Alison Brading, who died on 7 January 2011, was a well-known and much loved figure in The Physiological Society who will be sorely missed. To those who worked with her she was a source of inspiration, a vast fund of enthusiasm and scientific knowledge, and a loyal and supportive friend. Her services to The Society were extensive. She was elected in 1970, at a time when membership was strictly limited, peer-reviewed in competition with others, and largely male. She served on Council, was an editor of The Journal of Physiology, and Chairman of the editorial board of Physiological News between 1990 and 1992. She was elected to Honorary Membership in 2008.

Although stricken with polio in her late teens, she was fiercely independent and determined to lead a normal academic life. She showed indomitable spirit in dealing with her disability. Her early training was in Zoology at Bristol University. She came to the Department of Pharmacology, Oxford, to work with Professor Edith Bülbring of whom she became a life-long friend, establishing a trust to support young scientists when Edith died. She was a familiar and respected personality at Physiological Society Meetings, Lady Margaret Hall and the Pharmacology Department. Throughout her life, she made substantial contributions to our understanding of smooth muscle function.

Alison was born in 1939. Her father was an army officer and so, as was common in such cases, she attended boarding school while her father was posted abroad. As well as being academically gifted at school, she was also a superb athlete, winning the Victor Ludorum at Maynard School, Exeter, for her athletic achievements. During the long vacations she would visit her parents in Nigeria. She made three such trips, usually with her brother Roy but tragically on the last she contracted polio, which caused severe disease. She was hospitalised in an iron lung, first in Africa and then, after an emergency flight home, in England. She was fortunate to recover, but suffered permanent and considerable loss of motor function. She was unable to walk unaided and had restricted use of her respiratory muscles, which caused her particular discomfort with bronchial infections and even the common cold. All this was a considerable blow to someone who, until then, had been outstandingly fit and able. There followed a prolonged period of convalescence, which involved operations to improve the motor function of her hands.

Before Alison’s last trip to Africa she had applied for, and been accepted, to read medicine at Oxford. However, after two years of convalescence, she was informed that she would not be permitted to enter the medical course, because of her disability. Her subsequent life then involved an ongoing fight to remain independent and mobile. In her early years, with considerable will-power, she was able to walk distances using crutches (her ‘sticks’, as she called them) which placed considerable demand on her forearms and elbows. As she got older, however, walking became increasingly difficult, and she was forced to resort more to a wheelchair. Nevertheless she was supreme captain of this transport, issuing firm and precise commands to whosoever was pushing at the time. Alison was also undeterred by the prospect of international travel. She frequently went abroad, whenever possible with friends or relatives. Thus, she was able to visit most international scientific meetings to which she was invited. In 1976, for example, she travelled to Leningrad, Moscow and Kiev with Edith Bülbring and Tom Bolton, visiting palaces and places of local interest, and finally contributing to the Smooth Muscle Symposium in Kiev organised by Mykhailo Shuba. Alison also travelled extensively in Europe, the United States and the Far East, including Taiwan and Japan, where she had good friends and contacts. Even in the final year before her death she travelled to a scientific meeting in Japan.

Not discouraged by her early rejection from Oxford, Alison applied to read for a BSc in Zoology at Bristol and was accepted. She obtained a first-class degree and then chose to study for a PhD with Peter Caldwell, an expert membrane biophysicist, investigating the somatic muscles of the nematode roundworm Ascaris lubricoides. She qualified in 1965, but still held Oxford in her sights. It succumbed when she joined Professor Edith Bülbring at the Oxford Department of Pharmacology, as a post-doctoral research assistant, a position which continued until 1971 when she was appointed as a Departmental
Demonstrator, although she retained a close association with Edith. She was elected Fellow and Tutor in Physiology at Lady Margaret Hall in 1967 and University Lecturer in 1972; she became Professor of Pharmacology in 1996 and Emeritus Fellow at Lady Margaret Hall in 2005.

Although Alison’s PhD training was on nematode somatic muscle, all her subsequent work was in the field of mammalian smooth muscle. While in Edith Bülbring’s research group, she began to elucidate mechanisms that generate ionic asymmetry across the cell membrane. In smooth muscle this was a largely unexplored and open field. Although the Bülbring research group was internationally pre-eminent for the study of smooth muscle receptors and contractility, and for the first electrophysiological studies of smooth muscle using sharp microelectrodes, little was known about carrier-mediated ion transport. Alison’s work initially involved using radioactive tracers and flame photometry. The task proved difficult as smooth muscle cells are generally long and thin with transverse dimensions not greatly different in size from those of the local extracellular space; thus it can be difficult to identify ion fluxes specifically across the plasmalemma, especially when ion diffusion is slowed by binding to extracellular sites. Measurements of intracellular ion concentrations also required elaborate correction for the extracellular space.

Alison’s meticulous experimental approach set the scene for a more rigorous application, particularly of the radiotracer technique. Although initially part of the Bülbring group, she first published her work independently with Tadao Tomita from Nagoya, Johan Setekleiv from Oslo, and Alan Jones from Philadelphia who were visiting workers at the time. Edith did not have the now popular habit (and funding necessity) of group leaders adding their name to publications from individual members. As a result, Alison published only a couple of original papers with Edith although she did co-edit a book, ‘Smooth Muscle’, a comprehensive summary of smooth muscle research, with Edith (and T. Tomita and A. W. Jones) in 1970 and a later edition of this book in 1981. Alison’s early pioneering flux work was summarised in her paper, presented in a symposium at the Royal Society (Brading, 1973). Another brief publication from this period was with Tadao Tomita. They reported, at a meeting of The Physiological Society and published as a refereed abstract, that smooth muscle can generate action potentials in low sodium solution; indeed the rate of rise and overshoot was greater when extracellular Na⁺ concentration was reduced (Fig. 1). This was a crucial step in the discovery that smooth muscles generally have calcium-based rather than sodium-based action potentials. A full paper followed (Brading et al. 1969). The report was thus the forerunner of a major branch of smooth muscle physiology and pharmacology, including the clinical use of calcium antagonist drugs that influence smooth muscle contraction.

The analysis of ion fluxes and intracellular concentration continued to be a principal focus when Alison established her own laboratory in the Pharmacology Department, following her tenured appointment. She was joined by her first PhD student, Jonathan Widdicombe, and together they studied Na⁺-dependent ion transport across the plasma membrane. These included Na⁺/Na⁺, Na⁺/K⁺ and Na⁺/Ca²⁺ transport mechanisms.

The problems associated with radiotracer and flame photometric techniques continued to dog the smooth muscle field. Another technique, however, for recording local ion concentration was coming on-stream through the work of Roger Thomas in Bristol. He had developed the use of ion-selective microelectrodes (ISMs) for monitoring intracellular Na⁺, Cl⁻ and pH directly inside snail neurones. Alison was joined for a period by a post-doctoral assistant, Richard Vaughan-Jones, from the Thomas laboratory. Vaughan-Jones

**Figure 1.** a and d, action potentials, spontaneous and evoked, in normal [Na⁺], (Krebs solution) and b, c and e, in 10 mM [Na⁺], (sucrose substitution). Note the increase in rate of rise and overshoot in low [Na⁺], indicating that the action potential is calcium based. Taken from Brading et al. (1969).
started to use ISMs initially to measure intracellular Cl– and H+ ion concentrations (with Tom Bolton) in skeletal muscle, and later in cardiac muscle. Alison was joined a few years later by a further post-doctoral assistant, Claire Aickin, again from the Thomas stable. Claire extended the ISM technique to include mammalian smooth muscle. Applying the technique was difficult enough in tissues with relatively large cells, such as those of skeletal muscle and cardiac Purkinje fibres. Adapting the technique to the small contractile cells of smooth muscle required true perseverance, and not inconsiderable serendipity. But with Alison’s enthusiasm and support, and Claire’s expertise, it was achieved. This led to a major series of studies on the membrane transport of Cl–, H+ and Na+ ions, including the first description in smooth muscle of the Cl–/HCO3– exchanger and its participation in the process of intracellular pH regulation. Further ISM recordings of intracellular Na+ led to important functional work on the Na+/Ca2+ exchanger (Fig. 2; Brading et al. 1987), a transporter whose expression in smooth muscle had previously been questioned. This ISM work in the 1980s (and reviewed in Brading & Aickin, 1990), produced several milestone publications on the fundamental physiology of smooth muscles.

Alison’s work on Na+/Ca2+ exchange was paralleled by her studies of smooth muscle contractile activity, particularly the role of the sarcoplasmic reticulum as a receptor-operated store of releasable Ca2+. Indeed, she was among the first to moot for smooth muscle the possibility of capacitative entry of extracellular Ca2+ directly into intracellular stores as a means of rapid refilling, a phenomenon that to the present day is still being researched and debated. Indeed, a later doctoral student, Anant Parekh, now Professor of Physiology at Oxford, cut his teeth in Alison’s laboratory on studies of Ca2+ regulation, and has gone on to specialise in the study, in various cell types, of the ICRAC (capacitative entry) channel.

The 1980s saw Alison being joined by many visiting scientists from abroad, and her interest moved increasingly from taenia coli to other smooth muscles such as vas deferens and ureter. She formed collaborations with surgeons and clinical urologists, such as Jacek Mostwin, Gary Sibley and Mark Speakman, and later with others at the John Radcliffe Hospital in Oxford. This shift into more clinically oriented research began with investigations of the overactive bladder and the resulting incontinence it causes. The quest, an excellent example of a successful translational research axis for a basic scientist (and long before it was fashionable or politically encouraged) would occupy Alison for the next twenty-five years. Her research involved examination of bladder innervation and the effects of potentially useful drugs to relax the detrusor muscle. In addition, with the help of her clinical colleagues she studied the effects of partial outflow obstruction on the pig bladder. While collaborating on her clinical studies, Alison also investigated the fundamental cellular properties of detrusor muscles, thus helping to fuse more effectively both basic and clinical science. This work involved electrophysiological investigations by doctoral, postdoctoral and visiting academics such as Inoue, Burdyga, Teramoto, Nakayama, Parekh, Bramich and many others. Investigations were also extended to smooth muscles from a variety of other organs, and from a widening range of species, including pigs and even humans.

In addition to her research on the bladder, Alison in later years studied the properties and responses to drugs of anorectal smooth muscles. As with much of her earlier work, this was a largely unexplored area, ripe for development. Her interest focused on two areas: to what

![Figure 2. Sodium–calcium exchange in ureter of guinea-pig. Raising [Ca2+], hyperpolarizes the membrane, causes contraction due to the increase in calcium entry, and a reciprocal reduction in [Na+]. Lowering [Na+], allows the Na+/Ca2+ exchanger to hyperpolarize the membrane, while the reduction in calcium extrusion results in contraction (Fig. 1 from Brading et al. 1987).](image-url)
extent derangement of bladder (detrusor) function was associated with alterations in anorectal smooth muscle function, and whether diseases such as irritable bowel syndrome were associated with changes in the properties of anorectal smooth muscle. Many of her studies were again collaborative, notably with Mortensen, a consultant gastro-intestinal surgeon at the John Radcliffe Hospital. Most recently Alison studied the innervation and function of the anal sphincter and rectum in collaboration with Radomirov and Ivancheva of the Institute of Neurobiology, Bulgarian Academy of Sciences.

In her determination to be mobile after her convalescence from polio, Alison learned to drive a car in which the controls were modified. Although this could sometimes be rather scary for an unwary passenger, it enabled Alison to lead an essentially independent life, eventually commuting between her Department in Oxford and her cosy cottage in the outlying village of Thrupp. In later years, her relatives moved in next door, so that family members were gathered around her house. The house bordered the Oxford canal, and so she bought a narrow-boat and enjoyed trips in the company of friends and students. Just as she was captain of her wheel-chair, she was captain of her boat, issuing firm commands from the wheel-house, with crew members dispatched regularly onto the towpath to operate lock-gates and wave her through. For those involved, the trips were immensely sociable, and always memorable.

The job of a Tutorial Fellow at Oxford requires maintaining a research group, but also admitting, teaching and mentoring undergraduate students, in Alison’s case in Medicine and Physiological Sciences at Lady Margaret Hall. Her dedication to her research group was matched by her commitment to her College and her undergraduate charges. She was an extremely gifted and vigorous teacher, who talked with, rather than at, her students. She did not tolerate fools gladly, but she was genuinely caring about students’ welfare and academic development. And she was passionate about enthusing students with an understanding and respect for science. That was also true of her approach to her own scientific learning. In her early years in the Department of Pharmacology at Oxford it was not uncommon for Alison to appear suddenly on her ‘sticks’ in one’s office, enthusing about a marvellous paper she had just read in the most recent edition of The Journal of Physiology, often in an area far outside her own expertise. For her, it was a lifelong love affair with science, and with the teaching of science.

In the end, Alison was defeated physically by her disability. She contracted pneumonia and, with her respiratory difficulties, this was hard to fight for a prolonged period. But Alison’s spirit, even during this last illness, was never dimmed. In all, she should be celebrated for her tenacity in the face of early misfortune, for her energy and indomitable enthusiasm, for her loyalty and support of colleagues and friends, and for her broad and far reaching scientific and academic achievements. There is no doubt The Physiological Society has been the better for her.

**References**


