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Quantitative Measurement of 1/f Noise and Membrane Theory

Dear Sir:

In a recent note (1) I showed that electrical "noise" whose power spectrum varies reciprocally as the frequency ($1/f$ noise) should be generated when ions cross a potential barrier to enter or leave a membrane. Thus such noise would be expected, e.g. in the axonal membrane, and its *existence* cannot be used as evidence for or against any given membrane model.

Poussart (2) has now published an experimental examination of the quantitative variation of $1/f$ noise with the steady-state membrane current, assumed to be K^+. His results can have important implications in deciding between membrane models.

By my theory of membrane $1/f$ noise, the total noise power should be directly proportional to the total number of ions which cross the membrane interfaces per unit time. In a model which well represents many phenomena of the excitable membrane the permeability is primarily controlled at the external interface (3). As treated by activation energy, the flow of ions of species i across the external interface to enter the membrane is

$$J_i\,(\rightarrow) = k_0 \delta \tau_0 C_{i0} \exp\,(-\alpha_i + \varphi_0 \delta/2) \tag{1}$$

while the flow leaving the membrane across this interface is

$$J_i\,(\leftarrow) = -k_0 \delta \tau_0 C_{i1} \exp\,(-\beta_i - \varphi_0 \delta/2). \tag{2}$$

τ_0 is the fractional time ions can traverse the interface, being otherwise blocked by absorbed Ca^{++}. I have computed τ_0 by essentially the Langmuir isotherm (3):

$$\tau_0 = k_1/[1 + k_2 C_{Ca} \exp\,(-2V_0)]. \tag{3}$$

α_i and β_i are the heights of the interface potential barrier in the two senses; δ is the width of the barrier; and C_{i0} and C_{i1} are the concentrations just outside and inside the barrier, respectively. The electric field at the interface is φ_0, which corresponds to an interface potential V_0. (All potentials are measured in units of RT/F.) C_{Ca} is the Ca^{++} concentration in the external solution, and the k's are constants.

The net flow across the interface, for each species, is the

$$J_i = J_i\,(\rightarrow) - J_i\,(\leftarrow), \tag{4}$$

while the total *absolute* flow (the number of ions crossing the interface in either sense) is

$$\bar{J}_i = J_i\,(\rightarrow) + J_i\,(\leftarrow). \tag{5}$$

These equations are written for both Na^+ and K^+. It is assumed that α_{Na} and β_{Na} are considerably higher than α_K and β_K in the polarized condition, because of electrostriction, but that they are of about the same amplitude for K^+ and Na^+ when depolarized, when electrostriction is relaxed.

Similar equations are written for the internal interface, but since internal Ca^{++} is not a factor in excitable membranes, the τ_0 factor is not there included.

As the membrane potential is decreased, the flow-limiting factors in equations 1 and 2 are decreased, so that J_i (⟶) and J_i (⟵) increase. If these were the only terms involved in determining net diffusion, it would be expected that each would change at about the same rate, so that J_i and $\bar{J}_i$ would change in approximately the same proportion. Then the membrane noise would increase lineally with current.

Poussart finds otherwise: he shows the noise N can be represented by

$$N = A + B \tag{6}$$

where A is a constant, and B is given by

$$B = k\bar{I}_K^m . \tag{7}$$

$\bar{I}_K$ is the steady-state K^+ current, m is a constant varying from about 1.1 to 2.1 in various experiments, and k is another constant.

The departure of m from unity is explained by flow restrictions occurring elsewhere than at the external interface. If the potential barriers at the internal interface are higher than at the external, then as the flow restriction at the external interface is reduced with depolarization

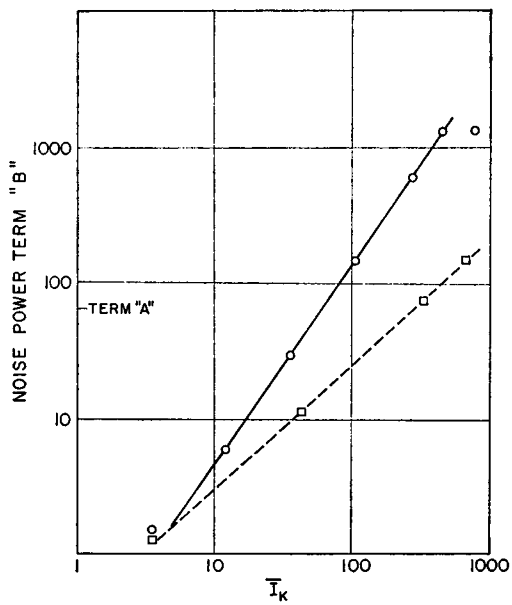

FIGURE 1 Calculated membrane noise according to Poussart's equation $N = A + B$, where $B = k\bar{I}_K^m$. The solid line is B vs. $\bar{I}_K$ for the normal case; the dashed line, no external Na^+.

(as seen from equations 1, 2, and 3), the net flow (given by equation 4) starts to be limited at the internal interface. This increases progressively with depolarization, particularly for Na^+, as the Na^+ external barrier especially is lowered by depolarization. The result is a reduction in J_{Na} (by equation 4), while $\bar{J}_{Na}$ is rapidly increasing. A similar but less pronounced effect occurs for K^+.

The noise N (equation 6) has two components: that due to the ions crossing the external interface, and that due to those crossing the internal. The absolute value of the latter is substantially constant, and determines the constant A in equation 6; that of the former increases steeply with depolarization, which is measured by $\bar{I}_K$; its value is given by the second term of equation 6.

A typical calculation of the noise power as a function of $\bar{I}_K$ is shown in Fig. 1, in which the constant term A has been subtracted. Here $A = 67$ and $m = 1.5$, the mean value found by Poussart.

Poussart finds that tetrodotoxin (TTX) does not affect the membrane noise, within his accuracy of measurement. By my theory of $1/f$ noise, this would imply that TTX does not act by the simple process of blocking the entry of Na^+ into the membrane pores, a hypothesis which also does not account for its effect on birefringence (4).

A prediction of the model is that removal of external Na^+ should reduce membrane noise, and make it substantially linear with $\bar{I}_K$; this is shown by the dashed curve in Fig. 1. The test of this prediction can have important theoretical implications.

Some remarks should be made on my treatment of the theory of $1/f$ noise. In my original calculations (1) I treated the return of ions in the direction of the resultant field as a "drift" of all the ions. More properly, it should be treated as a change in the probability of an ion passing across the barrier. Calculations have been repeated on this basis. The exponent calculated in the equation $N = kf^x$ is very close to -1.

As applied to semiconductors, it will be apparent that the model predicts no $1/f$ noise in the absence of an electric field (i.e., no current), since there is no force to displace the electrons through the semiconductor. This does not apply to the membrane case, however, since there is in general both an electric field and a concentration gradient present.

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