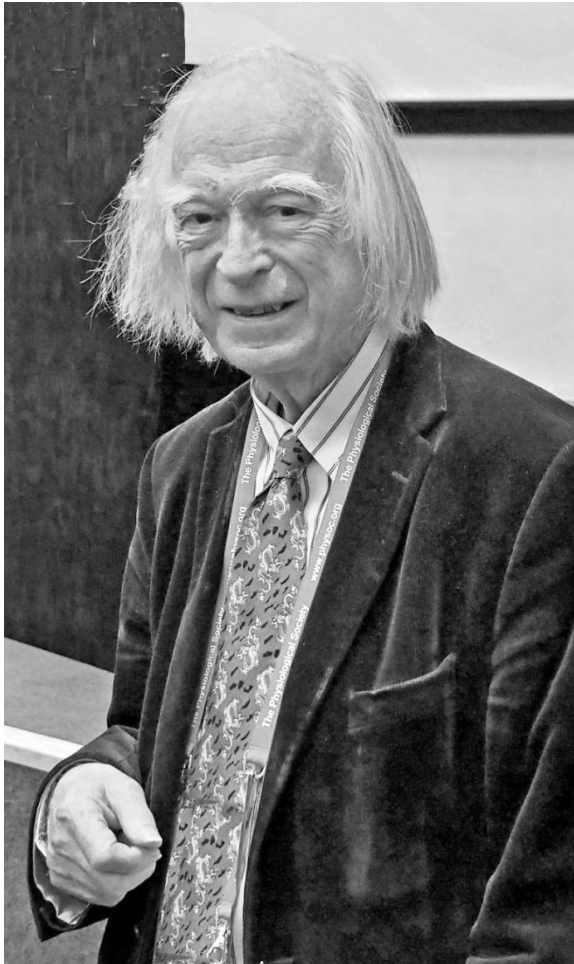


Carmeliet-Coraboeuf-Weidmann lecture

Denis Noble FRS



Biosketch: Denis Noble hardly needs any detailed introduction to this meeting since his work initiated, then stimulated, informed and underpinned that of so many in the field and is surely well known to you all. Denis is Emeritus Professor of Cardiovascular Physiology at the University of Oxford where he held the Burdon Sanderson Chair from 1984 to 2004. Extending from Hodgkin and Huxley's pioneering mathematical description of the propagated nerve action potential, he developed the first mathematical electrophysiological models of cardiac cells. This work began in 1960 (at University College London) using the discovery, made with his PhD supervisor Otto Hutter, of two of the main cardiac potassium ion channels. A core concept is that there is no 'primary oscillator' but that the heart's oscillatory pacemaking behaviour is an 'emergent property' of the complex electrophysiological and biophysical attributes of multicellular cardiac tissue. The project was later developed extensively with Dick Tsien, Dario DiFrancesco, Don Hilgemann and others, including Denis' late wife Susan, to provide the canonical models on which over a hundred cardiac cell models are based today.

Denis' insights as expressed in cardiac modelling found a wider platform. He was a co-founder of the 'Physiome Project', initially presented as a report from the Commission on Bioengineering in Physiology to the International Union of Physiological Sciences (IUPS) Council at the Glasgow Congress in 1993: its declared intent is to provide a "quantitative description of physiological dynamics and functional behaviour of the intact organism". At the Glasgow Congress, a seminal book given to attendees *The Logic of Life* (co-edited with Richard Boyd) revealed the potential breadth of the conceptual framework underpinning to the physiome project. In the preface, a quote from Nobel Laureate Sir James Black captured the mood with Sir James seeing the future of his science as "the progressive triumph of physiology over molecular biology".

In 2009, Denis was elected President of IUPS at its Kyoto Congress and then for a second term (in Birmingham, UK) in 2013. He delivered the opening plenary lecture at the Birmingham Congress, published as an article in *Experimental Physiology* (**98**, 1235-1243, 2013). Here his recent thinking towards a new understanding of evolutionary biology was expounded. This article, and other works in a similar vein, led to the special issue of the *Journal of Physiology* (**592**, June 2014) 'The

integration of evolutionary biology with physiological science'. This issue was provocatively sub-titled in the editorial '*Evolution evolves: physiology returns to centre stage*'. Some 35 eminent authors contributed to the 19 papers published there.

Denis wrote what is perhaps the first popular book on Systems Biology, *The Music of Life*. It has rightly enjoyed widespread critical acclaim. Over the last decade and more, his lectures and presentations have principally concerned the implications of physiological knowledge for evolutionary biology and *vice versa*. Denis has established himself as one of the leading thinkers in modern bioscience. (That rather fuzzy notion of the 'public philosopher' perhaps fits him well.) His deep scholarship ranges over the central ideas of biology and of the philosophy of science and is truly that of a polymath. As a physiologist and a leading proponent of the notion of 'emergence', he will relish that he continues a strand of philosophical thought whose name was coined by a founder member of The Physiological Society, George Henry Lewes (1817-1878).

Denis has published more than 500 papers as well as 11 books. His latest opus *Dance to the Tune of Life; Biological Relativity* will soon be published (by Cambridge University Press).

David Miller July 2016



Edward Carmeliet



Edouard Coraboeuf



Silvio Weidmann

The CCW lecture has been established to celebrate the contributions that Edward Carmeliet, Edouard Coraboeuf and Silvio Weidmann have made to cardiac cellular electrophysiology. It also recognizes their roles in establishing the Working Group in Cardiac Cellular Electrophysiology, which later became part of the European Society of Cardiology.

With the kind permission of Edward Carmeliet and the families of Edouard Coraboeuf and Silvio Weidmann, the lectureship is awarded annually to an outstanding European Cardiac Cellular Electrophysiologist. The story begins with Silvio Weidmann (1921-2005). After studying medicine at the University of Bern, in 1948 he went to the University of Cambridge to work with Alan Hodgkin and Andrew Huxley who were at that time well on their way to elucidating the properties of the nerve action potential. In Cambridge, Silvio was joined by Edouard Coraboeuf (1926- 1998). Together, in 1949, they published the first intracellular recording of a cardiac action potential. Edward Carmeliet also worked with Silvio Weidmann, in his case in Bern, where he carried out his PhD with pioneering studies on the potassium and chloride permeability of the heart. All three continued to make outstanding contributions to cardiac electrophysiology. Silvio Weidmann demonstrated the low conductance of the plateau of the action potential and the voltage dependence of the sodium channel as well as its sensitivity to local anesthetics. He also

demonstrated the diffusion of potassium between cells. Edouard Coraboeuf went on to identify early afterdepolarizations, which lead to torsades-de-pointes arrhythmias. He subsequently pioneered cellular studies on the human heart as well as characterizing the maintained component of the sodium current and its contribution to the plateau of the action potential. As mentioned above, Edouard and Edward had both worked with Silvio. Subsequently the two collaborated on work characterizing the chloride current. Edward Carmeliet (1930-) also pioneered studies of the control of the action potential duration; in particular the effects of heart rate and metabolism. He published seminal papers on virtually every cardiac potassium channel and on the mechanisms of action of antiarrhythmic agents. He also demonstrated the interaction of ionic gradients with channels and transporters.

As well as their own scientific contributions, all three have established their own schools of research as represented by countless successful careers of younger scientists worldwide.

Our Working Group owes much to this trio. Edward Carmeliet organized the first meeting in Leuven in 1977. The next year Edouard Coraboeuf organized a meeting in Orsay and, in 1980, the Working Group met in Bern at the invitation of Silvio Weidmann.

Past CCW Lecturers:

2012: Ursula Ravens (36th EGWCCE Meeting, Nantes, FR)

2013 David Eisner (37th EGWCCE Meeting, Athens, GR)

2014: András Varró (38th EGWCCE Meeting, Maastricht, NL)

2015: Barbara Casadei (39th EGWCCE Meeting, Milan, IT)

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