

## Voltage Fluctuations of Neural Membrane

THE resting membrane potential of the frog Ranvier node shows fluctuations for which, between 1 and 10,000 rad/sec, the power/cycle of bandwidth is inversely proportional to frequency ( $1/f$  noise), and for frequencies of less than about 1 rad/sec there may be an increase in the negative slope of the plot of log noise power against log frequency<sup>1,2</sup>.

This communication reports experiments on the amplitude distributions of the membrane noise voltage.

The arrangement was similar to that described before<sup>1</sup>: a three node preparation and a three terminal version of the electronic feedback isolation arrangement according to Frankenhaeuser<sup>3</sup> were used. The membrane potential of the middle node, lying in a pool containing Ringer or a testing fluid, was measured through one of the adjacent nodes, bathed in isotonic potassium chloride, by means of KCl-agar bridges to silver-silver chloride electrodes connected to a low noise, chopper stabilized electrometer amplifier. The membrane potential could be varied by means of d.c. injection through a 1,000 megohm series resistor through the other adjacent node. After filtering through a high pass filter (time constant 2 sec) to eliminate the d.c. component of the membrane potential and after further amplification the amplitudes of the noise voltage were sampled with 1.5  $\mu$ sec pulses at a rate of 1,000/sec. The amplitude of each sample was stored in the memory of a 128-channel sealer-analyser, with a channel width of 100  $\mu$ V of the input. From the resulting amplitude distribution the standard deviation, indicative of noise intensity, and the third moment ( $\Sigma x^3/N$ , where  $x$  is the noise amplitude and  $N$  the total number of samples), indicative of degree of skew, were calculated.

The relationship between noise intensity and membrane potential is shown in Fig. 1. Overall noise intensity is lowest for membrane potentials between -60 and -70 mV for this particular node. For smaller membrane potentials the spread of the intensities increases. This is because of a pronounced positive skew in the amplitude distributions. The intensity of the Gaussian noise component is minimal at the (supposed) level of the potassium equilibrium potential, which suggests that there is a relationship between Gaussian noise and passive potassium ion flux through the membrane.

Interfering with active ion transport (by the addition of 2,4-dinitrophenol to the Ringer in the bath together with an atmosphere of pure nitrogen) did not influence the Gaussian noise, nor did replacement of sodium chloride by saccharose. Replacement of sodium chloride by potassium

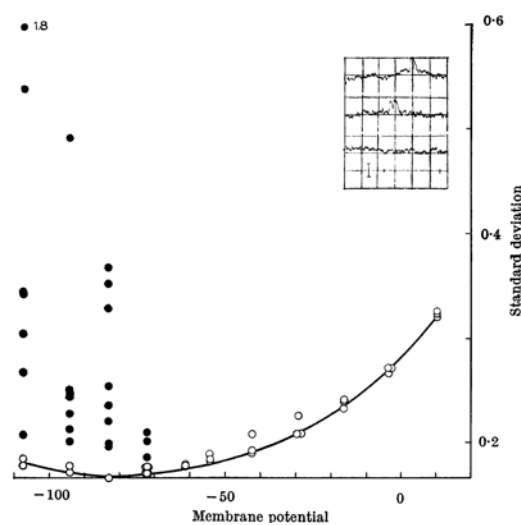


Fig. 1. Standard deviation of amplitude distributions of membrane noise voltage plotted against membrane potential.  $\circ$ , Gaussian distributions;  $\bullet$ , positively skewed distributions. Length of noise tracks analysed at each point was 12.5 sec. Inset is membrane noise (bandwidth 0.5-3,000 c/s) at a membrane potential of -90 mV. Units: 1 mV and 10 msec. A single miniature depolarizing potential is visible in the upper track, and a group of two in the second, while none are present in the third track.

chloride, however, shifted the Gaussian noise minimum towards zero membrane potential, the minimum either coinciding with the small remaining resting potential or lying between this potential and zero. Likewise it was found that 5 per cent tetra-ethylammonium Ringer, which is known to reduce the potassium conductance of frog node<sup>5,6</sup>, reduces the intensity of the Gaussian noise component.

We conclude that the Gaussian noise component is related to the passive flux of potassium ions and that its minimum indicates the potassium equilibrium potential. The position of the range of transition from Gaussian into skewed noise is independent of the actual resting membrane potential, recorded in the absence of d.c. injection. The tracks of skewed noise (Fig. 1, inset) show that skewness is caused by the irregular occurrence of miniature depolarizing potentials, spiked and with amplitudes of the order of 1 mV and lasting about 1 msec. These potentials occur both singly and in clusters, which vary from groups of a few additive miniature depolarizing potentials to high-amplitude, long-duration depolarizing bursts of noise (described by del Castillo and Katz<sup>7</sup>) in which the unit potentials cannot be distinguished. These phenomena

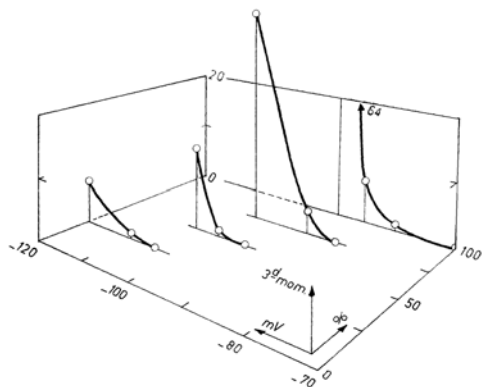


Fig. 2. Three dimensional representation of the relation between skewness (third moment), sodium chloride concentration in the bathing fluid (percentage of that in Ringer) and membrane potential. Length of noise tracks analysed at each point was 100 sec.

suggest that passive membrane sodium mechanisms are involved.

Interfering with active ion transport did not influence skewed noise, which excludes active transport and neither did replacement of chlorine ions by sulphate ions nor the addition of 5 per cent tetra-ethylammonium to the bathing Ringer solution, which excludes the involvement of chlorine and of potassium ions. Partial replacement of sodium chloride by saccharose resulted in a reversible shift of the transitional range towards more hyperpolarized levels, the shift increasing with the amount of sodium replaced (Fig. 2).

We conclude that skewed noise is related to spontaneous batchwise fluxes of sodium ions through passive transport sites within the membrane.

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A. A. VERVEEN

H. E. DERKSEN

K. L. SCHICK \*

Physiology Laboratory,  
University of Leiden.

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Present address : Department of Physics, Union College, Schenectady,  
New York.

<sup>1</sup> Derksen, H. E., *Acta Physiol. Pharmacol. Neerl.*, **13**, 373 (1965).

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