactive tracing

The Marine Biological Association on Citadel Hill

The library at the MBA

experiments by GM Spooner, vision by JAC Nicol, hearing by JAB Gray, muscle energy metabolism by P Caldwell, the neural control of movement by BL Roberts, to name just a very few, and none from the 12 other Nobel Prize winners who have worked in Plymouth!

THE PRESENT

Today, physiology continues to be a major component of the MBA's research programme, although other areas such as marine ecology and molecular biology are also well represented. Work using squid and octopus, as favourable model systems, continues apace, with Quentin Bone's interest in their muscles, Roddy Williamson's work on their vestibular and visual systems, and Euan Brown's work on the interactions between neurons and glia. Other areas include Eric Denton's work on fish communication systems, Tony Clare's work on the sensory cues used in settlement by marine organisms, and Colin Brownlee's study of fertilization and development using seaweed.

A healthy visitors programme continues

As before however, the MBA exists not only to carry out its own research programme, but to provide a base for anyone wishing to work on the sea or its organisms. Happily, despite these troubled times, a healthy visitors programme continues with current research on muscle physiology (R Woledge and NA Curtin), the blood brain barrier (NA Abbott), respiration (EW Taylor), vision (H Saibil, J Partridge and JB Messenger), ion channels (I Inoue), and the visceral nervous system (PLR Andrews), to name just a few (apologies to those not mentioned due to lack of space).

However, Physiology is no longer confined only to the MBA in Plymouth. The Plymouth Marine Laboratory (a NERC Research Institute) has long been interested in the physiology and bio-energetics of marine vertebrates and invertebrates, particularly in relation to their responses to environmental stress (BL Bayne, J Widdows & AJS Hawkins), and the University of Plymouth has a strong group, led by M Depledge, that uses physiological (and molecular) techniques to study how heavy metal and organic pollutants exert their actions. In addition, the University, in conjunction with Plymouth's Derriford Hospital, has recently (1991) formed the Postgraduate Medical School where TJ Wilkin heads a rapidly expanding department with research interests in diabetes, pancreatitis, osteoporosis, and pharmacokinetics. Plymouth has made some important contributions to Physiology in the past and it is clear from the growth in, and enthusiasm for, Physiology at present, that it is likely to feature in the Society's publications for many years to come.

The Meeting

It is some years since a Meeting of the Society was held in Plymouth, mainly because the MBA does not have the facilities for a large meeting. Although the University of Plymouth would have been pleased to host this meeting, it will take place in term time when accommodation and theatres are in use by the students. The May meeting therefore will break new ground for the Society in that it will be held in the local conference centre. The Pavilions Centre also contains a leisure pool and skating rink so members will have the opportunity for some light exercise during breaks! The Research Symposium on Neuromodulation and the Special Interest Group sessions are attracting some excellent contributions and, in keeping with the tradition of Plymouth Physiology, will have a strong, but certainly not exclusive, invertebrate flavour. A Meeting Reception will be held in the MBA Laboratory, so those wishingto see where famous physiologists have been squirted with squid ink or slipped into the shark tank, will have every opportunity. Whatever your interest in Physiology, I hope you will be able come to Plymouth, for no doubt there is an ideal marine preparation just waiting to help you with that very tricky problem you are working on!

Roddy Williamson University of Plymouth & Marine Laboratory

THE FUTURE OF THE MARINE BIOLOGICAL ASSOCIATION

The Marine Biological Association has proved to be a remarkably robust and versatile organisation over the past one hundred years or so, weathering many changes in fortune, shifts in funding sources and alterations in research priorities. In this it has been aided by its structure which is an extraordinary and uniquely British marriage of a research organisation with a learned society (currently 1500 members) set in the legal context of an incorporated academic charity.

Since its foundation, the MBA has concentrated on promoting the highest quality research into fundamental problems in marine biology. This has inevitably resulted in a strong accent on the physiology of marine organisms - more specifically on the way in which organisms sense and respond to their environment. The current physiological research programme focuses on inter- and intra-cellular signalling in animals and plants, using marine preparations, and on the information that is passed between individuals by chemical, optical or pressure signals. Marine animals and plants are especially attractive for this kind of research because of the diversity of their designs and life styles, and because it is feasible to trace evolutionary development.

Visitors programme still flourishing

The Citadel Hill has the best location of any laboratory in the UK for sampling the diversity of marine life. By combining this natural advantage with a welcoming atmosphere, a stimulating research environment and a diverse range of expertise, the MBA has historically attracted a large number of visiting workers and collaborators. Over the past ten years, the visitors programme has been resourced by the introduction of MBA Bursaries, by the availability of endowment funds and by valuable contributions from organisations such as the Physiological Society and the Fishmongers Company. The well-found laboratory has been provided through the Plymouth Marine Laboratory following a partnership agreement between the MBA and the Natural Environment Research Council signed in 1988. A lively and productive visitors programme is consequently still flourishing at Citadel Hill, albeit on a smaller scale than that enjoyed up to the mid 1980s. The growth of the in-house research programme of the MBA has placed additional demands on research space at Citadel Hill and the inexorable financial constraints have reduced the flexibility for providing animals and research resources for visitors. However, it appears that this trend may soon be reversed as a result of developments in the Association's educational programme.

Education and training have always been important components of the Association's activities. The famous MBA Easter Classes ran for more than seventy years and provided the foundation for a fascination in marine biology for several generations of marine scientists. These were stopped in the early nineteen seventies because of changes in academic regulations and funding structures.

A new National Marine Aquarium and Resource Centre

Over the past decade, the MBA has run an advanced Microelectrode Techniques workshop (in collaboration with the Physiological Society inter alia) and has sponsored two or three scientific meetings per year, also on occasion in collaboration with the Society. It has developed the 100 year-old Aquarium on site at Citadel Hill to communicate the importance and excitement of marine biology to the general public. The function of the Citadel Hill Aquarium will

The Laboratory at Citadel Hill

soon be transferred to a National Marine Aquarium which began life as an MBA initiative and is now being built in Plymouth by an independent incorporated charity established by the MBA. Plans are therefore being developed and funding sought to close the Citadel Hill Aquarium in 1998 and to convert the space into a Resource Centre to provide facilities for education, training and research.

Expanding teaching and research

The Resource Centre will provide modular teaching areas capable of holding up to four groups of 20, and a covered sea water hall with wet benches and holding tanks linked to a museum of specimens of local flora and fauna. The present Lecture Theatre will become a Visitors Laboratory for advanced training and for experimental studies. The combination of teaching and research areas with a high quality sea water system is essential. Holding healthy animals on-site broadens the range of experimental and behavioural studies that can be carried out and minimises the impact of the facility on the environment by reducing the need for animal collection.

The Resource Centre will open up new opportunities for physiological research, given the wide range of facilities in the laboratories of the MBA and the Plymouth Marine Laboratory (including molecular biological facilities, electrophysiology, visualisation techniques using confocal microscopy, electron microscopes, sea water system, ships, larval rearing, phytoplankton culture collection, National Marine Biological Library) and the breadth of scientific expertise in the two laboratories. The possibility of introducing new research initiatives to augment the facilities provided by the Resource Centre is therefore being explored.

These developments will coincide with the renewal in 1998 of the partnership agreement between the MBA and the NERC, which resulted in the formation of the Plymouth Marine Laboratory in 1988 and the refocusing of the MBA research programme. Discussions have already begun with a view to augmenting the achievements of the first decade of the partnership and encouraging new initiatives such as the Resource Centre to ensure that the wealth of resources embodied in Citadel Hill will be made available to a much wider community of students and research workers as we approach the millenium.

Michael Whitfield
Director
Marine Biological Association

EPITHELIAL & MEMBRANE TRANSPORT

The new Convenor for the Epithelia & Membrane Transport Group is:

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Email: pbrown@fs2.scg.man.ac.uk

Our thanks go to Professor Barry Hirst, the previous Convenor, for maintaining the Group over the last few years.

Important Announcement

The Group will hold the next Designated Session at the Bristol Meeting (2-4 September 1997).

Meetings Secretary's Office

SENSORY FUNCTIONS

There is to be a Sensory Functions Designated Session at the Bristol Meeting in September. This will feature a lecture on the cochlea by Professor Peter Dallos of Northwestern University. Abstracts for this Meeting must be submitted between Monday 19 May and Friday 30 May 1997.

The next Sensory Functions Group Session will be held in Cambridge in December and will be preceded by a research symposium. Full details of this will be provided in the next edition of the Magazine. There will be a Pfizer Prize round associated with the Session for which higher degree students presenting Oral Communications can enter (details on page 171 of The Gray Book).

Andy King

BACKRUNS OF THE JOURNAL OF PHYSIOLOGY

A complete set of bound Journals from 1948 (Vol. 107) to 1989 (Vol. 415) requires a good home. If anyone is interested, please contact:

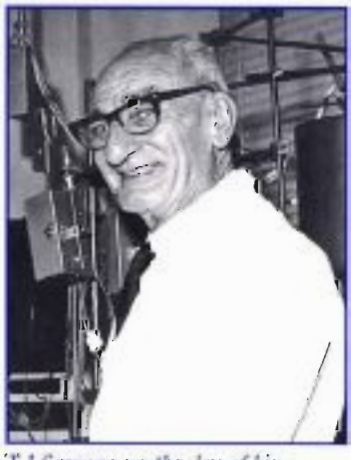
Professor R.D Keynes. Physiological Laboratory. Cambrdige University. Downing Street. Cambridge. CB2 3EG.

A Cardiff link with Sherrington

Dear Editor,

It was fascinating to read the interview with Mr T J Surman in the last issue, recalling his early days with Charles Sherrington at Oxford. Despite his translocation to Cardiff at the tender age of twenty, Mr Surman's early experiences here furnished him with endless reminiscences of his time with Professor T Graham Brown and his successor, Professor J M Peterson.

Surman joined the Department of Physiology in 1924, where Graham Brown was Head of Department until 1947. Sherrington and Graham Brown had already shown in the cat and dog that rhythmic movements could be elicited from the hindlimbs some time after severing the spinal cord, the inference being that a pattern generator for stepping movements might reside in the spinal cord. Later, Graham Brown made the key observation that rhythmic contractions of limb muscles, reminiscent of those during walking, occurred after spinal transections and after cutting the sensory nerves from the hind-limbs. The limb movement could not, therefore, be patterned by sensory input. He proposed a two half-centre model for the spinal pattern generator (see J Physiol, 1914, 48, 18-46), in which he visualized a pattern generator for each limb divided into 2 half-centres, one for flexor and one for extensor muscles. The two limb generators (centres) could be coupled in an in-phase or in an alternating mode, while the two half-centres were thought to be connected through inhibitory collaterals. In Cardiff, Graham Brown used the relatively new technique of cinematography to record limb movements of cats and pigeons.



T J Surman on the day of his retirement in September 1972 standing at the dissecting table in Stewart Stone's laboratory which, by then, had become his second home.

Graham Brown was a strong character and a strong climber. His mountaineering exploits often interfered with his teaching duties. This eventually led to discontent amongst students and staff. Ron Eccles' perusal of college papers revealed that in December 1925, a committee was set up to investigate several newspaper letters severely criticizing the medical teaching in Cardiff. In May the following year a committee appointed by the Senate of the College was set up "to enquire into the conduct of the Professor of Physiology in order to ascertain whether adequate grounds existed for proceeding with a notice of a motion to Senate proposing the dismissal of Professor Graham Brown". As Dean of the Faculty of Medicine Graham Brown overcame several attempts to dislodge him! After he retired, he was eventually obliged to leave his bachelor quarters in the Park Hotel and instead moved into a room in the Department. He gradually became hemmed in by piles of newspapers. One of Surman's duties was to ensure that a steady supply of pipe tobacco reached the hermitage.

One of the few pictures of Graham Brown surviving in the Department. It was probably taken before the war.

T J Surman then became chief technician to the new Head of Department, J M Peterson. There may be something in the Cardiff air (apart from coal dust), because Peterson also lived until last year. He died on June 18 1996, aged 97 years. Professor Magnusson Peterson (Pete) held the chair of Physiology in Cardiff from 1947 until 1966. He published a good deal on the estimation of haemoglobin and served on the subcommittee on Analytical Methods set up by the M R C in 1941. C R Harington was the chairman. The Ministry of Health was concerned at this time to survey haemoglobin levels in different groups of the population. The variability of the data then available suggested substantial instrumental error. The working group of which Peterson was a member used a reference Haldane type carboxyhaemoglobin standard, which was established at the National Physical Laboratory. The group selected the Haldane method for determinations in the field. What emerged was the M R C Haemoglobinometer manufactured to a specification laid down by the British Standards Institution. Peterson served from 1953-1960 on the editorial board of the Journal of Physiology, in the later years acting as chairman.

J M Peterson

Surman was regarded assomewhat authoritarian by a few of the younger technicians. They had great fun organizing practical jokes at his expense, especially when on Fire-watching duties during the war. Surman had to organize the Firewatch rotas at the old Institute of Physiology in Newport Road. At some time or other, the younger technicians decided his nickname should be a reversal of the last 3 letters of his surname. Forever afterwards, he was known as "Nam" Surman or just "Nam" to his close colleagues. Nam was always ready for a tea-room debate. When the discussion became animated, he was known on occasion to rise to his feet to make a point and, by the way of reinforcement, allow his false teeth to fly across the room.

David Willis
School of Molecular & Medical Biosciences
University of Wales, Cardiff

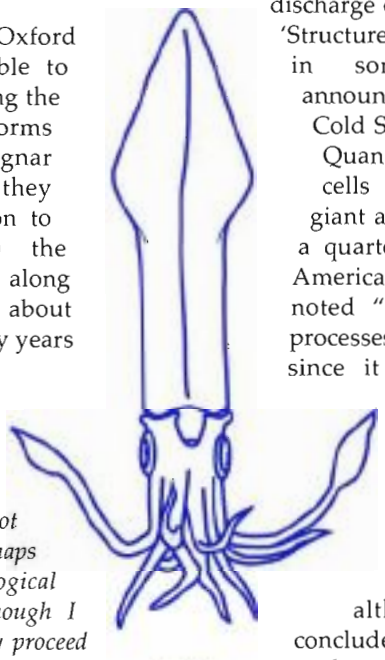
HOW THE SQUID GIANT AXON CAME TO PLYMOUTH

Squid are fast, jet propelled, ocean living animals that move in shoals, ranging in size from finger length to the giants that may be over 15 metres long. Not, on the face of it, a handy lab animal. But the discovery of the squid giant axon made these animals essential for neuroscientific research. How the axon was discovered and made widely available owes much to J Z Young. After reading zoology at Oxford, Young was awarded the University's Scholarship to study in Naples in 1928. Initially interested in fish autonomic nervous system (which he has studied ever since, in the past decade or so in collaboration with Paul Andrews) he became fascinated by the behaviour and nervous system of cephalopod molluscs, especially octopuses and squids.

Earthworms from a deck chair

When he returned to Oxford such animals were impossible to obtain, and he began examining the nervous system of earthworms with John Eccles and Ragnar Granit. In December 1932 they reported (in a Communication to the Physiological Society) the generation of nerve impulses along large diameter nerve fibres, about 300μm in the earthworm. Many years later Young recalled that collaboration

'I did the dissection, Eccles the recording, whilst Granit sat in a deck chair. We were not quite sure of his function. Perhaps he was deciding what logical methods we were to use, though I doubt whether scientists really proceed in the way that philosophers of science seem to suppose. It is a banal truism that all scientific workers operate with some hypotheses, but this alone does not adequately describe the motivation or process of their activities. Eccles, Granit and I were certainly not doing the work on earthworms to try to disprove the hypothesis that nerve fibres conduct. We were groping our way, trying to find new material for study. Disparagers can say this is not science, but we three seem to have been moderately successful scientists' (Young 1975).



Loligo

But Young had not entirely abandoned cephalopods: in 1929 he investigated the stellate ganglion in the mantle cavity of squid, and showed that large clear channels seemed to emerge from the structure, and by 1934 anatomical and physiological work convinced him that he was actually dealing with a nerve fibre of 500μm diameter.

Not for discovery... but Young demonstrated their function

The following year Young went to America and visited the marine laboratories at Cold Spring Harbour and Woods Hole where squid were available, to examine this suspected nerve fibre in more detail. He recorded action potentials, by stimulating the axon with a crystal of sodium citrate, and recording the repetitive discharge of the fibre. In a paper entitled 'Structure of nerve fibres and synapses in some invertebrates' Young announced his discovery in 1936 to a Cold Spring Harbour Symposium on Quantitative Biology. But the giant cells and their first branches (the giant axons) had been described over a quarter of a century earlier by an American naturalist LW Williams who noted "The very size of the nerve processes has prevented their discovery, since it is well-nigh impossible to believe that such a large structure can be a nerve fibre" (Williams 1909). The account was published by the American Museum of Natural History and appears not to have been widely circulated, although a review in *Nature* concluded `we did not expect very much in the way of novelty in a memoir of this kind, but the author is to be congratulated on the important discovery of a pair of giant nerve cells situated in the pedal ganglion and each giving off a giant nerve fibre' (Anonymous 1910).

Why was it ignored or forgotten for a quarter of a century? Perhaps its very size did stop people believing that it was a nerve fibre. BUT whilst Williams described the giant axons, Young did more, he **demonstrated** their

function. And he demonstrated that function in an environment where investigators could immediately repeat and extend the observations, thus quickly confirming and validating his findings. The American neurophysiologists who had seen his demonstration immediately began to investigate the preparation more closely.

'Getting results which made everyone else's look silly'

In 1937, the year after Young's announcement, a young Cambridge physiologist, Alan Hodgkin, was introduced to the squid giant axon at Woods Hole. In Britain he had isolated single fibres from the shore crab, which could be kept very conveniently in the Cambridge Laboratory, and had examined the early stages in the initiation of the action potential. He intended to continue the work at Wood's Hole but soon after he arrived, the crab supply failed, and Plymouth crabs had to be sent across the Atlantic for him, aboard the Queen Mary. Whilst he was waiting, Hodgkin was introduced to scientists working on the squid giant axon, as he wrote to his mother

> *`some scientists here have been getting most exciting results on the giant nerve fibres of the squid. As you know I spend my time working with single nerve fibres from crabs which are only 1/1000th of an inch thick. Well the squid has one fibre which is about 50 times larger than mine and Dr Cole has been using this and getting results which made everyone else's look silly. Their results are almost too exciting because it is a little disturbing to see the answers to experiments that you have planned to do coming out so beautifully in someone else's hands. No I don't really mind this at all. What I do dislike is the fact that at present English laboratories can't catch squids so that I don't see any prospect of being able to do this myself' (Hodgkin 1992).*

Squid giant axon - 'more for neurophysiology than any other single advance'

The technicalities of catching and keeping squid became as much a part of the scientific agenda as did the experimental work itself. Scientists and fishermen had much to learn about the most appropriate seasons and sites for fishing for squid, and how to handle delicate creatures. JZ Young arranged with the staff and fishermen at the Marine Biological Association's Laboratory at Plymouth how they might organise a regular supply. From the Summer of 1938, a limited and somewhat erratic supply of squid became available there, and Hodgkin, just back from America, packed his new equipment into a trailer and began a series of annual migrations to Plymouth that lasted for over 40 years. Years later he suggested 'It is arguable that the introduction of the squid giant nerve fibre by J Z Young in 1936 did more for neurophysiology and axonology than any other single advance during the past 40 years' (Hodgkin 1977).

Tilli Tansey
Wellcome Institute for the History of Medicine

References:

Anonymous (1910). Review of The anatomy of the common squid *Loligo pealii Nature* **83**:366.

AL Hodgkin (1977). 'Chance and design in electrophysiology: an informal account of certain experiments on nerve carried out between 1934 and 1952' In: The Pursuit of Nature, Cambridge University Press, pp 1-21.

AL Hodgkin (1992). Chance and design: reminiscences of science in peace and war, Cambridge University Press.

LW Williams (1909). The anatomy of the common squid, *Loligo pealii* Brill, Leiden.

JZ Young (1975). 'Sources of discovery in neuroscience' In: The Neurosciences: paths of discovery, ed F G Worden, J P Swazey, G Adelman, MIT Press, pp 13-46.

The following is from a book of poetry called BioGraffiti by John M Burns (publ. Norton, 1975).

Elucidation Blues

With a plethora
Of words
The would be
Explicator
Hides himself
Like a squid
In his own ink

Courtesy of John Chad

MY FIRST VISIT TO THE MBA

Andrew Huxley reminisces on his first visit to the MBA at the invitation of Alan Hodgkin

I finished the Part II course in Physiology at Cambridge in the Summer of 1939. I had two invitations to join members of the Department in research: one from Nevill Willmer (now, at age 94, a neighbour of ours in Grantchester), who was in charge of Histology in the Department, to work on cells in tissue culture, and the other from Alan Hodgkin (now Sir Alan, living in Cambridge, aged 83), to work on nerve conduction. Both were attractive propositions: tissue culture would have involved microscopy which was a long-standing hobby of mine, while nerve conduction was a physical process and I had always enjoyed physics, which I had taken as one of my options in Part I of the Tripos; indeed, my original intention when I went up to Cambridge had been to specialise in Physics.

In the end, I accepted Hodgkin's invitation, partly, I think, on personal rather than scientific grounds as I had got to know Hodgkin when we were both living in Trinity College, he as a Junior Research Fellow and I as an undergraduate, and he was much nearer to me in age than Willmer. Hodgkin planned to spend part of the Long Vacation at the Marine Laboratory at Plymouth and asked me to join him.

The MBA

Early in the vacation, I spent ten days in Belgium and Holland with John Gray (now Sir John; Secretary of the Medical Research Council, 1968-77) whom I had known from the age of six and who had been in the same Part II Physiology class with me. My diary (no more than a record of dates and engagements) tells me that I went to Plymouth on August 5th. We stayed in a boarding-house near the western end of the Hoe; the Citadel and the laboratory are at the eastern end. On two days, my diary has the word "Mothecombe", meaning that Hodgkin and I got walks at that attractive spot on the Devon coast.

Hodgkin was already an important figure in nerve physiology. In his first year of research, he had provided direct evidence that the "local-circuit currents" flowing ahead of an action potential were adequate to stimulate the next part of a nerve fibre; he had also been the first to record subthreshold electrical activity in nerves (single fibres from crab nerves) and (jointly with KS (Kacy) Cole in the USA) had measured the resting membrane resistance of the giant nerve fibre of the squid - discovered a few years earlier by J Z Young, who is now approaching his 90th birthday.

After the boat came in

Hodgkin had a first-class direct-coupled amplifier and oscilloscope, with high input impedance provided by cathode followers. His objective in going to Plymouth was to do more experiments on the squid giant fibre: squid do not live well in captivity, as they dash themselves against the walls of the tank they are kept in, so the only way to experiment on their nerves was to transport one's apparatus to the Laboratory at Plymouth and to start one's experiment in the evening, as soon as possible after the laboratory's boat had come in.

Hodgkin had not got a specific experiment that he was intending to perform. Our first idea was to measure the viscosity of the axoplasm of the giant fibre by dropping mercury down the fibre. In my part II practicals, I had been cannulating small blood vessels in the cat so I thought I could cannulate the fibre, which had about the same diameter. So I made a cannula, we inserted it into the fibre in its nerve trunk and suspended it vertically in a trough of sea water, which is an adequate Ringer's solution for squids and many other marine invertebrates. We put small drops of mercury into the cannula but were disappointed; they fell only a fraction of a

Early days at the MBA - Andrew Huxley and Alan Hodgkin (Courtesy of Archives Collection, MBA)

millimetre and came to a complete halt. Evidently the axoplasm was a gel, although it was liquid at the cut end of a fibre and at the place where the cannula had been inserted; it was later shown that it was calcium ions in the sea-water that caused the axoplasm to liquify.

Electrode inside the axon reveals the overshoot

But having the fibre suspended on its cannula suggested to Hodgkin that it might be possible to push an electrode down into the inside of the fibre so as to get a direct measure of the potential difference across the membrane. We pulled glass tubing down to a diameter of about 0.1 mm, filled it with sea water and pushed a chlorided silver wire nearly to its tip; I had made an arrangement with two small mirrors so that we could watch the electrode from both the front and the side as it went down and could guide it so as to avoid having it scrape the inside of the membrane. When the electrode tip was far enough beyond the damage where the fibre had been cannulated, we recorded a potential about 50 mV negative to the surrounding sea water; this was what was to be expected on the basis of measurements made with external electrodes on many excitable tissues. But when we stimulated the fibre, we got a surprise: the internal potential overshot and reached about 50 mV positive.

I confess that my own reaction was principally the excitement of recording an action potential so much bigger than anyone had done before, but Hodgkin was immediately aware of the implication that this was a refutation of the widely-accepted theory of Bernstein, namely that the action potential was due to the membrane becoming permeable to all ions so that the internal potential would rise towards, but not beyond, the external potential. Indeed, Hodgkin already had hints from external recordings on the much smaller fibres of crustaceans that the action potential might be greater than the resting potential, but uncertainties in calculating membrane potential from externally recorded potentials made these hints unreliable.

War work overshadowed nerve conduction

By this time, it seemed that war with Germany might break out at any moment, so we packed up and drove home on 30 August, only two days before Hitler marched into Poland. Hodgkin wrote a short note that we submitted as a letter for *Nature* and it appeared three weeks later.

The action potential of the squid fibre was also measured with an internal electrode during the same summer by Kacy Cole and Howard Curtis at the Marine Biological Laboratory at Woods Hole, Massachusetts. But they were unable to measure the resting potential as they used a capacity-coupled amplifier, which responds only to transient changes of potential; they therefore had no indication of the overshoot.

Hodgkin and I met a few times during the war but were both so busy with war work that we could not spend much time even thinking about nerve conduction, but we did publish a full-length paper in the *Journal of Physiology* in 1945. This contains some elaborate speculations about possible explanations for the overshoot; in retrospect it seems very stupid not to have thought of entry of sodium ions as the cause. Neither of us knew at that time of the paper by Overton, published in *Pflügers Archives* in 1902, giving excellent evidence for "the indispensability of sodium (or lithium) ions" for the excitability of muscle; if we had known of it, I am sure we would have jumped to the right conclusion at once.

Andrew Huxley
Grantchester
Cambridge

IT WASN'T ALL WORK - PLYMOUTH IN THE 1930's

Part of a written interview with Dr John Bateman, who was a Research Fellow at the Marine Biological Association's Laboratory at Plymouth in the early 1930s.

"How did you happen to go to Plymouth in 1931?"

By mentioning to AJ Allmand, my research supervisor at King's (London) that I had become interested in the application of chemistry and physics to biology, and had been fascinated by a public lecture at UCL by AV Hill. Allmand's kindness in mentioning me to Hill resulted in an invitation to meet him. The timing was just right, because AV had recently shown that the apparent heat production of muscle measured thermoelectrically was distorted by changes of vapour pressure attributable to the accumulation of osmotically active metabolites. AV had very cleverly isolated this phenomenon as a means of measuring the vapour pressure depression of aqueous solutions, replacing the muscle on one surface of his differential thermopiles by bits of filter paper soaked in the solution of interest, the other surface being covered similarly by a reference solution. A constant ambient aqueous vapour pressure was established by surrounding the thermopile by a cylinder of filter paper soaked in the reference solution. The whole assembly was immersed in a thermostat and the steady state temperature difference between the two thermopile surfaces was measured by a galvanometer... Some of the uses of this instrument had been published by AV, but it was, for him, a diversion from his central interest and thus sensible to turn it over to somebody else. So I was invited to UCL to learn the technique and to pick up some physiology, which I did by working with material easily available in the Department, erythrocytes and frog skin.

A V Hill

The time came when AV suggested that the Plymouth laboratory would be the best place to work, since osmotic regulation in marine animals could be studied and the new vapour pressure thermopiles were particularly suitable for measurements on small volumes of haemolymph.

"What do you remember about the Plymouth laboratory itself?"

Situated at the far end of the Hoe, on a rocky bluff at the foot of the old Citadel Hill. Not a very large site; probably not much changed over the years. The seaward side was occupied by the Aquarium and associated offices and (I think) a few preparation rooms. There was an underground passage to a landing platform on the rocks - a good place for swimming in those days when the sea was fairly clean. On the landward side was another building with laboratories, offices and, at the Hoe end, the excellent library on the first floor. In between, an open courtyard lined by (slate?) tanks with running seawater, containing some of the latest catch - I remember mostly dogfish, conger, crabs. One helped oneself ... The buildings were kept open day and night. No one thought of theft or vandalism in those days and I never heard of any incident.

Getting set up owed everything to Hill's assistant, JL Parkinson, "Parky", who spent a few days with me in Plymouth. I was given a decent sized laboratory and a concrete

basement room for the thermopiles ... It may interest people versed in today's computerised techniques to know how primitive, though ingenious and effective, but labour-intensive, the set-up was. The thermostat bath was a large metal rubbish bin filled with water stirred with air from the laboratory compressed air tap. The source of heat was a flame from the uncovered jet of a Bunsen burner. The movement of the meniscus of a column of mercury across the bevelled tip of a wide-bored surgical needle, in response to temperature changes in the bath, provided continuous adjustment of gas flow to the burner.

"What laboratory work did you do in Plymouth?"

Mainly measuring adaptation of shore crabs (*Carcinus maenas*) and swimming crabs (*Portunus puber*) and a few smaller marine invertebrates, when immersed in solutions of different composition and decreased osmolality with respect to sea water.

"What about the permanent staff?"

Being there out of season I probably had more opportunity than most to get to know the staff. **Dr EJ Allen**, the Director, was self-effacing, and although very busy, he was never in a hurry and was immensely helpful to me personally, spending time in the library showing me where to find source material with which as a chemist I was rather unfamiliar. I don't know whether he ever raised his voice; the following anecdote might suggest never. One day I was chatting in the lab with Dr Cooper when Dr Allen walked in. Cooper, without warning, picked up a large beaker from the bench and dropped it on the floor, where of course it shattered. Dr Allen merely looked amazed and walked away without a word. As Cooper then explained, the beaker was a commercial sample of "unbreakable" glass - secure perhaps against impact with a wooden floor or lino but defenceless against concrete.

Dr William Atkins was, I think, Deputy Director or equivalent. A man with a varied background: FRS; chemist; physiologist; botanist; strict Irish Protestant; once heavyweight champion of Ireland; year-round swimmer in the sea. Author of innumerable papers on urea, osmosis, balloon fabrics, diatoms, photoelectric cells, preservation of fishing nets, cryoscopy, grass, seawater, the cause of gape in hens. Tall, balding, rather dour and easily provoked; anti-communist. A story circulated around the lab that somebody ventured to congratulate him on the rumoured birth of a child. "Who told you that?" he snapped ... He was kind enough to me. When I went to dinner at his house he proved to be an entertaining host with a rather majestic but less reticent wife who confided that they had met in a Plymouth boarding house. There was no sign of a child in the house, so I began to suspect an unfounded rumour, when suddenly the discourse was interrupted by the dramatic entrance of a maid who announced "Master Billy's crying!" Both parents dashed out and one heard heavy steps on the stairs and an alarmed voice shouting "What is it, old man?".

The crew of SS "Salpa": I don't remember their names but they were tough. The "Salpa" was the laboratory's collecting trawler, a vessel exquisitely sensitive to the slightest motion of the sea. One of the crew (it might have been the captain) declared proudly that everyone sailing aboard the "Salpa", himself excepted, became seasick no matter how smooth the sea. Confronted with somebody who appeared resistant he would tie string around a piece of raw mutton fat, swallow it, then pull it out. He claimed 100% success.

Red sea bream

"What do you remember about occasional visitors?"

AV Hill visited occasionally. He had a house near Ivybridge in the hinterland. And he was very much attached to the MBA and to the Laboratory, proud of its importance and prominent, then or later, as President. Ancel Keys of the Scripps Institute came to visit via Copenhagen where he had worked in Krogh's laboratory. There he had shown that eels in seawater excreted salt through their gills in order to maintain the much lower internal osmolality characteristic of teleosts and most terrestrial vertebrates... Keys and his wife Winnie (a Hollywood beauty, I thought) duly arrived. I had booked them into what I considered a nice boarding house. They were not in the least amused. Stairs to climb, bathroom to be shared. Sea impossibly cold for swimming. In La Jolla, they said, everyone had a nice little bungalow on the beach and the sea was comfortably warm and pleasant in spite of the ubiquitous sting rays. Anyway they roughed it with fairly good grace and we got along quite well, though Keys could be exasperatingly brash ... AV Hill arrived one day and he was more irritated than I. As he was standing outside enjoying the fresh air, Keys with evident provocative intent posed a

T P Feng and J B Bateman, with spider crab in Plymouth c. 1931. Photograph given by AV Hill to the Physiological Society Archives, reproduced courtesy of the Wellcome Institute Library, London

question about the hydration of haemoglobin and whether the Hill thermopiles were sensitive enough to detect it. AV's response was to turn to a workman who happened to be nearby and engage him in conversation about paint... I think it was simply an expression of AV's habit of indulging in technical discourse on his own terms, at his own time and place. Another example (though this takes us away from Plymouth). He once gave me a lift to Cambridge. I must have tried some sort of "shop" talk. He deflected the question by saying that Meyerhof, on a similar trip, had talked unceasingly about creatine phosphate. "I threatened to throw him out and make him walk if he wouldn't shut up". After that, as if to sharpen the point, he started singing a favourite Devonshire tune, with an assurance and a true intonation that for some reason surprised me. Of course this may also have been his oblique way of saying "that's a stupid question".

Detlev "Det" Bronk came for a few days. The Keys - Bronk visits overlapped, giving me an amusing opportunity to observe them together when we went for a walk. There was throughout a sort of veiled hostility, a mutual distrust. Toward evening we were getting hungry and by way of experiment I insisted that we buy fish and chips and eat them out of paper bags. Anticipated roles became somehow reversed. The brash Californian was outraged by the prospect of losing dignity. The man from Pennsylvania displayed the tolerance due to a spoilt child (myself I presume), as though this were something slightly louche that the English might do in informal moments as long as there were no important personages to see what they were up to.

T P Feng arrived in AV's lab when I started there, and he soon joined me in Plymouth - I don't think he did any experiments but we stayed in the same boarding house, and did a lot of talking. He was a pleasant, even jolly companion, especially when some oddity of the local culture provoked a sort of unbelieving, articulate amusement halfway to an outright guffaw, which he would no doubt have considered discourteous. Once, at a Physiological Society dinner we chatted at such length that somebody asked what we could have been talking about. I don't recall my reply but it might have been 'cheese', 'tea' or 'Schubert', in that order. Feng was politely fascinated by Schubert though a little mystified; knowledgeable about tea and generous with gifts imported from China; but absolutely bowled over by the wonderful exotic idea of cheese, unthought-of in his own country.

There was very little evidence of group activity or social exchange; everyone had his own project I suppose and time was short. However there was one laboratory steward in charge of the dark room, who enjoyed showing some of us pictures of a visitor taking part in very uninhibited frolics with a group of young girls in a secluded cove. So perhaps it wasn't all work.

Tilli Tansey
Wellcome Institute for the History of Medicine

1000th MEETING OF THE SOCIETY

The 1000th Scientific Meeting is a significant event in the history of the Physiological Society: this will occur in 1999. Any members, or others, who wish to make suggestions for how this event may appropriately be celebrated may contact Professor Brian Whipp at the Department of Physiology, St George's Hospital Medical School, Cranmer Terrace, London, SW17 0RE.
Telephone: 0181 725 5390
Fax: 0181 725 2993
email: b.whipp@sghms.ac.uk

CHANCE AND DESIGN IN ELECTROPHYSIOLOGY

In 1977 Cambridge University Press published a book THE PURSUIT OF NATURE, Informal Essays On The History of Physiology. These are extracts from a chapter entitled "Chance and Design in Electrophysiology: An Informal Account of Certain Experiments on Nerve Carried out between 1934 and 1952" written by Sir Alan Hodgkin.

My aim in this lecture is to give you some idea of the informal background to the series of papers on nerve conduction which my colleagues and I wrote between the years 1937 and 1952. I believe that the record of published papers conveys an impression of directness and planning which does not at all coincide with the actual sequence of events... But over a long period I have developed a feeling of guilt about suppressing the part which chance and good fortune played in what now seems to be a rather logical development...

My first two papers... were published in the Journal of Physiology in 1937 under the title "Evidence for electrical transmission in nerve". The aim of the papers is stated in the first two sentences: the method is straightforward; fire an impulse at a local block and see what happens beyond - and the result now seems so obvious that one wonders whether the work was worth doing at all. I suspect that this was one of the papers which caused a very distinguished biologist to say, 'The trouble with you Cambridge electrophysiologists is that you never discover anything; you think hard, decide what is right and then work away until you prove it'. In defending myself and my colleagues against this accusation I must come clean and dispel any impression of tidy planning which our papers may have created...

Chance and good fortune were equally important in my next piece of research. I had grown interested in cable theory... and... followed a suggestion by Professor Adrian that I should work on crab nerve. I found it very easy to split crab nerve into fine strands and one of the strands I picked up turned out to be a single axon to judge from its enormous all-or-nothing action potential. This really was a great piece of luck as I had no dissecting microscope and the chances of picking up one of the half-dozen or so 30 μm fibres in a nerve trunk a millimetre thick are not very high. The next day I borrowed a dissecting microscope and from that time to this I have never worked on a multifibre preparation again. (What, never? Well, hardly ever.)

Loligo vulgaris

Soon after I got the preparation going I noticed that a shock which was just below threshold produced something like a small graded action potential, which grew rapidly in size as the stimulus approached threshold. This clearly was exactly what was needed to explain Bernard Katz's results and I was very pleased to be getting evidence of something as unorthodox as a graded response in a single nerve fibre... Herbert Gasser, who was then Director of the Rockefeller Institute in New York... invited me to spend a year working in his group, and it was a valuable experience to work in a big well organized laboratory and helped to turn me from an amateur into a professional scientist. But the contact which had the greatest immediate effect on my scientific life was with Cole and Curtis at Columbia. Cole asked me to visit him at Woods Hole in June.

Meanwhile I visited St Louis, on the way to a 3 week holiday in Mexico, which was then a wild and remote country, and also an incredibly inexpensive one where you could live for less than a dollar a day. In St Louis I stayed with Joseph Erlanger who was exceedingly nice to me, but expressed total disbelief in subthreshold activity in myelinated axons and was also very sceptical about the local circuit theory. I had tried hard but without any success to isolate single myelinated axons from cat spinal roots... [but] I got a good idea from a conversation with Erlanger in which he said that he might be convinced if I could alter conduction velocity by changing the electrical resistance outside a nerve fibre. Somewhere on that holiday... I saw that it would be very easy to alter the electrical resistance outside a crab fibre from a high value in oil to a low one in a large volume of sea water. I did the experiment as soon as I got back to New York and obtained

a large effect on conduction velocity. This was one of the few occasions on which everything went according to plan and this time no hidden snags emerged... When I got to Woods Hole in June, Cole and Curtis very kindly let me use their amplifier and I was able to repeat the experiments on squid axons as well as making some other tests of the local circuit theory... Curtis and I also did a few long-shot experiments trying to push electrodes up the cut end of a giant axon. I think we both came away with the idea that it might not be too difficult to record action potentials with an internal electrode...

When I got back to Cambridge in the autumn I decided to set up the kind of equipment used in the Rockefeller, with racks, electronic timing, d.c. amplifiers and so on... It took three or four months to get all the equipment built and to be ready for experiments again. I had worked very hard for the previous six years and as there was obviously going to be a European war I thought it best to choose a straightforward problem which would leave time for non-scientific activities. So I decided to use my new d.c. amplifier to check how close the action potential came to the resting potential. Andrew Huxley, who was doing the Part II Physiology course, joined me in some of the experiments. We measured external electrical changes in Carcinus axons immersed in oil and took the resting potential as the steady p.d. between an intact region and one depolarized by injury or isotonic potassium chloride... I decided to continue the experiments at Plymouth where I had worked several times since my first visit there as a schoolboy in 1931. I bought a trailer which I attached to my ancient car and with some difficulty managed to drag the bulk of my equipment from Cambridge to Plymouth in July 1939. After a few weeks, Andrew Huxley joined me... [and] said he thought is would be fairly easy to stick a capillary down the [squid] axon and record potential differences across the surface membrane. This worked at once, but we found the experiment often failed because the capillary scraped against the surface; Huxley rectified this by introducing two mirrors which allowed us to steer the capillary down the middle of the axon. The result was that the action potential of nearly 100 mV was about twice the resting potential of about 50 mV... However, within three weeks of our first successful impalement, Hitler marched into Poland, war was declared and I had to leave the technique for eight years until it was possible to return to Plymouth in 1947.

Huxley and I wrote a cautious note to Nature about our results and for the first few months of the war I tried to work on a full paper. But this didn't get very far as it had to be done in the evenings after a long day at the Royal Aircraft Establishment, Farnborough, where I was working on aviation medicine with Bryan Mattews. After I had switched to radar, there were other things to study in the evenings and by June 1940 the war had gone so disastrously, and the need for centimetric radar was so pressing, that I lost all interest in neurophysiology and did not even both to keep my copies of the Journal of Physiology.

By 1944 the position of the Allies had improved, radar was less demanding and I had married Peyton Rous's daughter, Marion, whom I first met in New York in 1937. There seemed to be a reasonable chance of getting back to Physiology and I was feeling happy enough to start thinking again about nerve... Andrew Huxley was working on Naval gunnery and his visits to Malvern (where I worked on radar) enabled us to finish the paper about the action potential and resting potential which we had started in 1939... When I returned to Cambridge in August 1945 I continued working on crustacean nerve using almost exactly the same equipment as before the war... [and when] Andrew Huxley was released from the Admiralty... we were able to continue the very happy collaboration which we had started in 1939... Towards the end of 1946 and in the early part of 1947 we spent much time speculating about the kind of system which might give rise to an action potential.

A propagated action potential was calculated by Huxley in 1947 and incorporated the main features that emerged two years later from the voltage-clamp experiments - i.e. a rapid rise in sodium permeability followed by a slower decay, and a slow rise of potassium permeability...

Towards the end of 1946 Bernard Katz sent me a manuscript in which he showed, among other things, that crab axons became inexcitable in salt-free solutions. As this agreed with my own experience of squid axons I began to think the Woods Hole result was wrong and that there was hope for the sodium theory. In January 1947 I decided to test the theory by measuring the effect of sodium-deficient dextrose solutions on (1) the action potential recorded externally from single crab axons, and (2) the longitudinal resistance of external and internal fluids in parallel...

Alan Hodgkin at the MBA in 1976 (Courtesy of Archives Collection, MBA)

These experiments were brought to an end by the first of our many energy crises, in this case precipitated by an exceptionally prolonged cold spell which lasted until the end of March 1947. It was soon found that national coal stocks were exhausted and the central heating was switched off in many buildings, including university laboratories. We then had no cold room in our part of the laboratory and I remember that David Hill took the opportunity of carrying out a series of experiments at 4°C. But you can't dissect single fibres at such temperatures and I spent the time writing at home or talking with Andrew Huxley in Trinity where he could be seen cranking a Brunsviga calculating machine with mitten-covered fingers. I started experimenting again in April but by then the summer vacation was approaching and I had decided to do the sodium experiments properly at Plymouth using the squid axon and an internal electrode. I found it hard work to get going again. The Plymouth laboratory had been partly demolished in the great air raids of 1941 and was being rebuilt; squid were in short supply and I'd forgotten much of the technique. Worst of all I was short of a partner. Bernard Katz wasn't free till September and Andrew Huxley was just getting married...

Katz and I first spent several weeks in July 1948 trying to perfuse squid axons with virtually no success, except that we learnt that calcium ions would liquefy axoplasm. Having failed here we started to try to make and insert double spiral electrodes. This didn't work either until we realized that one should first pre-drill the axon with a smooth glass capillary. Then things started to move and by using short shocks and constant currents with different external solutions we obtained indirect information about the permeability changes to sodium and potassium. Andrew Huxley arrived in mid-August and settled down to make the feed-back amplifier work. We managed to do a few voltage-clamp experiments, which were published in 1949...

During the next year Huxley and I spent a fair amount of time improving the equipment and we returned to the attack at Plymouth in June 1949. At first squid were in poor supply and we took a few weeks to get going. But by mid July 1949 Katz had joined us, there was a fine supply of living squid and in the next month we obtained virtually all the voltage clamp records that were used in the five papers published [in the Journal of Physiology] in 1952...

Extracts from A L Hodgkin (1977) In: The Pursuit of Nature, pp 1-21 Cambridge University Press Reprinted with permission

Extract from Presidential Address given by J N Langley to the British Association (Physiology Section) in 1899.

"Those who have occasion to enter into the depths of what is oddly, if generously called the literature of a scientific subject (like physiology), alone know the difficulty of emerging with an unsoured disposition. The multitudinous facts presented by each corner of Nature form in a large part the scientific man's burden today and restrict him willy-nilly, to a narrower an narrower specialisation. But that is not the whole of his burden. Much that he is forced to read consists of records of defective experiments, confused statements of results, wearisome description of detail and unnecessary discussion of unnecessary hypotheses. The publication of such matter is a serious injury to the man of science: it absorbs the scanty funds of his libraries, and steals away his poor hours of leisure."

Courtesy of Cecil Kidd

MICROELECTRODE TECHNIQUES: THE PLYMOUTH WORKSHOP

For the past 14 years in the first two weeks of September people have gathered at the laboratory of the Marine Biological Association on Plymouth Hoe to take part in this postgraduate Workshop. The purpose is simple - the 16 students learn as much as they can in the 2 weeks they are there from the 40 or so experts who come at various times to teach diverse applications of glass micropipettes and related topics. A Workshop (rather than a course) because the aim is to teach and improve technique, unlike the well known courses at the MBL in Woods Hole, which teach academic rather than technical aspects of cell physiology. However, the big attraction of the Plymouth laboratory is essentially academic - this is not only the home of the squid axon, but also that of many other interesting creatures, carefully catalogued and with many secrets, that can be simply observed, or pressed into service to provide experimental preparations. In this sense the present Plymouth Microelectrode Workshop is a direct descendent of the comparative physiology course for undergraduates run by the MBA each Easter until the late 1970s - you go to Plymouth because of the biology and the unique academic environment of the MBA.

The beginnings of the course

The first Workshop in 1984 took place at a time when electrophysiology and glass pipette techniques were changing fast, yet undergraduate practical training was declining. Microelectrode techniques that had been the domain of membrane biophysicists were now being applied in areas such as developmental biology and botany. The resolution, new insights and possibilities of the emerging patch clamp methods were becoming increasingly obvious. Formal training in the theory and practice of microelectrode recording for PhD students and post-docs working in cell physiology was needed urgently. The timing and location were spot on, and the drive to start the Workshops was provided by Anne Warner (at UCL) and Eric Denton (then Director of the MBA).

Most of the UK electrophysiological community was involved in some way and the 'cooperative' nature of the Workshops has paid dividends in keeping them running for 14 years. Generous finance was obtained, and still is received, from the Research Councils MRC and BBSRC, The Physiological Society and The Company of Biologists, with initial help from the Nuffield Foundation. Techniques taught on the first Workshop were voltage clamp, patch clamp, ion sensitive microelectrodes and intracellular injection. There were 12 students and, following the essential principle that technique is best taught with 1 demonstrator per student, the same number of teachers were present for the 2 weeks. Visiting lecturers were David Colquhoun, Bernard Katz, Richard Keynes, Martin Thomas and Roger Thomas.

Now as then and a high demand

The organisation is essentially the same now as then - the practical core adheres to the 1 to 1 teacher/student principle, with 3 days spent on each of three techniques for each of the now 16 students. A day is spent with electronics and with microscopy, lectures cover the basic techniques, and lectures and demonstrations are given of recent developments. The range of techniques has been extended to include optical methods -fluorescent indicators and flash photolysis- now used in conjunction with microelectrodes, making a total of seven core techniques and 3-4 demonstrations. For most experiments a local creature provides the tissue - squid, dogfish, amphioxus, skate, tunicates, crayfish and seaweed.

Most learning is done at the bench - students have usually had at least a year of experience and sufficient frustration to know the questions they need to ask. Students are mainly PhD students (usually 10-12) and postdocs retraining or extending their skills (usually 4-6). Most are from the UK, 3-4 from other European countries and occasionally one from the US. Importantly, friendships are made among contemporaries from different institutions who would otherwise not meet so easily. Demand for places is high, 50-60 high quality applications each year, enough to justify a second Workshop of the same kind. The number of teachers who come to pass on their skills has increased to about 30 who stay for a week each, and in addition there are 10 or so visiting teachers who stay for a day or two. The teachers are committed to the workshop band, coming back each year to set up, teach and finally dismantle the equipment. There is an atmosphere of controlled chaos as an empty lab is transformed in a couple of days to 7 working set-ups, and relief and sadness when the adventure is over for another year. Some of

Sepia officinalis

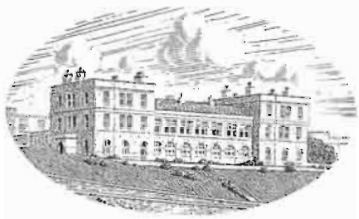
the equipment is owned by the Workshop, but much state of the art instrumentation and optics are kindly loaned by manufacturers and suppliers.

As well as the exotic creatures of the aquarium and seawater tanks, the MBA facilitates the Workshop in many ways. The indigenous electrophysiological Research Fellows and postdocs provide an essential interface between the MBA lab research and the Workshop, teaching with the visiting teachers for the two weeks. Guest house accommodation close to the lab is readily found out of season by the MBA Visitors coordinator, there are excellent caterers in the MBA common room, and pubs and restaurants nearby for the evening. The walk across the Hoe in morning sun or storming rain, the view across Plymouth Sound, and the smell of the sea on entering the lab, are a good start to any day.

David Ogden
Division of Neurophysiology
National Institute for Medical Research
Colin Brownlee
Marine Biological Association
Anne Warner
Dept of Anatomy & Developmental Biology
University College, London

The changing look of past course leaflets

VACATION COURSES IN MARINE PHYSIOLOGY 1962



WITH APPROVAL OF THE COUNCIL OF THE MARINE BIOLOGICAL ASSOCIATION

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Students seeking admission to a Course are advised to communicate, BEFORE 30 APRIL 1962, with Dr E. J. Denton, Marine Biological Laboratory, Plymouth, who will give further information on application. Those preparing for an honours course in Physiology will be given priority.

Students are requested to state in their applications the stage they have reached in the course of their studies and the designation and date of their final examination (*if any*).

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FIRST COURSE - 9 SEPT. - 21 SEPT. 1968
SECOND COURSE - 23 SEPT - 5 OCT 1968

Application Forms and further information can be obtained from Mr J. V. Howarth, Marine Biological Laboratory, Citadel Hill, Plymouth.

FINAL DATE FOR APPLICATION 30th APRIL 1968

An extract from "Sea Anemone Experiment" taken from the MBA, Physiology Class Course Notes 1967.

Facilitation, rates of conduction, and slow contractions

Read preliminary account in Pantin, J exp biol., 12, 119 (1935). Settle anemone (which lives on Buccinum shells inhabited by hermit crabs) either on a glass plate, or onto an empty shell, this is best done the day before you wish to do the experiment. An hour or more before experimenting, place radial hooks (bent pins) with an attached length of cotton, into the radial sphincter. The anemone is less liable to get fed up with the experiment and walk off if its foot is smeared with vaseline.

SO HOW DO ANAESTHETICS WORK?

From channels to synapses, Bill Winlow discusses what is known about anaesthetic actions and why the pond snail is a good model for their study.

If we knew the answer to the above question, then surgical procedures would be safer, but the job description of anaesthetists would be very different and the drug companies would be spending lots of money on new better targeted compounds. At the moment we still don't know the side effects of general anaesthetics, from their real anaesthetic actions.

Currently used volatile anaesthetics are based on derivatives of ether and chloroform that were first introduced in 1846 and 1847 respectively. Although many of the actions of general anaesthetics have been described in the ensuing 150 years, we are still a long way from understanding the key cellular events that underlie general anaesthesia. In recent years Nick Franks and Bill Lieb, working at Imperial College, have espoused the view that anaesthetics may act on proteins within cell membranes and support for this view is gradually increasing. The membrane expansion hypothesis, based on Meyer and Overton's independent work at the turn of the century is no longer a viable explanation for the actions of general anaesthetics, with the result that i) the only unifying principle of general anaesthesia is that general anaesthetics somehow interact with surface and subcellular membrane components; ii) no single cellular mechanism seems to explain their widespread effects in the central nervous system.

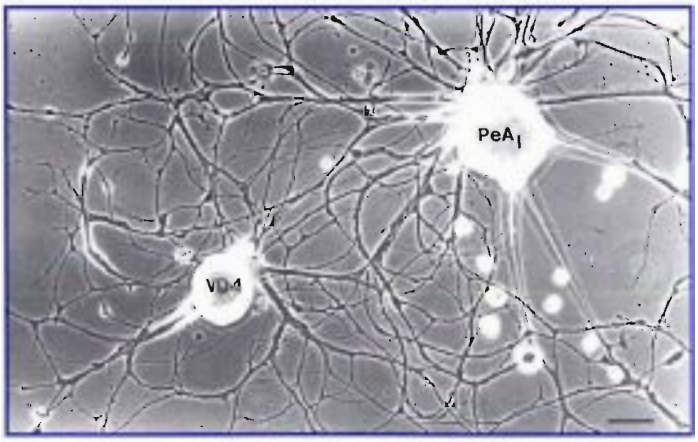

Fig 1 The peptidergic neurone VD4 growing in culture with pedal A cluster neurone, with which it makes monosynaptic inhibitory connections after 24 to 48 hr. in culture as it does in the intact brain (from Spencer et al, 1996).

Lymnaea stagnalis (Courtesy of Munir Qazzaz)

Snails in anaesthetics research

Over the last fifteen years we have established the pond snail, *Lymnaea stagnalis*, as a model system for anaesthetics research and other snails such as *Helix* and *Aplysia* have been used in Elliott's lab in Dundee and Lukowiak's lab in Calgary. At first sight these may seem strange preparations to use, but they offer many advantages for those who would try to disentangle the complexities of anaesthetic function.

In *Lymnaea*, the nervous system is easily accessible, the cells are large and pigmented (orange, yellow or white) and individual neurones are uniquely identifiable from one preparation to the next. In addition, the animal has an interesting behavioural repertoire, for those who have time to watch it, and is currently being used for studies on respiratory function by Naweed Syed's group, also in Calgary. Fortunately the animal becomes anaesthetised in the normal clinical concentration range for volatile anaesthetics and can be used to study their actions on neural networks, synaptically coupled cells, single neurones or at the subcellular level.

Lymnaea neurones survive and grow well in culture, where they may be studied in isolation, without the background activity of the rest of the nervous system to complicate events. Cultured neurones preserve both their characteristic action potential shapes and neurotransmitter identity. Excitingly, it is also possible to reconstruct identified synapses in culture and to look in detail at the pre- and postsynaptic actions of the anaesthetic (Fig 1).

Pathways to silence

Different neurones respond to anaesthetics in different ways and we were interested to discover that although many neurones gradually hyperpolarized and became silent in the presence of anaesthetics, others went through a period of bursting activity known as paroxysmal depolarizing shifts (PDS), prior to

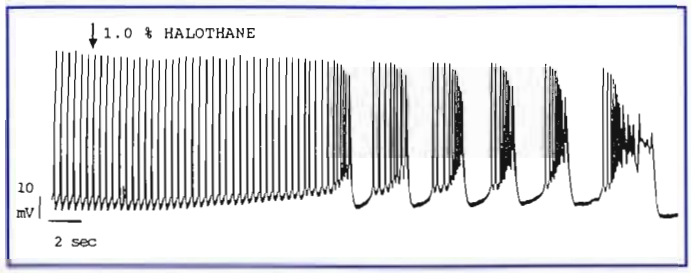

Fig 2 Paroxysmal depolarizing shifts triggered in an isolated M group neurone by 1% halothane delivered in snail saline at the arrow (from Winlow et al, 1992).

becoming quiescent. In the presence of halothane, these PDS-like events were also generated by isolated neurones in culture (Fig 2), indicating that they are an intrinsic property of the neurones themselves and not necessarily due to synaptic interactions within a neural network. How PDS is generated is still a matter for conjecture, but it seems to involve blockage of the potassium currents involved with the repolarization of the action potential coupled with a rising intracellular calcium concentration.

Channels and anaesthetics

Many ion channels are affected by general anaesthetics. Commonly used inhalation and barbiturate anaesthetics produce dose dependent effects on the spontaneous discharge of identified neurones, abolish the calcium dependent components of action potentials and block chemical synaptic transmission. These studies imply that calcium channels may be selectively affected by anaesthetic agents. Both low voltage-activated and high voltage-activated channels are known to exist in molluscan neurones (Haydon & Man-Son-Hing, 1988) and we have demonstrated that L-type calcium currents are blocked in a dose dependent manner by halothane.

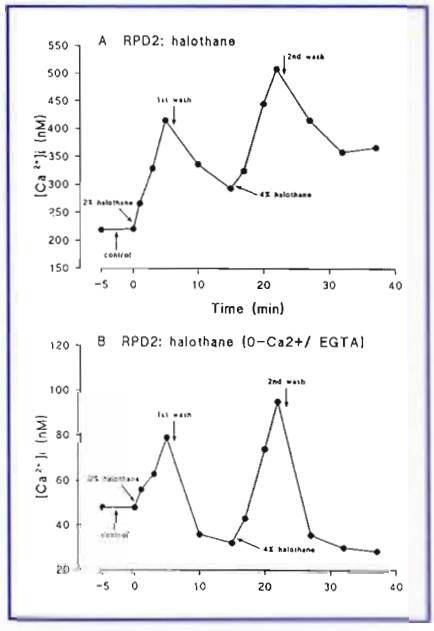

Fig 3 Effect of halothane on $[Ca^{2+}]_i$ of the neurone RPD1. In A the cell was exposed to halothane in normal saline, whilst in B a zero calcium/EGTA saline was used, resulting in a lowered $[Ca^{2+}]_i$ as might be expected (from Winlow et al, 1996).

Both ligand and voltage gated Ca^{2+} channels occur in all highly evolved groups of animals, including vertebrates, and may be potentially regulated by secondary messenger systems. Recent work in Leeds has also demonstrated that several voltage activated potassium currents are blocked by both halothane and barbiturates. The actions of anaesthetics on sodium currents are complex and have been studied in Elliott's lab. One should not assume that anaesthetics always block or partially inactivate channels, since in some *Lymnaea* neurones an anaesthetic induced potassium current ($I_{K(An)}$) causes hyperpolarization (Franks and Lieb, 1988).

Volatile Anaesthetics Raise $[Ca^{2+}]_i$

In many tissues from rat hepatocytes and cardiac myocytes to hippocampal and snail neurones, intracellular calcium $[Ca^{2+}]_i$ is raised by inhalation anaesthetics and we have recently shown that halothane induced rise in $[Ca^{2+}]_i$ is derived from intracellular sources (Fig 3).

Decoupling and blocking synapses

Although we now know that anaesthetics block many channels at clinical concentrations, we discovered early in our work that they also caused a concentration dependent increase in membrane conductance in many neurones (Fig 4). It is still not clear which channels are being affected, but the clear implication is that as well as **blocking** some channels, anaesthetics enhance the **opening** of others.

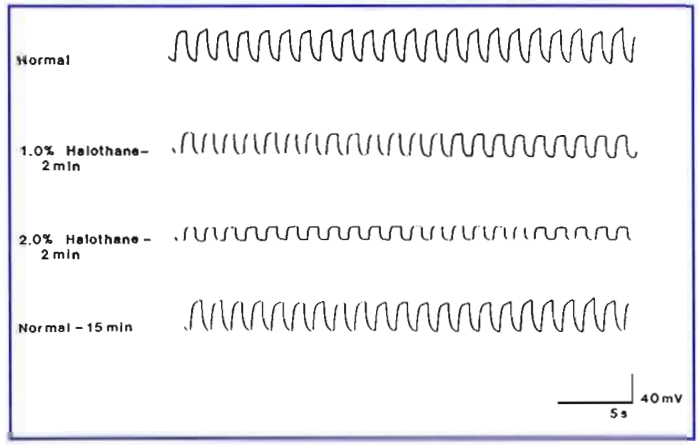

Fig 4 Concentration dependence of the conductance change seen on exposure of the neurone VV1 or 2 to different concentrations of halothane. There is a concentration-dependent reduction in the voltage drop across the membrane, which implies an increase in conductance across the membrane (from D Girdlestone, PhD. Thesis, University of Leeds, 1986).

One of the consequences of increased membrane conductance appears to be the reduction of coupling between electrically coupled neurones by volatile anaesthetics. The

simplest explanation for this is that that a general increase in membrane conductance, will cause current to flow preferentially through the cell membranes, rather than through the gap junctions between them. Of course the gap junctions can themselves be decoupled by rising $[Ca^{2+}]_i$ and we do not yet know whether this is a factor in the decoupling of the electrical synapses in the presence of volatile anaesthetics.

Chemical synapses are also key targets for general anaesthetics and they block the actions of many different transmitter systems. Recently, in conjunction with colleagues in Calgary, we have looked for the first time at the actions of halothane on peptidergic transmission at reconstructed identified synapses. We found that the excitatory and inhibitory actions of an identified neurone on different follower cells were mimicked by the signal molecule FMRFamide and that these connections were blocked by 2% halothane. Excitatory transmission was abolished at lower anaesthetic concentrations than was inhibitory transmission. Furthermore, the postsynaptic responses to exogenously applied FMRFamide in the presence of halothane, were quite different from one another: in 1% halothane the excitatory responses were substantially reduced or abolished, whilst the inhibitory responses were maintained and enhanced in duration and continued to be maintained, though at reduced amplitude, in concentrations of 4% halothane. It is probable that the ion channels or second messenger systems linked to these FRMFamide receptors were differentially affected by the anaesthetic. Current work in Franks and Lieb's laboratory suggests that $I_{K(An)}$ is also activated by FMRFamide.

In conclusion we can see that anaesthetic agents interact with membrane components both at the cell surface and intracellularly. It is probable that they modify many different conductances both directly and indirectly by alteration of metabolic processes, which themselves raise free $[Ca^{2+}]_i$ in a number of different preparations and may also alter the actions of other second messenger systems. As yet we do not know the real targets for anaesthetic actions and it is difficult to separate the genuine actions of anaesthetics from their side-effects. The fun goes on and there is still much to do!

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BSE eclipses other dementia research

An article argues that government money allocated for BSE research (projected at £24 million in 1997-8) would be 'infinitely more useful' if it were ploughed into investigating other more common dementia conditions such as Alzheimer's (£1.97 million last year).

THES 1266 *21 February 1997* p.2

Source: SPIN

Ode to an Academic Audit

Oh mockery of academe,
With goodness, measured by the ream,
Where audit for the "Chair" aloof,
May rest on firm financial proof!

Could Harvey, Newton, Darwin, Keynes
Find entry to these novel scenes?
Would they, as budding thinkers new,
Gain access to good peer review?

In Senate Court, the scene is droll,
Accountants now, take Monarch's role.
Some thinkers from the tumult flee -
This Alice's once found imagery.

Did Carroll, in his board and gown,
Predict the things, which make some frown?
Did he foresee these grand charades,
With College Boards, as packs of cards?

John Anon
A West London Medical School

DYNAMICS OF THE SWIMMING LAMPREY

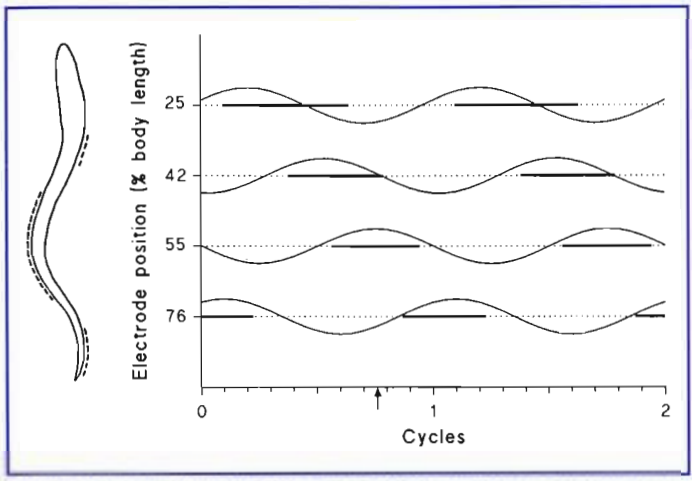

Fig 1. Relative timing of muscle activation and body curvature in a swimming lamprey. EMG electrodes placed superficially at 4 positions along the left side of the body (as viewed from above), at 25%, 42%, 55% and 76% of the body length, measured from the head. Solid bars represent EMG activity, while sinusoidal traces indicate extent of body curvature away from the left side, and hence relative muscle length at corresponding electrode positions. Sketch on the left indicates active muscle at the time indicated by the arrow on the x-axis. Data from Williams et al. 1989.

Most fish swim by passing waves of lateral bending along the body from the head toward the tail. Such waves are obvious to the eye in anguilliform swimmers, such as the eel and lamprey, in which nearly the entire body participates in the passage of the wave (See Fig 1). The occurrence of a travelling wave is harder to discern in most other fish, in which the lateral movement only becomes obvious in the tail region. How these movements generate thrust from the water to propel the fish forward has fascinated scientists for many years (Lighthill, 1969).

A curious travelling wave: muscle stimulation does not coincide with body curvature.

Early work based mainly on films of swimming fish (such as that of Gray, 1933) showed that the time course of the bending of the body at any particular point is roughly sinusoidal during steady swimming (See Fig 1). It was natural to assume that as the wave of bending passes down the body, the muscle is active on the concave side (where the muscle is shortening) and inactive on the convex side of the body (where the muscle is lengthening). Simultaneous recordings of electromyographic (EMG) signals and films of swimming lampreys have subsequently shown, however, that what is happening is more complicated than this. Just behind the gills, the swimming muscle is indeed stimulated primarily during shortening. As can be seen at the most rostral electrode position in Fig 1 (25%), EMG activity begins just before the muscle reaches its maximum length and continues throughout most of the shortening process. However, by the time the leading edge of the EMG signal has passed halfway down the body (see Fig 1, electrode position 55%), muscle stimulation starts halfway through the previous lengthening portion of the cycle and ends before the muscle is halfway through its shortening phase. Hence for a significant fraction of the cycle, muscle is active while it is being lengthened by external forces. Since the power generated by the muscle is given by the product of force and rate of shortening, the power will be negative if the muscle generates force while being lengthened.

Why do fish generate negative power in active muscles?

Muscle alone can provide the energy to power swimming. To understand the overall energy balance it is necessary to know what forces are being generated by the muscle during the swimming cycle. It has not been possible with existing technology to measure the muscle force in a swimming fish, so force has been measured in experiments on isolated fish muscle (Altringham & Johnston, 1990; Rome *et al*, 1993; Curtin & Woledge, 1996). Patterns of movement and electrical stimulation have been imposed on isolated muscle preparations so as to mimic what occurs during the intact animal's locomotion.

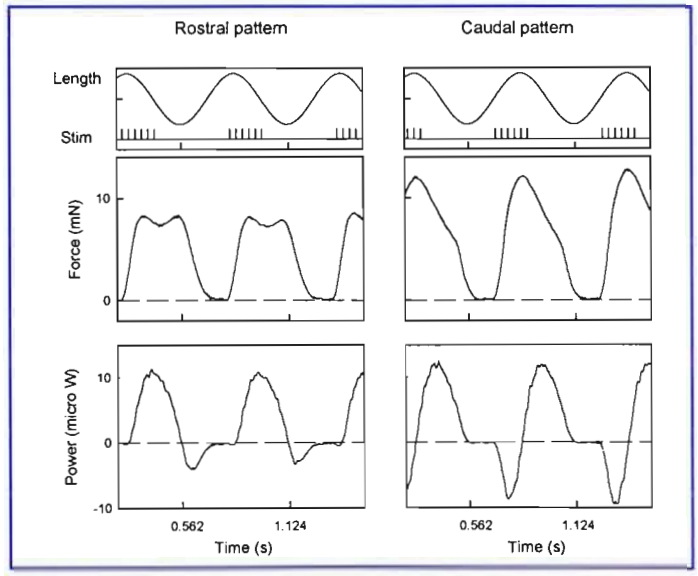

Fig 2. Force and power generated by isolated lamprey muscle during rhythmic activation. Sinusoidal length changes imposed with servo apparatus. Stimulation applied with similar timing to that occurring in more rostral (left panels) or caudal (right panels) parts of the body. Unpublished data, Curtin & Williams.

Fig 2 shows an example of one such experiment on isolated lamprey muscle, where the movement and stimulation patterns recorded at the rostral and at the caudal end during swimming were imposed, and power was calculated from measured force and movement. Only with positive power can muscle supply the mechanical energy for swimming, and yet significant amounts of negative power are produced, especially when the stimulus timing matches that occurring in the caudal half of a swimming lamprey. Negative power must be subtracted in the overall energy balance. So what is the function of the lengthening active muscle? Is it required as a brake to stop or minimise lengthening, or does it provide appropriate stiffness for the interactions between the body and the water? We don't know the answers to these questions because we don't know exactly what are the sources of the external forces that overcome the force generated by the muscle. Some must come from pressure forces generated in the water and some from passive recoil of connective tissue, notochord and skin.

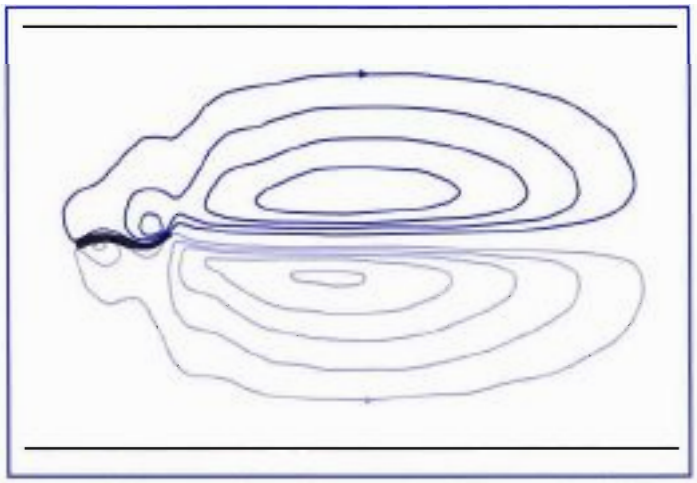

Fig 3. Fluid dynamics of anguilliform swimming in an enclosed tank, as viewed from above. From a standing start near the right-hand side of the diagram, the animal swims through 8 cycles of activity to the position shown. Blue lines are contours of instantaneous stream function, which indicate the structure of the two-dimensional fluid flow. Dark blue: clockwise flow; pale blue: anticlockwise. Unpublished data, Carling, Williams & Bowtell.

The lamprey moves the water and the water moves the lamprey: modelling the system.

To understand what the fish gains by relative timing which produces negative power, we must unravel the complex interactions amongst the muscle, the mechanical responses of the body of the fish, and the fluid dynamics of the water. In order to achieve this it is necessary to develop models of the fluid dynamics of swimming which account for viscous forces in the surrounding water as well as inertial forces propelling the creature along. Such models require large scale computations and the techniques of computational fluid mechanics to provide the necessary detail (Williams *et al*, 1995; Liu *et al*, 1996). Fig 3 shows the fluid flow around a model anguilliform creature which is swimming from the right to the left side of the tank, as viewed from above. Here only the changing body shape has been specified; the creature propels itself, accelerating and decelerating rhythmically in each cycle, in response to forces generated in the water by its changing body shape.

The whole picture

Rather than specifying the changing body shape (as for the computation illustrated in Fig 3), a mathematical description of a simplified anguilliform body has been developed. The model consists of a series of jointed rods connected with force-producing elements and elements of stiffness and damping. This model has successfully reproduced the behaviour of a lamprey on a slippery bench (Williams *et al*, 1995), but the real test will come when the differential equations of the body model are combined with those of the fluid mechanics to predict both the changes in body shape and the resulting swimming movements of the lamprey.

Although anguilliform swimming seems a relatively straightforward form of locomotion, its study involves understanding the complex interaction of many elements. Through a combination of physiological, mechanical and mathematical approaches, insight is being gained into the dynamics of lamprey swimming.

Acknowledgements

The muscle physiology research reported here was supported by the Wellcome Trust; the fluid dynamics work was supported by the Biotechnology and Biological Sciences Research Council.

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"Molecular Biology in Cardiovascular Research"

September 1 1997; University of Bristol; Wills Hall

A one-day Symposium focusing on "Molecular biology in Cardiovascular Research" will be held at the University of Bristol on Monday Sept 1, 1997 - immediately preceding a 3 day meeting of the Physiological Society in Bristol. Molecular biological techniques for investigating cellular function have made a huge impact on research over the last few years, and many of us now appreciate the immense power of these methods. There is a large collection of research groups in Bristol working in the Cardiovascular area (in Physiology, Pharmacology, Biochemistry, and also in Cardiac Surgery & Cardiology - together we form the "Bristol Heart Institute"). The objective of this symposium is to focus on cardiovascular research from a molecular biological aspect and will, we hope, have large national and also substantial local interest.

We have attracted many of the top workers in this field to talk at the symposium - Harry Fozzard (Na ion channels), Gary Yellen (K channels and arrhythmia), Ken Philipson (Na/Ca exchange), Chris Higgins (Cl channels and CF), Colin Nichols (modulators of K channels), Bob Meech (H channels), Burton Horowitz (smooth muscle K channels), Alan North (Purinergic receptors) and Andrew Halestrap (Lactic acid transport). We have also deliberately left one of the speaking slots open, in case a major discovery is made in the next 8 months, and then we can invite someone to talk on a "hot" topic! There will also be a poster session at the symposium, for those who would like to present data but do not have the opportunity to speak.

The symposium will be held at "Wills Hall of Residence" - a beautiful Oxbridge-style college just outside the centre of Bristol. There is a modern Conference Centre on site, accommodation will also be provided in the Hall. However, we are limited to 150 people, so send in your registration early ! The symposium is sponsored by the Physiological Society, British Heart Foundation, Axon Instruments, Pfizer and Smith, Kline & Beecham. Details of the Symposium and the main Physiological Society meeting can be found on the Bristol Department of Physiology Wen Site.
This is just one of five different symposia which will be held either before or after the Bristol Physiological Society meeting. Before the meeting there will be two other one-day symposia: "Neural mechanisms controlling respiration" organised by Dr Julian Paton, and "Gating of transmission in Sensorimotor pathways" organised by Dr Richard Apps. After the Physiological Society meeting there will be a one day symposium on "The Neuron in Tissue Culture" organised by Dr Laurie Haynes, and a two day meeting on "Myocardial Injury: Current knowledge and future directions" organised by Prof Andrew Halestrap & Dr Saadeh Suleiman (this is the annual meeting of the "British Society for Cardiovascular Research").

We hope to welcome a large number of you in Bristol between 1 and 5 Sept 1997!

Allan Levi, Phil Langton, Chris Garland (Cardiovascular Symposium organisers)

MEDIA FELLOWSHIPS

Wendy Purcell talks about her experiences with the BBC World Service Unit under the Media Fellowships Scheme

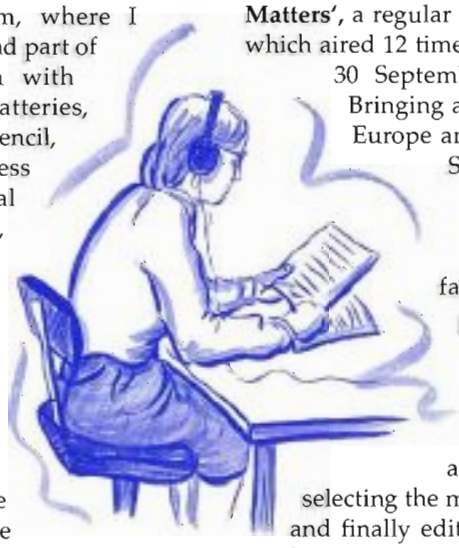
As a research scientist and academic manager working in a university, I had dealt with the press prior to my Media Fellowship. In conjunction with the university Press Office, I had issued several press releases about exciting developments in our research and duly responded to print and radio journalists. As Head of Division of Physiology, Pharmacology and Toxicology, I had also been called upon to discuss my academic areas. In particular, I recall sitting up between midnight and 2 am as part of a live discussion programme on drugs of abuse for Radio 5 Live. It was these experiences of communicating science to the general public that triggered my interest in applying for the Media Fellowships Scheme.

I spent a most enjoyable couple of months during Summer 1996 working as The Wellcome Trust media fellow with the BBC World Service Science Unit, under the auspices of the Media Fellowships scheme. Of the many and varied activities I undertook during this academic sabbatical, two are worthy of special note.

British Association
Promoting Science & Technology

Part of the 'hack pack'

The first, was my week at the British Association Annual Festival of Science, at the University of Birmingham, where I really felt like a journalist and part of the 'hack pack'. Laden with tape machines, tapes, batteries, microphone, notepad and pencil, I attended numerous press conferences and several public lectures; at each, asking questions and 'capturing' speakers for interview, and all with a pressure of time that was at once thrilling and stressful. Then there was the work of trying to entice interviewees (often shy ones!) back to our 'home room' either for a live interview down an ISDN line back to the studio or onto tape in time to edit and 'wire' the story back to base. All this was done in competition with other 'media hacks', who were often other BBC outlets! Every facet of the media was represented at the festival, all hungry for copy to fill blank paper or screens with words and images generated by active scientists; all the 'hacks' were there solely to help bring science to the public.



The BBC World Service output from the festival exceeded all previous records and was much appreciated by the many 'customers', both in News and the Vernacular Services. In total, a team of just four picked about 35 stories from the 400+ presentations and filed 21 despatches, 14 of them voiced, 11 for Newsdesk, 3 for Britain Today with 3 further illustrated despatches/packages for Britain Today; 21 packages for language services including 2 packages for Newsday, 3 live interviews and 2 live discussions for Newshour. In addition, for regular BBC World Service programmes, a special 14 item edition of 'Science in Action', a package and 2 interviews for 'Soundbyte', a package and 3 interviews for 'Discovery', an interview for 'Global Concerns', 4 interviews for 'Health Matters' and a scripted talk for 'Science View'. So working from 8 am to 10.30 pm each day, with a 'Balti' each evening paid dividends, although memories of a 'green curry' still linger!!

A producer in the making

The second was as **Producer of 'Health Matters'**, a regular World Service programme, which aired 12 times across the globe between 30 September and 3 October 1996. Bringing a programme to listeners in Europe and the Middle East, Africa, South Africa, Asia/Pacific and the Americas was an enormous challenge for me and a great leap of faith for the regular producer, who offered me the chance to 'take over' her programme. I was charged with picking the stories to cover, arranging the interviews, selecting the music, briefing the presenter and finally editing the programme, doing all the paperwork and writing a factsheet for listeners. My programme dealt with a test for Alzheimer's disease, genetic screening and bad breath! Altogether, this was a scary and

exhilarating opportunity. Sitting studio side, with 'cans' and deck saying 'And cue music!' was enormous fun, and a creative outlet for me. Putting together just 15 minutes of a programme took some days of work: liasing with external agencies such as the Alzheimer's Disease Society and the British Dental Association to ensure accuracy; dealing with the Gramphone Library to pick appropriate music (The Police 'Don't stand so close to me!' to link into the bad breath story) and then arranging studio time. I also had the chance to interview one of the guests and the daunting task of taking a razor blade to my own words - 'journalist edit thyself' - never easy! All in all, an exhausting and completely satisfying opportunity to bring science to the public across the world. What Media Fellow could ask for more!

Other experiences included interviewing scientists from all over the globe, writing packages on complex scientific issues for translation to a world audience, contributing to an educational programme on the A to Z of science, writing and voicing news despatches and editing out all the 'erms' from taped interviews! With chinagraph pencil and razor blade in hand, cutting a 30 minute interview to just one or two minutes certainly exercises ones editing skills!

"Hello, I'm calling from the BBC..."

From day one in the BBC World Service Science Unit, my fellowship was both fun and exhausting. All the staff in the unit were very supportive and generous with their time. After an interesting couple of days reading the output of the unit, listening to some of the programmes on tape and attending my first editors meeting I was trained to use the EDiT system. I was given my own News and Current Affairs password, work area in the computer system, telephone and desk and I was off. My first task was to get interviews with scientists who had published a paper in The Lancet about the higher number of girls born to parents exposed to dioxin pesticides after an accidental leak in Italy, so much so that the sex ratio was significantly altered. Telephone calls to Italy and then the Centre for Disease Control and Prevention, in Atlanta, USA, revealed that the authors were attending a conference, Dioxin '96, in Amsterdam. So after tracking down the conference office, and finding the hotels where the scientists were staying, an interview was duly arranged. I was amazed at how many 'doors' were opened by the words 'Hello, I'm calling from the BBC and ...'. Everyone was so helpful and supportive of our request to bring their story to the wider public.

Running my own stories

After this initiation, I was then introduced to the various outputs of the unit. From 'packages', which were 3-4 minute pieces of cue, narrative and actuality (tape inserts of speech/music), to 'despatches', one minute scripts and 'blurbs', short tasters put into the menu for language services to select longer pieces. Also, deadlines which although not quite yesterday, were fast and furious. So at the next editors meeting, I was given my own stories to run with and file. Sitting in a 'self-op' studio with an eager scientist at the other end of a telephone, to get a one minute taped piece - but conducting an interview for some 15-30 minutes was my next challenge. Setting up the studio, running the tape deck and trying to ask open-ended questions to scientists who were at once enthusiastic and reticent about making claims was indeed interesting! My stories included everything from bad breath to the age of the universe! 'Acid heads not so bright'; 'Bad breath: it's all in the mind?'; 'New understanding of cystic fibrosis'; 'A stressed mind in a sick body'; 'It's all in your genes: why worry?'; 'Tuberculosis: tackling a global emergency'; 'Babies prefer pop to classical music'; 'More than meets the eye?'; 'Amnesia? Some things you never forget'; 'Fungi used to control river blindness'; 'Why fungi matter'; 'Female hormones make you happy - men too!'; 'Dying stars used to date the universe'.

Shunning the media

One disappointing, and most revealing, experience during the fellowship was an interaction with scientists who had published an article in *Nature*. The paper provided a new insight into Alzheimer's disease and offered hope for novel therapeutic strategies to tackle this crippling condition. After approaching several of the authors, none would comment about the work without recourse to the senior author. When contacted, this scientist said she wished for the paper to speak for itself and did not want publicity. After explaining to her that the paper did indeed speak to other scientists, but that the general public (who incidentally funded her work through taxes!) were also worthy of consideration and would like to join us in understanding the implications of her teams work, she would not agree to an interview. For me, this served to highlight the problem with communicating science.

Trivializing science? No

Some scientists appear to be afraid of communicating with the media. There are suggestions from certain quarters (often scientists themselves !) that science has to be oversimplified, or somehow cheapened to appear in the public domain. There is only one way to deal with this criticism - ignore it, they're wrong! The efforts that the science journalists working at the BBC World Service Science Unit made to preserve scientific integrity, but promote understanding were enormous.

We, the scientists, need to remember why we are doing research, who funds it and that we have a duty to inform the public. We need to encourage scientists to climb down from their ivory towers, and remind them that the media and science journalists are there to help us make the climb. The Media Fellowship scheme is an excellent way of promoting this important activity. Seeing the other side of the fence during my time with the BBC World Service Science Unit has encouraged me to promote the public understanding of science in my own work and to chivvy often reluctant colleagues to do the same.

As an academic engaged in teaching, learning and research, I am often called upon to 'translate' complex issues for communication to students, colleagues and peers orally and in writing. Tasks which are shared with science journalists. The fellowship afforded opportunities to further develop my communication skills and share my enthusiasm for science with others. Special thanks go to all at the BBC World Service Science Unit.

Wendy Purcell
Head of Division of Physiology, Pharmacology & Toxicology
Deputy Director of Cellular Toxicology Unit
University of Hertfordshire

IT WAS A PERFECT PIECE OF CALAMARI

"Deep fried to a golden brown, curled invitingly around bright-yellow lemon wedges"

I have been frying squid since I was fourteen and I thought I knew everything there was to know about it. [My favourite Greek restaurant] 'Its Greek To Me' proved me wrong. Their calamari compared to my best efforts the way a bottle of Chateau Rothschild compares to a cheap carafe of Gallo. And the damnable thing was, I couldn't figure out how they were doing it. Unfortunately 'It's Greek To Me' never shared recipes with the public. Even for fried squid.

Usually I ate there, but today I had ordered it to go. And today, as I bit into it, sitting behind the wheel of my rusted-out Honda Civic parked facing frozen Lake Calhoun in downtown Minneapolis, I experienced a revelation. As the squid filled my mouth, everything else fell away... An image of a jar of Jif was filling my mind. Then something like a striped paper bag at a circus, a time a similar flavour flooded my senses. "It tastes like... tastes like.. PEANUTS" I fairly shouted to myself. Peanuts! They must be cooking it in peanut oil. That's it. That's the secret...

Scents conjure up memories so quickly and vividly...memories can carry smell into our consciousness...

The secret of the calamari had been literally, right under my nose many times, but I didn't get it until I took the dish out of the restaurant. When I'd eaten it at one of their tables, bathed in the fragrance of roast lamb, onions and rosemary, I hadn't been able to notice it... Smell is a subtle thing. A few molecules rising through the nasal passages, making contact with the brain - what a difference they make.

'It was Greek To Me' Fried Calamari

1 lb. Cleaned squid, including both tubes and tentacles
1 cup all-purpose wheat flour
$^1/_2$cup peanut oil, preferably of hearty flavour
$^1/_2$cup water
Juice 1 lemon
Salt and pepper

Marinate squid in water and lemon juice for about 1 hour in refrigerator. Dredge pieces of calamari through the flour mixture thoroughly coating each side and fry in peanut oil for about ten minutes, until you see a golden crust more than halfway up the sides of the squid. Turn the squid and fry it until the other side is browned - about three minutes. Serve with lemon wedges, over hot rice or warm pitta bread.

Extracts from an essay by Alice Cascorbi about how she set out to replicate an elusive recipe for squid. Http://natsci.ucsc.edu/scicom/SciNotes/9502/squid.html

With courtesy of John Chad whilst surfing the Internet for 'squid pieces'

SYMPOSIUM ON RESPIRATORY CONTROL MECHANISMS AND SENSATIONS: DELHI AND BHARATPUR JANUARY 6-7 1997

John Widdicombe and I had been having some lively discussion through letters for about nine years, about sensory mechanisms underlying cough. Finally last year we agreed that we should have a small symposium on "Respiratory Control Mechanisms and Sensations" in Delhi in January 1997 and proceeded to get together people who seldom (or never!) saw eye-to-eye on mechanisms of cough and dyspnoea. The result was a two day symposium which turned out to be most enjoyable and stimulating. The speakers were: Ashima Anand (Delhi), Robert Banzett (Boston), Balram Bhargave (Delhi), Abe Guz (London), Kieran Killian (Hamilton),

Tea and coffee were freely available throughout the "formal" proceedings at the Bird Sanctuary

Speakers at the symposium

Sukhamay Lahiri (Philadelphia), Haq Nizamie (Ranchi), Autar Paintal (Delhi), Nanduri Prabhakar (Cleveland), Hans Raj (Delhi), Krishnan Ravi (Delhi), Vijay Singh (Delhi), Susan Ward (London) and John Widdicombe (London).

The venue of the symposium was the Vallabhbhai Patel Chest Institute of Delhi University. However on the second day we went to the Bharatpur bird sanctuary (about 150 km from Delhi), and I gave a modified poster presentation on "Control of ventilation and heart rate during rapid locomotion"; this was in order to remind us that through the ages mammals could have had few possibilities of running rapidly (a basic need for survival) without interruption for more than 50 to 100 metres through forested areas. The final discussion was held after dinner. Abe Guz did a splendid job chairing this session which finally brought opposing views closer and established the great need to develop simpler methods of anaesthetising the vagi of humans.

Ashima and I hope that the proceedings will become available before long at cost price to members of physiological societies and to students. Those interested should write to me (address in Grey Book; Fax: 91-11-7257471).

Autar Paintal
DST Centre for Visceral Mechanisms
Vallabhbhai Patel Chest Institute
India

Autar Paintal deliberates with his modern visual aids

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March 1997 Vol. 499 part 2

March 1997 Vol. 499 part 3

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Experimental Physiology

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Mini Review Articles

Full-length Papers

Physiological Society Symposium: Impaired Endothelial and Smooth Muscle Cell Function in Oxidative Stress

Physiological Society Symposium: Fetal—Placental Interactions

Rapid Communications

No notice is carried for more than three successive editions. Notices are starred so that readers can see at a glance whether this is the first (one star) or final (three stars) appearance of the notice. Notices for the Autumn 1997 edition (to be distributed on 25 July) should reach the Administration Office by 9 June.

Open Meeting at The Royal Society
DISCUSSION MEETING
AGEING: SCIENCE, MEDICINE AND SOCIETY
7-8 May 1997
Organised by Dr R Holliday, Professor J Grimley Evans, Professor T B L Kirkwood, Dr P Laslett and Professor L Tyler. Further information from the Science Promotion Section, The Royal Society, 6 Carlton House Terrace, London SW1Y 5AG. Tel: 0171 839 5561 ext 2574/2575, fax: 0171 930 2170, WWW address: http://britac3.britac.ac.uk/rs/ ***

TRAINING COURSES IN CELL CULTURE FOR NEUROSCIENCE
11-16 May & 14-19 December 1997, University of Bristol
An intensive training course including lectures, seminars and 25 hours' hands-on practical work under supervision. Theory and application of good tissue culture practice, handling neural cell lines, instruction in dissection and primary culture techniques for the peripheral and central nervous system from basic to advanced level. Includes cell typing, transduction and hybridoma methodology. Suitable for neuroscientists with little or no experience in tissue culture methods.
Sample programme and further information from Dr L W Haynes, School of Biological Sciences, University of Bristol, Woodland Road, Bristol BS8 1UG. Tel: 0117 928 8656, fax: 0117 925 7374, email: L.Haynes@Bristol.ac.uk*

FETAL AND NEONATAL PHYSIOLOGY SYMPOSIUM
in association with the IUPS Congress
25-29 June 1997, Cambridge
This symposium has been organised by the Fetal Commission of the IUPS and will contain invited lecturers, oral communications and poster presentations. It will include eight sessions: fetal programming, fetal endocrine development, placental structure and function, growth and metabolism, cardiovascular development, fetal lung and respiratory control, fetal brain, transition at birth.
Further information from Mrs Sharon Holder, R & W Publications (Newmarket) Ltd, Goodwin House, Willie Snaith Road, Newmarket, Suffolk CB8 7SQ. Tel: 01638 667600, fax: 01638 667229. ***

International School of Biophysics "A. Borsellino"
NEURONAL CIRCUITS AND NETWORKS
15-27 June 1997
Ettore Majorana Centre, Erice, Italy
The school will present an updated review of neuronal mechanisms underlying brain functions, and is particularly suited to students from different scientific backgrounds.
Further information from Vincent Torre, SISSA, Via Beirut 2, 34014 Trieste, Italy.
Tel: +39-40-22 40 470, fax: +39-40-37 87 249, email: torre @sissa.it, WWW address: http://www.sissa.it/~torre/ ***

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

BRAIN & MOVEMENT
A symposium to be held immediately after the IUPS Congress in St Petersberg
6-10 July 1997
Moscow, Russia
Topics will include central pattern generators, mechanisms of interlimb co-ordination, adaptive capacities of spinal cord in motor control, supraspinal mechanisms of motor control, posture and locomotion, motor learning and modelling of motor control. Registration fees: $300; students $100.
Abstract submission: 1 February 1997.
Further information from Elena Biryukova, Institute of Higher Nervous Activity & Neurophysiology, RAS, Butlerov str 5a, 117865 Moscow, Russia.
Fax: +7 338 85 00.***

EUROPEAN PANCREATIC CLUB 29TH ANNUAL MEETING
9-12 July 1997
King's College, London
Further information from Dr Giovanni Mann, President, European Pancreatic Club, Biomedical Sciences Division, King's College London, Campden Hill Road, London W8 7AH. Email: g.mann@kcl.ac.uk or Ms Theresa Potter, Congress Secretariat, tel/fax: 0171 333 4371, email: theresa.potter@kcl.ac.uk ***

INTERNATIONAL POTASSIUM CHANNEL CONFERENCE
17-19 July 1997
University of Ulm, Germany
This conference will bring together many experts in the field of potassium channels to present and discuss the most recent developments in potassium channel research including structure-function expression/localization/diversity as well as regulation, modulation and pharmacology of potassium channels. There will be twenty invited speakers and participants will also able to give poster presentations. The deadline for submission of abstracts, which will appear as an official supplement to The European Journal of Physiology (Pflügers Archiv), is 9 May 1997.
Further information and abstract forms from Prof Stephan Grissmer, Dept of Applied Physiology, Universität Ulm, Albert-Einstein-Allee 11, D-89081 Ulm, Germany. Fax: +49 731 502 3260, email: stephan.grissmer@medizin.uni-ulm.de ***

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

THIRD INTERNATIONAL SYMPOSIUM ON RESEARCH FOR AQUACULTURE: FUNDAMENTAL & APPLIED ASPECTS
24-27 August 1997
Barcelona, Spain
Scientific sessions will include reproduction, nutrition & metabolism, growth & development, pathology, applied research on aquaculture, and a free session on comparative physiology & biochemistry. Sessions will comprise plenary lectures, state of the art, oral communications and poster presentations. There will also be workshops on specific subjects related to the sessions.
A satellite Symposium on Insulin and IGF superfamily peptides and related molecules is planned for 28 August 1997 in Barcelona.
Further information from Joaquim Gutierrez, Dept of Physiology, Faculty of Biology, University of Barcelona, 08028 Barcelona, Spain. Tel: +34 3 402 1532, fax: +34 3 411 0358, email: joaquim@porthos.bio.ub.es **

Meeting of the British Society for Cardiovascular Research
MYOCARDIAL INJURY: PRESENT KNOWLEDGE AND FUTURE DIRECTIONS
5-6 September 1997, Bristol
Further information from Dr M-S Suleiman, Bristol Heart Institute, University Department of Cardiac Surgery, Bristol Royal Infirmary, Bristol BS2 8HW. Fax: 0117 928 3581, email: M.S.Suleiman@bris.ac.uk **

THE NEURON IN TISSUE CULTURE
One-day symposium sponsored by Becton Dickinson (UK) Ltd, The British Neuroscience Association & the European Tissue Culture Society
5 September 1997, Bristol
Plenary and keynote lectures on progress in the physiology, neuropharmacology and developmental biology of the neuron in vitro. Free communications are invited for poster presentation; selected authors will be offered an oral presentation.
Further information about registration, submission of abstracts and accommodation from Dr L W Haynes (address given above) or Mr Paul Eros, Becton Dickinson (UK) Ltd, Between Towns Road, Oxford OX4 3LY. Tel: 01865 748844, fax: 01865 781578. *

EUROPEAN WORKING GROUP ON CARDIAC CELLULAR ELECTROPHYSIOLOGY
21st Meeting
12-13 September 1997
Tours, France
Pre-registration forms and information from Professor Jorge Argibay, CNRS physiologie des cellules cardiaques et vasculaires, Faculté des sciences, Parc de Grandmont, 37200 Tours, France. Tel: +33 47 36 7012, fax: +33 47 36 7112, email: argibay@univ-tours.fr or from WWW address: http://www.univ-tours.fr/garnier/ccv_home.html *

TITLE	PURPOSE	ELIGIBILITY	AWARDS	APPLICATIONS
AFFILIATE TRAVEL GRANT SCHEME	To enable Affiliates to attend meetings and symposia overseas	Affiliates in the British Isles who have not already received a grant under this scheme (Eligibility continues for a year after election to Membership of the Society)	Up to £600	Applications are considered at the end of January, March, May, July, September and November
BENEVOLENT FUND	To assist persons who have contributed to the advancement of Physiology and are in necessitous circumstances	Physiologists, their staff and dependents	Depends on circumstances	Applications are reviewed immediately on receipt
DALE FUND	To promote new physiological research in the British Isles	Physiologists working in the British Isles	Travel for collaborative research, learning new techniques, practical workshops and training courses: up to £800. Travel to conferences and symposia: up to £300	Applications are considered throughout the year
EASTERN EUROPEAN AND THIRD WORLD SUPPORT SCHEME	To support centres of scientific excellence where high quality physiological research is threatened by lack of resources	Centres of physiological research in Eastern European and Third World countries demonstrating scientific excellence and financial need	Up to £10,000 per annum, for up to three years	Applications are considered at the end of August
RUSHTON FUND	To promote new physiological research in the British Isles	Young physiologists working in the British Isles who are not yet Members of the Society	Travel grants for collaborative research, learning new techniques, practical workshops and training courses: up to £500	Applications are considered throughout the year
VACATION STUDENTSHIPS	To enable undergraduates to undertake research projects in the summer vacation	Undergraduates in the UK and Eire in their second year or above, for work in the laboratory of a Member of the Society	Up to £500, for maintenance (no support available for consumables or other research expenses)	Applications must be submitted by 30 April

The Physiological Society

VACATION STUDENTSHIP SCHEME APPLICATION FORM

Details of Host Applicant

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

Address .....

.....

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

Three recent publications:

Details of Student

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

Degree or other course currently being studied:

Course Title .....

Department .....

Institution .....

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

Previous Studies and Relevant Work Experience

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

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

.....

.....

.....

.....

Details of Proposed Research Project

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

Summary of Costs

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

Living expenses per week: £.....

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

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

Funding sought or received from other sources for this project

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

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

.....

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

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

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

Trinity College Meeting....

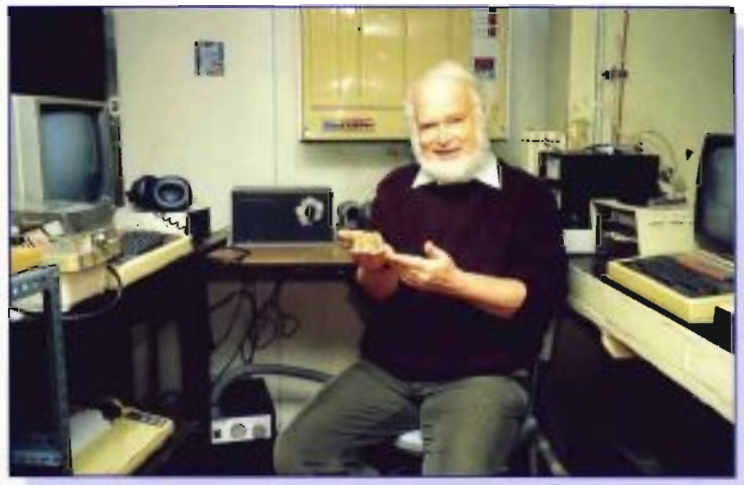
Photography by Martin Rosenberg

Dr Marina Lynch

Physiology front door

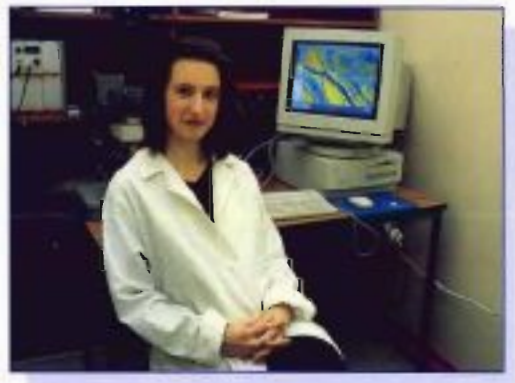
Dr Helen Harty

(L-R) Siobhan McBennet, Ciara Murray, Anne Kelly, Patricia Mullany, Veronica Campbell and Eamon O'Donnell



Dr Fred Andrews

(L-R) Grainne Boylan and Dr Mary McElroy



Dr Veronica Campbell

Back cover: Palinurus elephas, Courtesy of Professor Roddy Williamson.