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EDITORIAL

Bernd Nilius: The Bard of ion channels. Congratulations on 65th birthday

Alexei Verkhratsky · Ole H. Petersen

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This year, we celebrate the 65th birthday of Bernd Nilius, the outstanding physiologist and cell biologist, as well as prominent contributor to various aspects of theoretical medicine. Bernd Nilius' career began in the era of a divided world, in the East German University of Halle. From the very first day, Bernd dedicated his efforts to studies in electrophysiology, thus continuing the traditions of Julius Bernstein who brought worldwide fame to Halle's physiology department.

The first decade of Bernd's research was devoted to deciphering mechanisms of cardiac excitability and excitation–contraction coupling. Bernd was one of the first cardiologists, who investigated calcium channels in heart muscle using the sucrose gap voltage-clamp technique [3]. Using this technique, he was able to measure, for the first time, the acetylcholine-induced outward currents associated with activation of muscarinic cholinoreceptors in atrial cardiomyocytes [4]. Similarly, he was one of the first to document calcium-induced inactivation of calcium current in cardiac cells [7].

In 1985, Bernd went to the USA to the laboratory of Dick Tsien, where he made seminal observations of low- and high-threshold single-channel calcium currents. After fruitful years in Halle (from where Bernd published ~80 papers), and a brief period of chairmanship of the Max Planck Research Group for Molecular Cell Physiology in Jena, Bernd became a full professor of physiology at KU Leuven where he leads a group which has made and continues to make outstanding contributions to ion channel physiology.

Calcium channels The physiological importance of transmembrane Ca^{2+} flux was recognised by Fatt and Katz who, in the 1950s described Ca^{2+} action potentials in the crayfish muscle, and in 1958, Fatt and Ginsborg demonstrated directly membrane action potentials that were due to inflow of Ca^{2+}. From the beginning of the 1960s, Ca^{2+} action potentials were recorded from mollusc and amphibian neurones, and in 1967, Harald Reuter performed the first recordings of calcium current using the double sucrose voltage-clamp technique on Purkinje fibres. In 1975, Susumi Hagiwara suggested that Ca^{2+} channels may be represented by several different populations with distinct biophysical properties, and subsequently, low- and high-threshold Ca^{2+} currents were recorded from several types of neurones and muscle cells. In 1985, Bernd, working together with Peter Hess, J.B. Lansman and Richard Tsien, performed direct single-channel measurements of unitary low- and high-threshold Ca^{2+} channels in ventricular myocytes (Fig. 1 [5]). By employing barium ions as charge carriers, long-lasting openings of a 25 pS channel could be easily resolved from burst-like openings of 7 pS channels in single patches (called “combi” patches by Dick Tsien). Thus, for the first time, both channel types could be clearly separated at the single-channel level and were baptised as T-type (from “tiny” and “transient”) and L-type (from “large” and “long-lasting”).

Transient receptor potential channels In 1993, Bernd entered a new field of research, namely transient receptor

A. Verkhratsky (✉)
The University of Manchester,
Oxford Road,
Manchester M13 9PT, UK
e-mail: alex.verkhratsky@manchester.ac.uk

O. H. Petersen
School of Biosciences, Cardiff University,
Museum Avenue,
Cardiff CF10 3AX, UK
e-mail: PetersenOH@cardiff.ac.uk

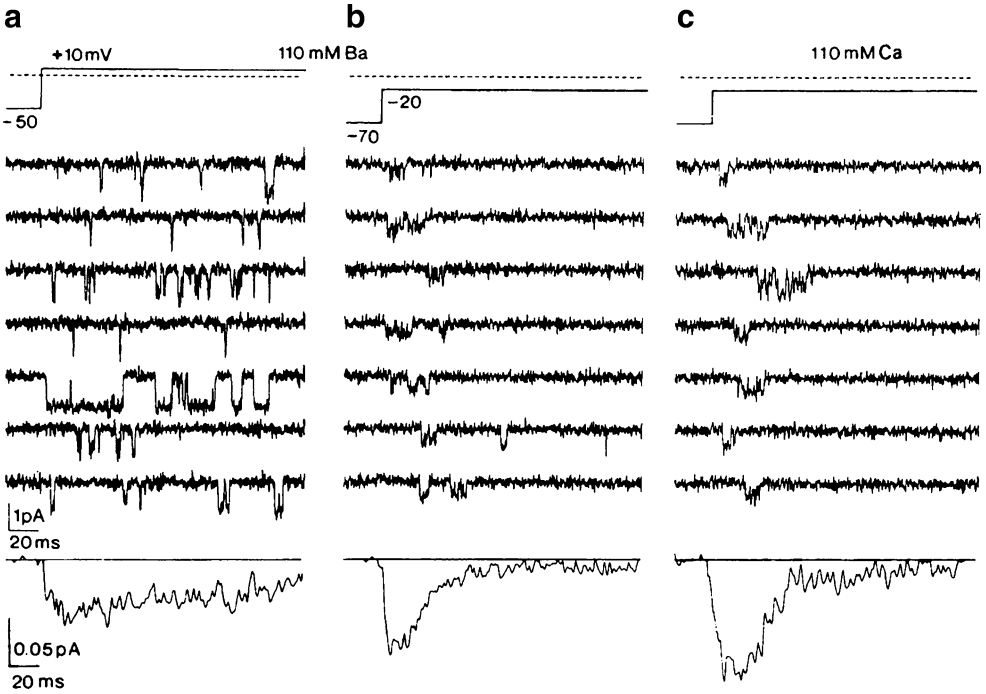

Fig. 1 Single-channel recordings of T-type and L-type channels made by Bernd Nilius from ventricular myocytes in 1985; the *traces* show the large and long-lasting L-type channel openings and the tiny and transient T-type Ca^{2+} channels activation. Reproduced with permission from B. Nilius, P. Hess, J.B. Lansman and R.W. Tsien, A novel type of cardiac calcium channel in ventricular cells, Nature 316 (1985), pp. 443–446

potential (TRP) channels, when he published an electrophysiological characterisation of an ion current, which appears in endothelial cells following discharge of intracellular stores. This is the current associated with store-operated calcium entry [2]. Later on, investigations of store-operated calcium channels were very much instrumental in discovery of various members of the TRP channel family. A rather substantial part of these discoveries was made by Bernd Nilius. Indeed, it was he who produced the first functional characterisation of several TRPs, most notably TRPC3/4, TRPV4/5/6 and TRPM 4/5/6 and TRPV1, e.g. [1, 10, 13, 14].

Subsequently, Bernd was the driving force behind the fundamental discovery of temperature-dependent gating of TRPs, which explained how the wide palette of these channels covers the whole range of physiologically relevant temperature changes (Fig. 2 [11]). Bernd also demonstrated the role of TRPM5 in temperature-sensitivity of taste [8], and soon thereafter, he discovered the molecular mechanism of temperature sensing by TRP channels [12]. Bernd published the first phenotype of TRPM4, indicating a mast cell gain of function resulting in anaphylaxia and an increased type 1 allergic response [9]. He further discovered a wide range of pathological potential of TRPM4 in variety of diseases [6].

Overall achievements The breaths and depth of Bernd Nilius' research is outstanding. In the last two decades, Bernd became the world leader in the studies of ion channels. Apart from his outstanding contributions to studies of Ca^{2+} channels and TRP channels, Bernd was at the forefront of the investigations of volume-regulated anion channels and made a detailed description of endothelial calcium channels. Overall, Bernd has published more than 400 papers and chapters, which have been cited more than 14,600 times (current H-index 63). Bernd is an outstanding lecturer, and he delivered hundreds of lectures around the world at the most prestigious meetings and conferences. In 2007, The Royal Belgian Academy of Medicine awarded Bernd the prestigious Lucien Dautrebande Prize in Pathophysiology for his outstanding work on TRP channels (Fig. 3).

In 2005, Bernd became Editor-in-Chief of Pflügers Archiv–European Journal of Physiology. His impact on the journal's international standing has been remarkable; he rapidly increased the journal's popularity among physiologists and turned it into a world-leading outlet for high-quality publications. In addition, Bernd served and continues to serve as a member of the editorial boards of many top-ranking journals including *Physiological Reviews, Journal of Physiology (London), The American Journal of Physiology, Cell Calcium, The Journal of Cellular Physiology and Biochemistry*. Bernd is a member of Academia Europaea, where he is also a member of the Physiology and Medicine Section Committee.

Bernd is a true academic; his enthusiasm for science and intelligent approach to research is remarkable. He has an encyclopaedic brain, which also excels in knowledge of poetry, history and music. Most importantly, Bernd has a deeply rooted understanding of loyalty and friendship, which many academics in the world appreciate deeply. We hope very much that the coming years will witness

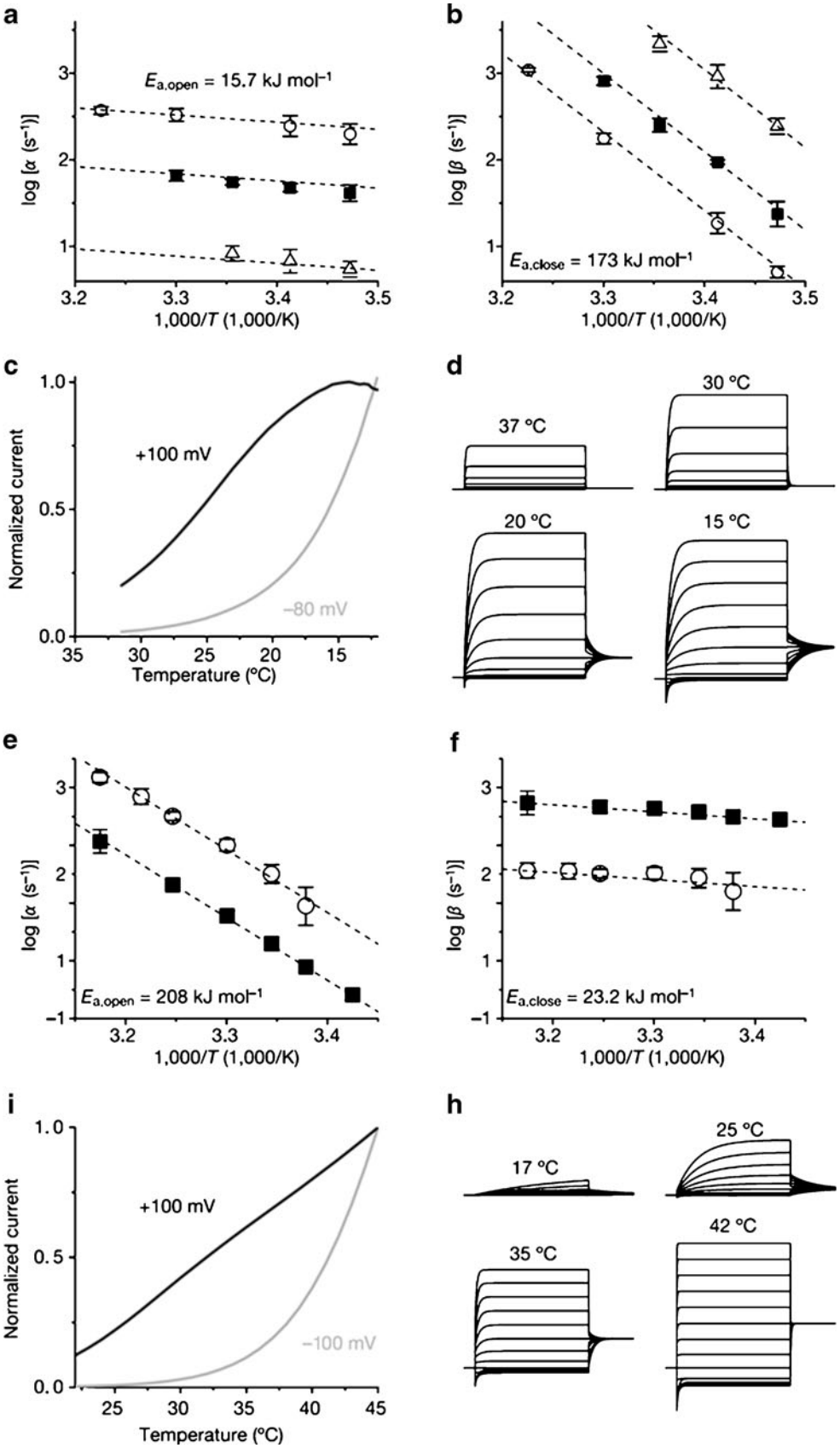

Fig. 2 The famous two-state model for predicting the temperature-dependent behaviour of TRPM8 and TRPV1. **a**, **b** Arrhenius plots of alpha and beta for TRPM8 measured at +160 mV (*open circles*), +60 mV (*filled squares*) or −80 mV (*open triangles*). **c** simulated TRPM8 current at +100 and −80 mV as a function of temperature. (**d**): Simulated TRPM8 currents in response to voltage steps. **e**, **f** Arrhenius plots of alpha and beta for TRPV1 measured at +100 mV (*filled squares*). **g** Simulated TRPV1 currents at +100 and −100 mV as a function of temperature. **h** Simulated TRPV1 currents in response to voltage steps. Reproduced with permission from Voets, Droogmans, Wissenbach, Janssens, Flockerzi & Nilius, The principle of temperature-dependent gating in cold- and heat-sensitive TRP channels. Nature 430, 748–754, 2004

Fig. 3 Bernd Nilius (*left*) receives the Dautrebande Prize in Pathophysiology from Her Majesty Queen Fabiola at the Royal Belgian Academy of Medicine in Brussels on 10th March 2007

further advancements of Bernd Nilius' science, for the pleasure of himself and for the benefits of the world at large.

Happy birthday Bernd!

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