Professor Roger Woledge was an eminent physiologist who made major contributions to the knowledge and understanding of an unusually wide range of topics in muscle physiology. He was instrumental in major developments in muscle energetics research from the 1960s until his death. His published works span 54 years and include those which provide a direct link between classical work on muscle thermodynamics and current thinking, in which energetics is integral to the understanding of the molecular events underlying muscle contraction.

His father, Brian, was Head of French at University College London (UCL) and his mother, Christine, was as also a very good linguist, but both Roger and his sister, Jane, were encouraged to study science. An early passion for horses that stayed with him for the rest of his life evoked a vague ambition to become a vet but Roger went to UCL to study Physiology following an informal interview with G.L. Brown, then Head of Department. He enjoyed practical sessions more than lectures, partly due to partial hearing loss starting from an early age. His excitement
for science really developed in his final year when he was encouraged to read up-to-date research literature which he found more inspiring than the textbooks. Roger always liked quantitative work and excelled at physics and mathematics, despite not having A-level maths. As an undergraduate he found that the dry abstraction of physics could merge with biology, for example in muscle thermodynamics, to produce the logic of physiology he found compelling.

He remained in the UCL Department of Physiology until his retirement, becoming Professor of Experimental Physiology and subsequently Head of Department. He became Director of the newly formed UCL Institute of Human Performance based at the National Orthopaedic Hospital in Stanmore in 1994. Although retirement of university academic staff was at that time compulsory at the age of 65, this made little difference to Roger’s working life. He continued his productive research career, particularly with colleagues at Imperial and King’s Colleges, Queen Mary University of London (QMUL) and the Royal Veterinary College (RVC) until his death.

While he was always based in London, Roger liked participating in conferences abroad and working with research students. Consequently he formed many very successful research collaborations. We can describe only small fraction of them in the space available here, but we hope to give some idea of the breadth of this research and influence.

**Research Career**

Following his 1st degree in 1959 Roger was awarded a Medical Research Council Scholarship for research training under the supervision of AV Hill, who was a Nobel Prize winner and dominant figure in British physiology in the first half of the 20th Century. AV oversaw the start of Roger’s life-long fascination for muscle research. His early work involved measuring the heat produced during contraction in frog muscle, followed by measurements on tortoise muscle, and in later years, mouse, lizard, fish and wild rabbit muscle. AV believed that “if you are any good” there was no need to do a PhD but Roger was persuaded that this was the appropriate route to an academic career by Doug Wilkie, who acted as his PhD supervisor. Roger was the Sharpey Scholar in the Department of Physiology (1962-1965) while doing his PhD. The work resulted in one of the field’s iconic papers (1); it describes the slow contractile properties and high efficiency of tortoise muscle which remains the most efficient muscle studied. This paper introduced the now widely accepted idea that high power output and high efficiency are mutually exclusive properties of striated muscle. Roger interpreted the contrasting energetic properties of frog and tortoise muscle in terms of AF Huxley’s 1957 two-state cross-bridge model. The use of mathematical models continued throughout his career. He much enjoyed the challenges of both laboratory and modelling research.

In the 1970s muscle energetics research was focused on untangling the so-called “energy gap”: more heat and work produced during contraction than could be accounted for by immediate ATP turnover. Roger, mostly working with his life-long collaborator Nancy Curtin, accurately measured both biochemical changes and energy output from frog muscle under a variety of experimental conditions (2). A key piece of solving the puzzle was the value of the heat and work expected from ATP breakdown and resynthesis from phosphocreatine. This required knowledge of the molar enthalpy of phosphocreatine breakdown under physiological
conditions which Roger's group determined using in vitro calorimetry, quite a methodological leap for a physiologist. From these experiments and others, it became clear that a large part of the unexplained energy output (the "energy gap") was due to the heat that accompanied the binding of Ca\(^{2+}\) to troponin and parvalbumin, the latter being unknown when the experiments started, rather than concurrent ATP use. Roger's work on muscle energetics extended from the cellular to the molecular level in experiments with Takao Kodama. They used calorimetry to quantify the thermodynamics of steps within the actin-myosin cycle, using purified proteins (3). In the 2000s, Roger returned to work on the biochemistry-energy link with Mike Ferenzi, Tim West and others. These experiments represented an amalgam of the earlier work on cellular energetics, calorimetry and mathematical modelling of the cross-bridge cycle. They took advantage of newly-developed fluorescent probes for the ATP metabolites Pi and ADP to examine on a millisecond time-scale the energetic events in the cross-bridge cycle (4).

In 1985 Roger published the classic monograph "Energetic Aspects of Muscle Contraction" with co-authors Nancy Curtin and Earl Homsher (5). This was the publication in which Roger took most pride. From about the time of the publication of the monograph, Roger's attention turned increasingly to understanding the energetics of muscle contracting during normal in vivo function, which was an undeveloped field at the time. The standard muscle physiologist's aim was to explore intracellular mechanisms of the cross-bridge cycle and activation by Ca\(^{2+}\), which entailed very reductionist experimental designs: constant speeds of shortening, fused tetanic contractions etc., which are not the usual patterns during muscle function in vivo. During a research visit to the Marine Biological Association in Plymouth he and Nancy Curtin, following wise advice from Vic Howarth and Quentin Bone, tried dogfish muscle. It turned out to be ideal for studying contractions that mimicked swimming. The pattern of action potentials and muscle length change during swimming were already known, and the two major fibre types, pure white and bright red, were well segregated in different parts of the body and could be easily dissected. A series of experiments followed which brought together the physiological and zoological approach to muscle which showed how the individual muscle fibres turn over energy and produce power during contractions that mimic swimming (6). Much of this research was done during what Roger called his "science holidays" at the MBA in Plymouth during short summer visits which he enjoyed enormously. Besides the results being interesting in themselves, Roger also valued them because they extended the small range of muscles about which there was detailed knowledge of mechanics and energetics. Comparative muscle physiology remained a keen interest for the rest of his life. When he died Roger was part of a team headed by Alan Wilson at the RVC, which is investigating the muscles from African animals, including very fast-moving cheetahs, to discover whether their speed is reflected in the energetic properties of their muscles.

Also in the late 1980s, Roger started working on intact human muscle, the focus becoming the effects of ageing on muscle function. The prevailing view at the time was that the decline in muscle performance with age was simply down to loss of muscle tissue. In a series of publications, principally with Suzanne Phillips and Stuart Bruce, Roger demonstrated that in addition the specific force (maximum force/cross-sectional area) also declines (7). Controversial at the time, it is now accepted that the declines in specific force and power not only account for a significant proportion of the overall decline in muscle performance with age,
but are associated with adverse outcomes, including increased mortality, whereas the decline in muscle size is not. An observation by David Jones’ group that women with osteoporosis were particularly weak led Roger to design a series of studies that showed that women lose specific strength around the time of the menopause, disproportionately to men of similar age, and that hormone replacement therapy slows this decline in women (8). His suggestion that oestrogen could be having an effect at cross-bridge level was highly controversial but has been supported subsequently by studies by other groups.

His interest in working on intact human muscle, led to his becoming Director of the UCL Institute of Human Performance (1994-2003). There he became involved in many strands of human muscle physiology spanning studies of individual muscle characteristics to those of whole body movement and gait. Detailed 3D gait analysis studies revealed age-related changes in walking patterns that may contribute to the important clinical problem of falls in older people (9). Towards the end of his life working with Stuart Bruce at King’s College London (KCL), he devised studies of the effects of cooling older people’s muscles, thus combining his innovative translational ideas, falls being commoner in cold weather, with his long-standing interest in using muscle energetics to inform models of cross-bridge kinetics, as set out in a late review written with Chris Barclay and Nancy Curtin (10).

**Beyond Research**

Roger was a gifted teacher who honed his skills as a Teaching Assistant in the early part of his career at UCL, also giving evening classes at the Regent Street Polytechnic covering the whole physiology curriculum. He put considerable effort into preparing lectures and practical classes in the belief that physiology teaching could be made more accessible and enjoyable than he felt had been the case when he was an undergraduate. He had endless patience with those who had difficulty understanding a particular topic. For several years he played a key role in the UCL final year BSc "Muscle Course", the starting point for many muscle physiologists. He particularly enjoyed devising projects and discussing results with students. While Director of the Institute of Human Performance at Stanmore he developed an MSc programme which had a huge impact, giving clinicians the research knowledge and skills to evaluate and modify their clinical practice for musculo-skeletal conditions. He was awarded an Honorary Fellowship of the Chartered Society of Physiotherapy in recognition of this contribution to the academic development of the profession. His enthusiasm, clear delivery and sense of fun made him as popular with students as he was with his peers and colleagues. After formal retirement, in addition to his work at Imperial College and RVC, Roger continued to assist supervising research students and to work on human muscle at both KCL and QMUL. Some of this work involved biomechanical analysis for which his mathematical and modelling skills were invaluable.

Always quick to see the potential of emerging technology, Roger was early to embrace computerisation using punch cards on huge main frame computers to substantially enhance the interpretation of experimental data. He felt his earlier work was generally descriptive, which was typical of physiology at that time, and was keen to adopt any technology that would yield further knowledge of mechanisms, which was his real interest. To that end he continued to develop impressive computing skills which, along with his broad interest in physiology, were much sought after and used by colleagues and students alike.
Roger was an exceptional person who combined his remarkable intellectual knowledge and ability with a great sense of humour. He had a real interest in whatever research people were doing and gave generously of his time and expertise to anyone who approached him. Despite his phenomenal intellect, his broad interest and personality made him a very approachable man who never made one feel they were asking a stupid question. As a result of this generosity of spirit, combined with his expertise in data analysis and statistics, he became mentor, colleague and friend to many.

Roger Woledge made a great contribution to muscle research over a long period of time and maintained his productivity right up to the time of his death. In addition to his intellectual and practical skills, he had an enormous sense of fun and a real zest for life. He was doing one of his favourite recreational activities, riding his horse in Epping Forest, on the last day of his life and that seems fitting. His many attributes resulted in him being mentor, colleague and friend to many people. He is much missed.

References

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