Noise-Mediated Spike Timing Precision from Aperiodic Stimuli in an Array of Hodgekin-Huxley-Type Neurons

Xing Pei,*,† Lon Wilkens,*,‡ and Frank Moss*,†

University of Missouri at St. Louis, St. Louis, Missouri 63121

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The influence of noise on the detection and timing precision of neural signals is a topic of current interest. Experimentalists and theorists have recently studied its influence on neural responses to aperiodic stimuli and in relation to temporal encoding schemes. We explore these topics using an array of noisy Hodgekin-Huxley neurons stimulated by a single pulse-type stimulus, which is either subthreshold or suprathreshold. The timing precision is improved by internal noise only for deterministically subthreshold stimuli. A classical statistical formula captures the dominant features of the simulation   [S0031-9007(96)01771-1]

Attempts to understand how individual neurons or neuronal networks encode information have occupied neuroscientists for decades. The most frequently used encoding scheme—*rate* coding—is based on short time averages of the rate at which neurons fire, or generate action potentials (spikes). In 1972, populations of leaky integrate-and-fire stochastic neurons demonstrated rate coding in a simulation [1]. But rate coding in a single neuron is slow (limited by the mean firing rate and by the averaging time of the detector neuron), and only highly redundant ensembles of many neurons using rate coding can speed the response. Recently, much interest has centered on developing *temporal* encoding schemes [2], wherein information is carried in spike patterns interpreted during a much shorter time window [3,4]. These ideas are embedded in a more general question— one of information transmission efficiency: Are neurons noisy and slow transmitting only a small amount of information plus much noise [5], or are they fast, efficient, largely noise free, and capable of transmitting spike patterns which only seem to be noisy but, in fact, are deterministic and very complex [6,7]? In the latter case, one would expect complex patterns, recognizable by single or networks of detecting neurons, to emerge. The feasibility of submillisecond coincidence detection, which might be important for the interpretation of such patterns, has been demonstrated in noise free dendritic trees [8] which are capable of large computational power [9]. However, if one admits the possibility that at least some internal noise may be present, one is perforce led to a statistical consideration of spike timing precision [9]. Much effort has been put into this question, using both experiments [10–13] and numerical models and theories [8,12–15]. What is missing from this body of work is a consideration of the effects of noise on the response precision of deterministically subthreshold single stimuli, which are surely important in the peripheral if not the central nervous system. Deterministically subthreshold stimuli are defined to be those which can evoke *no* spikes in the absence of noise.

At the same time, it has become a widely used practice to stimulate with an "aperiodic" single sample, that is, a finite length time course, taken from a noise distribution [11,16–21]. Experimentalists often repeatedly apply this same sample (it thus becomes periodic unless presented at random times) in order to average the responses [11,16–20]. The problem with this procedure, when considering response timing precision, is that the stimulus sample often contains both subthreshold and suprathreshold features, and, as we show here, the internal noise of the neuron affects these two features in quite different ways. Added internal neuronal noise can improve the timing precision of deterministically subthreshold stimuli, and optimal noise results in maximal improvement, similar to stochastic resonance [16–20,22–31]. By contrast, noise only degrades the timing precision of suprathreshold stimuli. The effects of periodically forced, subthreshold stimuli on a giant squid axon have been reported recently [32].

We report here the results of a numerical simulation of 1000 Hodgekin-Huxley (HH) neuron models connected in parallel and converging, through excitatory synapses, on a summing center Σ, as shown in Fig. 1(a). The HHs are identical simple 4 conductance (Na, K, leak, and stimulus) models, as shown in Fig. 1(b), with the current through each conductance given by

$$I_x = g_x(m_b - E_{ext}), \qquad (1)$$

where g_x is the channel conductance ($x =$ Na, K, leak, or synaptic stimulus, syn), m_b is the membrane potential, and E_{ext} is a constant external driving force. Each HH includes an internal Gaussian noise ξ_n, of zero mean and standard deviation σ, which is temporally correlated with correlation time τ (equal to the integration time step), but is uncorrelated with the noise in any other HH in the array. All HHs are subject to the same stimulus $S(t)$, applied as a synaptic conductance change $g_{syn}(t)$; see Fig. 1(a). The stimulus can be deterministically subthreshold or suprathreshold. All HHs are subject to the same magnitude noise intensity σ, which is an independent variable. Similar arrays have been previously
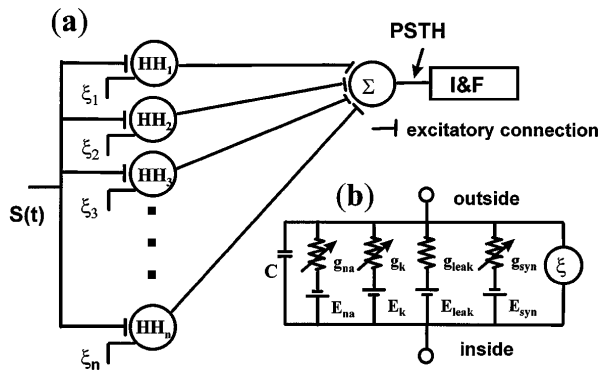
FIG. 1. (a) A schematic diagram of the parallel array of Hodgekin-Huxley (HH) neuron models convergent on a summing center Σ through excitatory synapses. The simulation involved 1000 identical HH models in the array. (b) A diagram of a single HH model showing the usual channel conductances plus the stimulus, $S(t) = I/g_{\text{syn}}(t)$ common to all HHs and the noise $\xi(t)$, independent for each HH.

studied with the single sample noise stimulus repeatedly applied [17] as well as an array of on-off devices with a single frequency periodic input [33].

In our simulation, a biologically reasonable input, $S(t) = (At/t_0)\exp(1 - t/t_0)$, of maximum amplitude A and characteristic time t_0, *was applied only once*. The post stimulus time histogram (PSTH) of all spikes from the HHs was collected at the output of the summing center. This quantity mimics the stimulus $S(t)$, but is somewhat different in shape. We define the spike timing precision P, based on the shape of a smoothed data set obtained as a five point moving average of the PSTH,

$$P = (\text{PSTH})_{\text{max}}/W, \qquad (2)$$

where $(\text{PSTH})_{\text{max}}$ is the maximum value of the smoothed data, and W is the width at $(\text{PSTH})_{\text{max}}/e$. A subthreshold stimulus $S(t)$, and the resulting PSTHs (unsmoothed) for three different noise intensities are shown in Fig. 2. We note that for both small and large noise, Figs. 2(b) and 2(d), respectively, the timing precision is smaller than for some intermediate noise intensity 2(c). On the other hand, the PSTHs for suprathreshold stimuli are similar except that P is monotonously degraded by increasing noise intensity. Figure 3 summarizes this finding, where in 3(a) we show the timing precision versus internal noise intensity for two subthreshold stimulus amplitudes. Note that larger stimulus amplitudes result in larger spike timing precisions. Moreover, for each amplitude, there is an optimal noise intensity which maximizes the precision, and the optimal value of noise is smaller for larger amplitude stimuli. By contrast, Fig. 3(b) shows that, for suprathreshold stimuli, the noise induced optimization vanishes. Larger stimulus amplitudes and smaller noise intensities both lead inexorably to larger response spike timing precisions as expected, the stimulus amplitude effect on timing precision having also been observed in both recent [11] and classical [34] experiments.
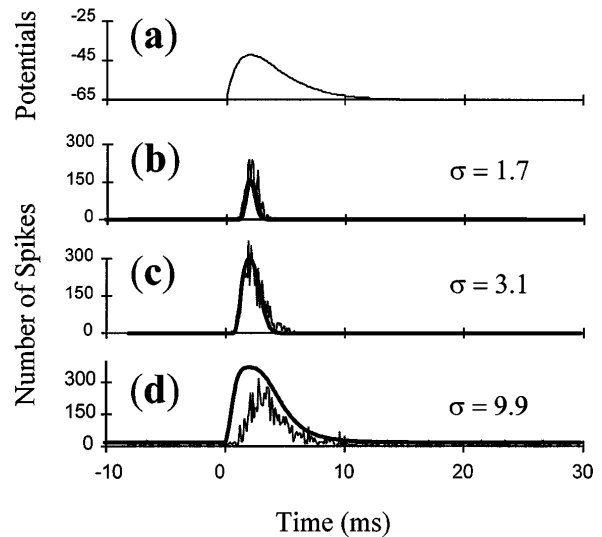

FIG. 2. (a) An example subthreshold stimulus. (b)–(d) The PSTHs resulting from the stimulus in (a): for small noise (b), optimal noise (c), and large noise (d). The solid curves in (b)–(d) are the predictions of Eq. (3) for $A = 23.6$ mV, $\Delta_0 = -40$ mV. The noise standard deviations (in mV) shown were common to both the numerical simulations and the theory.
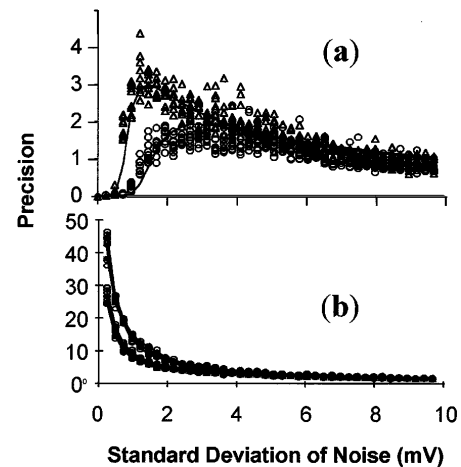

FIG. 3. The spike timing precision versus internal noise intensity. (a) Deterministically subthreshold stimuli of larger amplitude, $A = 24.5$ mV (upper data set—triangles), and smaller amplitude, $A = 23.6$ mV (lower set—circles). The solid curves are the predictions of Eqs. (3) and (4) for $\Delta_0 = -40$ mV, where A is used as an adjustable fitting constant, obtaining $A = 24.0$ mV (upper set) and $A = 22.5$ mV (lower set) for the fits shown, which deviate from the A values used in the numerical simulation by less than 5%. (b) Suprathreshold stimuli for larger (upper data set) and smaller (lower data set) amplitude stimuli. Sequential points are connected by straight lines as a guide to the eye, since the theory is not applicable to suprathreshold stimuli. In both panels, the multiple symbols at each noise intensity represent the results of separate simulations for the same conditions but differing realizations of the noise. The scatter thus indicates the statistical variability of the simulation. It is worth noting that for noise intensities above about 4 mV, the precisions of both suprathreshold and subthreshold stimuli are approximately equal.

Figure 4 shows the behavior at three constant noise intensities with increasing stimulus amplitude. For the smallest noise, the threshold is close to deterministic and is clearly distinguishable. Increasing stimulus amplitude *always* results in improved timing precision, whereas increasing noise intensity improves the precision only of deterministically subthreshold stimuli and only over a limited range.

Because the results of our simulation seem entirely reasonable, it should be possible to capture the main features with a simple analytical formula. Classically the leaky integrator with a threshold has been investigated as a first passage time problem with a time varying threshold [35–39]. By contrast with these prior and perhaps more biologically motivated calculations, we begin with a formula from the classical engineering literature [40], which is an exact result for the mean threshold crossing rate ν, of a Gaussian, band-limited noise of standard deviation σ, whose mean is located a distance Δ from the threshold.

$$\langle \nu \rangle = \frac{f_0}{\sqrt{3}} \exp\left[-\frac{\Delta^2}{2\sigma^2} \right], \qquad (3)$$

where the shape of the power spectrum of the noise is low pass rectangular with upper cutoff frequency f_0. We now make the familiar adiabatic assumption: that the mean of this noise evolves identically in time with the stimulus $S(t)$, and that the mean crossing rate is given instantaneously by Eq. (3), that is, we pretend that the statistics are stationary; whereupon $\langle \nu \rangle \to \langle \nu \rangle(t)$. The temporal changes in $\langle \nu \rangle(t)$ evolve on the scale of t_0, and the adiabatic assumption requires that $t_0 \gg 1/f_0$. With this we can allow the threshold-to-stimulus (noise mean) distance in Eq. (3) to become a function of time,

$$\Delta \to \Delta(t) = \Delta_0 - S(t), \qquad (4)$$

where Δ_0 is the distance from the threshold to the baseline of $S(t)$. Equation (3) thus gives the time evolution of the mean $\langle \nu \rangle(t)$, which is actually the time evolution of the PSTH, assuming that one threshold crossing results in the generation of one spike [41]. The PSTH is shown by the solid curves in Figs. 2(b)–2(d). The maximum value

of $\langle \nu \rangle(t)$ occurs at $t = t_0$, the characteristic time of the stimulus, and is given by

$$\langle \nu \rangle_{\max}(t_0) = \frac{f_0}{\sqrt{3}} \exp[-(\Delta_0^2 - 2\Delta_0 A + A^2)/2\sigma^2]. \quad (4)$$

The equation for the two times at which $\langle \nu \rangle_{\max}(t_1, t_2) = \langle \nu \rangle_{\max}(t_0)/e$ is transcendental but was solved numerically for the width $W = t_2 - t_1$, thus giving the precision, $P = \langle \nu \rangle_{\max}/W$ as shown by the solid curves in Fig. 3(a).

Beyond the adiabatic assumption, a second approximation inherent in this analysis neglects the fact that there is a refractory time built into the HH model. Though neither approximation is well represented by the HH dynamics, the fits to the numerical data based on Eq. (3) are surprisingly good. Though a more refined, accurate, and biologically motivated theory, such as the one due to Cowan [42], could be applied, we believe the simple physical transparency of the present calculation has value as an aid to understanding the dynamics of spike timing precision.

To summarize, we have shown that the spike timing precision due to subthreshold stimuli can be enhanced by internal noise, whereas the precision due to suprathreshold stimuli is only degraded by it. In response to spikes arriving at the summing center, a single spike will or will not appear at the output of the integrate-and-fire, or decision neuron, shown in Fig. 1(a), in response to a single applied stimulus at the HH inputs. We are currently studying the statistics of the decisions both with this numerical model and with our experimental crayfish tailfan/sixth ganglion preparation [43].
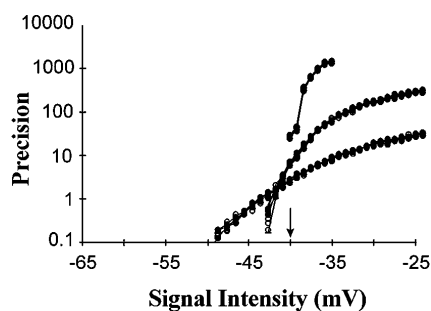
FIG. 4. The spike timing precision versus stimulus amplitude for three noise intensities: $\sigma = 0.2$ mV uppermost data set, $\sigma = 1.7$ mV middle data set, and $\sigma = 4.6$ mV lowermost data set. The deterministic threshold is marked by the arrow.

*Center for Neurodynamics.
†Department of Biology.
‡Department of Physics and Astronomy.

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