Letters to the Editor

A Comment on the Sensitivity of Fish to Low Electric Fields

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The sensitivity of sharks, skates, rays, and similar animals to extremely low electric fields is a popular topic in the nonlinear analysis community. It has been considered often in general editorial comments (Tsong, 1994; Glanz, 1996) and very recently in the "New and Notable" section of *Biophysical Journal* (Moss, 1997). Indeed, the sensitivity of some fish to electric fields appears to be astounding. Behavioral evaluation of the lowest field perceived by rays, found earlier to be 10 nV/cm in water (Kalmijn, 1982), has recently been reduced to 1–2 nV/cm (Kalmijn, 1997). Such a field, if applied directly to a sensory cell, produces a change in the transmembrane potential that is absolutely negligible in comparison with spontaneous fluctuations. On this premise, the usually accepted evaluation of 10^{-7} for the signal-to-noise ratio (SNR) is obtained (Block, 1992)—a really astonishing value. It seems impossible to detect such a low signal by ordinary means, thus lending credence to the idea that detection requires methods qualitatively different from traditional techniques of linear analysis. It has been said that in order to reach the sensitivity of fish "artificial devices . . . should work at liquid nitrogen temperature" (Glanz, 1996).

Let us take a closer look at the actual biological situation to evaluate both the signal produced at the cellular level by the external field and the noise in the membrane potential in a receptor cell.

We start with the evaluation of the potential drop induced by the external field on the membrane of the electroreceptors. To make a straightforward comparison with the former evaluation, we will consider a field of 10 nV/cm, the value already used to calculate an SNR $= 10^{-7}$. This value was obtained by assuming that the potential drop through the membrane of a receptor cell was equal to that occurring over the cell length (10 μm). Actually, the weak field generated by the prey is measured over a much longer distance: the Lorenzini ampulla is a relatively insulated organ, connected to the external water through insulated canals filled with a conductive jelly (Waltman, 1966; Kalmijn, 1974; Murray, 1974). A simple way to enhance the electric signal before contamination with the noise in the membrane potential of the receptor is used; elasmobranchs (fish like sharks and rays) take advantage of their extended body. The potential drop on the receptors in the sensory epithelium corresponds to that occurring between the canal pore and the ampulla (5 cm for the longest canals in medium-sized dogfish) and is therefore of the order of 0.05 μV for a field of 10 nV/cm. A factor of 5×10^3 is therefore introduced with respect to the former evaluation.

The noise in the membrane potential has been evaluated by applying basic physical principles (Weaver and Astumian, 1990; Block, 1992). Schematically, a cell membrane can be represented as a first approximation by an equivalent circuit in which membrane resistance (R) and capacitance (C) are combined in parallel. Considering the voltage drop across a cell membrane, it is known by the Johnson-Nyquist theorem that $\langle V_n^2 \rangle = k_B T/C$, where k_B and T have their usual meaning. For a spherical cell of radius r (10 μm), and assuming the specific capacitance of a lipid bilayer is 1 μF/cm^2, C is about 3 pF; therefore, $\langle V_n^2 \rangle^{1/2} =$ 30 μV. This is a lower limit for the noise that one might expect on the voltage across the membrane of an average-sized cell. This value cannot be lowered; however, $\langle V_n^2 \rangle^{1/2}$ is inversely proportional to the square root of C and therefore decreases with increasing membrane surface. Moreover, it is important to evaluate the number of cells that connect the same area in the central nervous system. Figs. 1D and 1F in Murray (1974) show that electroreceptors in each ampulla at the bottom of a canal number about 10,000, divided among a small number of swellings; the number of fibers innervating each ampulla (five) is about the same as the number of the swellings and they project to the same brain area. Therefore it is conceivable that the output of 10^4 cells are averaged in certain areas of the brain, and in this case the voltage thermal fluctuations might be as low as 0.6 μV root-mean-square.

Biological excess noise is to be expected because ion channels switch continuously from the open to the closed conformation also because of thermal fluctuations. However, the current flowing through the open channel is due to the electrochemical gradient through the membrane, and the nonequilibrium situation is the actual source of the excess noise. The excess noise depends on the number and types of channels that are open in the resting condition. It is possible to retrieve experimental evaluations of $\langle V_n^2 \rangle^{1/2}$ in receptor cells. For instance, the amplitude for the voltage fluctuations in retinal bipolar cells (cell membrane capacitance of 11 pF) of the larval amphibian axolotl, a kind of salamander, was evaluated to be 100–300 μV (Tessier-Lavigne et al., 1988), whereas the voltage noise of an insect

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photoreceptor (cell membrane capacitance of 14 pF) is $\sim$100 μV (Stephenson, 1988).

We made numerical simulations of the equivalent electric scheme of a cell membrane to obtain qualitative insight into the dependence of voltage noise on cell parameters. The obvious result was that voltage fluctuations due to the switching of ion channels decrease when the ion channel kinetics are fast compared to the membrane time constant, suggesting a possible way to minimize nonequilibrium noise in specialized structures. As for the fundamental thermal noise, a decrease of the excess voltage noise with the square root of the cell surface is to be expected.

A reasonable estimate of the voltage noise due to ion channel switching in a single electroreceptor is therefore 200 μV (based on the data by Stephenson (1988), normalized for the difference in cell radii); by the same reasoning used for thermal noise, we consider that averaging this noise over 10^4 cells results in a final root-mean-square value of 2 μV. However, it is worth recalling that the responses to voltage steps lasting 0.5 s in the excised ampullary organ have a dynamic range between -100 and 20 μV (Lu and Fishman, 1994a,b), and that a variation in the discharge of the nerve fibers has been measured for voltage steps of 3 μV, which suggests that the noise at low frequencies is only a fraction of a microvolt (and each nerve fiber averages over just 2×10^3 electroreceptor cells). Clearly, only direct experimental measurements can reveal how much noise originates in the electroreceptors and how its spectral distribution is shaped.

The evaluation of SNR using the estimates of voltage noise (2 μV) and voltage drop (50 nV) reported above yields an SNR value of $\approx 10^{-2}$ for a canal of 5 cm. This value, however, should be divided by 10 according to the lowest evaluation of the threshold field, 1–2 nV/cm (Kalmijn, 1997). This evaluation, very different from the usually accepted value of 10^{-7} for the SNR, is in agreement with considerations reported by Weaver and Astumian (1990) (see their Table 1 and the explanation reported in their note 2).

Could ordinary techniques detect signals with such SNR? By "ordinary techniques" we mean not only averaging of different units with independent noise, but also Fourier analysis or similar processing. Fourier analysis is a powerful tool for the detection of small signals, sorting them out of the noise contributions at different frequencies. This sorting out is in principle only limited by the time of observation. In a cell Fourier analysis may be implemented if the transduction system acts as a selective amplifier around a resonance frequency, as seems to occur in the excised electric organ (Lu and Fishman, 1994a). As for further averaging, about 1000 canals of different length are present in a single animal (A. J. Kalmijn, personal communication) and the longest ones (about 20) are nearly parallel; i.e., to a reasonable approximation 20 equivalent units can be averaged. This could also help reduce the noise originating in the ohmic resistance of the canals.

Thus with the present evaluation of SNR we propose that ordinary tools can work, whereas the former evaluation of 10^{-7} seemed to rule out this possibility. Only the experimental study of the system under physiological conditions can give direct answers to questions about how electroreception operates. However, there are insufficient reasons to assume that traditional techniques such as linear analysis do not work. The hope that systems exhibiting stochastic resonance can improve SNR has recently been denied by a clear-cut note in *Nature* (Dykman and McClintock, 1998).

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