Letter to the Editor

Re: Collective dynamics of ion channels in biological membranes

To the Editor.

This journal recently published a notable report concerning interactions between ion channels in biological membranes (Babinec and Babincová (1996) Gen. Physiol. Biophys. 15, 65). Starting from nonlinear nonequilibrium statistical thermodynamics, the authors developed a model in which, given certain parameter configurations, spontaneous macroscopic fluctuations may be observed that could possibly cause such systems to be extremely sensitive to very weak external field gradients. The physical nature of the channel interactions was not treated in their report.

In an earlier publication (von der Heydt and von der Heydt (1980) Z. Physik B 37, 249) an interaction between membrane channels by way of a current-induced voltage drop in the electrolyte spaces bounding the two sides of the membrane was termed "current interaction" and taken as the basis for extensive semi-quantitative model calculations. Along with channel density, single-channel conductance etc., the electrical resistance of the spaces immediately adjacent to the membrane played a major role here. In the case of myelinated nerve fibres, the axon membrane at the node of Ranvier is also expected to present a considerable so-called series resistance that might give rise to current interactions. This is a preparation in which with a measurement technique optimized in every respect, by current-proportional electronic positive feedback, it is possible largely to compensate errors in sodium-current measurement due to series resistance (see Zaciu et al. (1996) Gen. Physiol. Biophys. 15, 89). However, there are some unavoidable, preparation-induced limitations (Bohuslavizki et al. (1994) Gen. Physiol. Biophys. 13, 357), and the method fundamentally allows only an average compensation because the morphological peculiarities of the nodal gap structure (see e.g. Berthold and Rydmark (1983) Experientia 39, 954) make it inevitable that the current interactions will not be equally strong for all the sodium channels involved. This consideration also applies to the potassium channels in the nodal membrane, but with the substantial difference that these tend to be situated paranodally (see e.g. Black et al. (1990) Trends Neurosci. 13, 48) and hence can be expected to exhibit a considerably greater series resistance, which cannot be adequately compensated because there is no clear criterion for the optimal degree of compensation. This could mean that even under optimized experimental conditions, potassium-current recordings at the nodal membrane are systematically more greatly affected by current interactions than sodium-current recordings.

From all the above it follows that true single-channel recordings cannot be used to calculate the behavior as seen in conventional voltage-clamp recordings of more complex systems, such as the node of Ranvier, without quantitative data on the parameters of the current interactions. Therefore even identical types of channels could show measurably different behavior in the two kinds of measuring conditions. Apart from the above-mentioned current interactions, of course, if the channel density were high enough other influences such as gating-induced (i.e., intramembrane) interactions of neighboring membrane channels would be conceivable. Whether sodium channel densities of about $1000/mm^2$ (Schwarz und Vogel (1995) in: The Axon (Eds. Waxman et al.) pp. 257, Oxford University Press) are sufficiently high should be investigated; if so, such ion channel interactions could be avoided, if at all, only with true single-channel preparations.

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