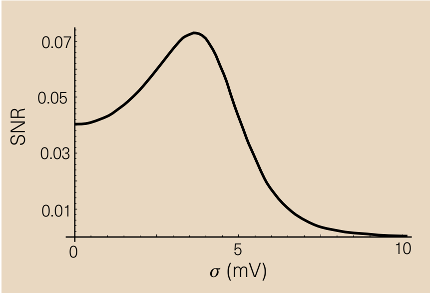

Figure 1 SNR against the σ, calculated using equation (1), for $E_{rms} = 1$ mV cm^{-1} at room temperature ($k_B T = 25$ meV), and the parameters $z = 10$ electronic charges, $r_{cell} = 100$ μm, $f_c = 10^7$ s^{-1}, $r(0) = 10^6$ s^{-1}, and with $\Delta f_a = 100$ s^{-1}, appropriate for a detector around 50–60 Hz (ref. 9).

plot of the actual numerical value of the SNR against noise amplitude for a specific set of parameters is shown for $E_{rms} = 1$ mV cm^{-1}. Although we selected values to maximize the SNR within experimental constraints, the SNR does not approach unity.

To achieve a SNR > 1 with $r(0) < f_c$ (which is necessary to derive any benefit from added noise), the factor $z^2/\Delta f_a$ would have to be much larger than 1. In principle, this could be achieved by a system with a tremendous sensitivity to an applied field ($z > 10$), or by a detection mechanism that is sensitive only in a very narrow band of frequencies ($\Delta f_a \ll 100$ s^{-1}) centred around the signal frequency. However, in the absence of experimental evidence for such properties of cells, we conclude that, as for other mechanisms of single-cell stochastic resonance[8], the mechanism of Bezrukov and Vodyanoy cannot explain experiments in which fields of less than 1 mV cm^{-1} are claimed to cause effects on single cells[2].

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Bezrukov and Vodyanoy reply — The possibility that the mechanism of stochastic resonance might account for the sensitivity of organisms to industrial low-frequency magnetic and/or electric fields has inspired much discussion[1,2,10]. In a recent Letter[6] we formulated a physical model of stochastic resonance that permits quantitative analysis of the phenomenon in a variety of systems. Astumian and co-workers apply our results to the intriguing but difficult question of the role of stochastic resonance in signal detection at the level of a single cell. For a 'typical cell' of 100 μm radius, they come to a conclusion that stochastic resonance increases cell sensitivity to small signals, but that this increase is not significant enough to account for the effects reported by others[2]. Although we agree with their treatment of our theory, we show that for smaller cells stochastic resonance can improve signal detection considerably.

Astumian and co-workers address two possibly related but altogether different questions: whether electrical power lines pose a significant health hazard and whether non-equilibrium noise can play a role in small-signal detection by single cells. Although the health-hazard question unfortunately cannot be answered by our physical (not physiological) theory, the question about a role of stochastic resonance in signal detection is in the domain of our model.

Here we would like to demonstrate that the choice of the system parameters is crucial. The vertical arrow in Fig. 2 shows the $f_c/r(0)$ value used by Astumian and co-workers, which gives an increase in the cell sensitivity of about 1.8 times. However, consider a cell of 10 to 30 μm diameter. Using their reasoning that the corner frequency, f_c, is limited by cell membrane capacitance (that is, ignoring a possible frequency dependence of the channel response[11]) and taking into account that the number of channels (and thus $r(0)$) is proportional to the membrane area, we obtain a increase in $f_c/r(0)$ of two to four orders of magnitude. This increase in $f_c/r(0)$ will correspond to a 10- to 100-fold improvement in signal-to-noise ratio, suggesting a significant role for stochastic resonance in signal detection. The r.m.s. value of optimal noise only doubles (Fig. 2). It can be shown that for $f_c/r(0) < 10^5$, the dependence of optimal noise on this parameter is slower than logarithmic:

$$\sigma_{opt} \cong \sqrt{\ln \frac{f_c}{r(0)}} \qquad (2)$$

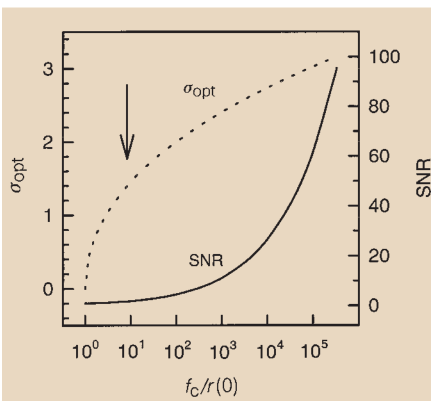

Figure 2 Signal-to-noise ratio (SNR) and optimal noise r.m.s. amplitude σ_{opt} against the ratio of the noise bandwidth f_c to the equilibrium rate $r(0)$, calculated from the stochastic resonance model[6].

Indeed, the decrease in the equilibrium rate $r(0)$ will decrease the initial signal-to-noise ratio, but there is another parameter, Δf_a, that is as significant as $r(0)$, and that was arbitrarily chosen by Astumian *et al.* as 10^2 s^{-1}. In principle, the theoretical limit on Δf_a is defined by the device lifetime τ, and in the case of a human being is $\Delta f_{a\,lim} = 1/(2\pi\tau) \approx 1/(2\pi \times 75 \text{ years}) \approx 4.2 \times 10^{-10}$ s^{-1}. Individual cells on average do not live that long, so reducing the limiting frequency resolution to about 10^{-8} s^{-1}, but this is still quite different from 10^2 s^{-1}.

One of the main conclusions of our Letter[6] is that stochastic resonance is an inherent feature of a variety of systems with threshold-free behaviour. Indeed, a News and Views article in the same issue[12] mentioned a particular electronic device that can be described by our model, and predicted some other applications including biological ones. We were delighted to see yet another application made by Astumian *et al.* to describe stochastic resonance at the single-cell level. As for the health-hazard question mentioned above, resolving it will require joint efforts by physicists, physiologists and epidemiologists. What is clear at the moment is that specialized cells and organisms do have extraordinary electrical sensitivity[13,14], and that some sensory biological systems and neuron circuits do show stochastic resonance[15,16].

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