Suprathreshold Stochastic Firing Dynamics with Memory in P-Type Electroreceptors

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Weakly electric fish generate a periodic electric field as a carrier signal for active location and communication tasks. Highly sensitive P-type receptors on their surface fire in response to carrier amplitude modulations (AM's) in a noisy phase locked fashion. A simple generic model of receptor activity and signal encoding is presented. Its suprathreshold dynamics, memory and receptor noise reproduce observed firing interval distributions and correlations. The model ultimately explains how smooth responses to AM's are compatible with its nonlinear phase locking properties, and reveals how receptor noise can sometimes enhance the encoding of small yet suprathreshold AM's.

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There has been much interest over the past decades in the nonlinear dynamical properties of excitable systems. Studies of single cells and cell networks have revealed various forms of synchronized activity to physical stimuli or input from other cells (see, e.g., [1,2]). Also, there has been much interest in the mechanisms by which cells or ion channels respond to minute signals, and to the effect of noise on such responses [2–4]. Many sensory stimuli, such as sounds, contain an oscillatory component, and the encoding of stimuli into neuronal firing patterns involves phase locking to this component. This is the case for electroreceptors involved in active electrolocation and electrocommunication tasks in weakly electric fish [5,6].

In particular, "probability"-type electroreceptors or "P-units" are continuously driven by a highly periodic quasisinusoidal electric field [electric organ discharge (EOD)] generated by the fish. When the amplitude of this EOD is constant, a P-unit always fires near a given EOD phase, but skips a random number of EOD cycles between firings, as shown in Figs. 1a and 1d. The probability P of firing in an EOD cycle is a smooth increasing function of the instantaneous EOD amplitude [5,6]. P-units can thus encode amplitude modulations (AM's) of this EOD or "carrier," arising from environmental stimuli, into the frequency of "randomly" phase locked firings.

The dynamical origin of this firing pattern, and especially its implication for signal encoding in excitable systems, are the focus of our Letter. Studying these implications is possible only once we have a biophysically justified model of P-unit activity. Theoretical studies of various forms of deterministic phase locked firing abound (see, e.g., [1,7,8]). None account, however, for the smooth pattern of skipped cycles seen in P-units, for which interspike interval histograms (ISIH) have many peaks at contiguous multiples of the EOD period, and the peak maxima fall on a bell-shaped curve. This pattern is similar to those seen in the context of stochastic resonance [4], where a subthreshold stimulus and dynamical noise together produce the smooth skipping pattern; those patterns, however, lack interspike interval (ISI) correlations displayed by P-units (see below and Fig. 1c). Subthreshold deterministic chaos [9] does produce similar ISIH's. However, unless noise is added to the dynamics, ISIH's do not have the smoothness described above [10] and, even then, there are no significant ISI correlations. Also, a detailed deterministic ionic model [11] for studying P-unit tuning curves does not display the skipping patterns seen in the data, and a stochastic P-unit model [5] which reproduces skipping and frequency response data has no firing dynamics or ISI correlations.

A P-unit is composed of 25–40 receptor cells and a nerve fiber making synaptic contact unto upwards of 16 active neurotransmitter release sites per receptor cell [12]. Although intracellular recordings are not yet possible, there is much indirect evidence that the EOD amplitude changes individual receptor potentials, which govern

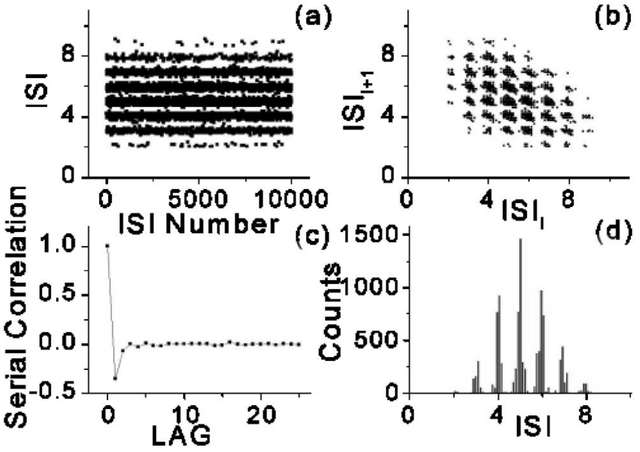

FIG. 1. Analysis of 10 000 consecutive interspike intervals from a P-unit of the weakly electric fish A. Leptorhynchus (data courtesy of Mark Nelson, Beckmann Institute, Illinois, USA; we focus on such "nonbursty" units). Time is in EOD cycles; the EOD frequency is 755 Hz. The firing rate is 145 Hz which corresponds to $P = 0.192$. (a) Raster plot of ISI duration versus ISI number, (b) return map, (c) serial correlation, and (d) histogram.

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the rate of release of a neurotransmitter onto the nerve. The probability P that the nerve fires in an EOD cycle is proportional to the amount of transmitter that binds on target channels in the nerve membrane. Fluctuations in release rates are thus one expected source of current noise [5,13,14]. Others include conductance fluctuations through various ion channels in the receptor cells and the nerve fiber. Noise has been implicated in recent studies of "passive" electroreceptors [2,3] that detect low frequency electric field fluctuations without using an EOD. In contrast to the EOD and AM's studied here, those studies involve much slower oscillations, with typically many firings per cycle.

Noise is known to perturb periodic phase locked patterns (see, e.g., [15]). Our model suggests that P-unit firing results from suprathreshold dynamics with refractory effects, perturbed by a significant amount of intrinsic receptor noise. It is inspired from an analysis of ISI correlations. We assume that the ith firing time is given by $t_i = n_i T + \xi_i$, where T is the period of the external forcing, n_i is a positive integer that increases with i by integer jumps, and the ξ_i are independent and identically distributed random values. The ξ_i represent jitter in the firing times around multiples of T. Defining the random variable $m_i \equiv n_i - n_{i-1}$, we can write for the serial correlation of intervals $I_i = t_i - t_{i-1}$ at lag one:

$$\frac{\langle (I_{i+1} - \langle I\rangle)(I_i - \langle I\rangle)\rangle}{\langle (I_i - \langle I\rangle)^2\rangle} = \frac{(\langle m_{i+1}m_i\rangle - \langle m_i\rangle^2)T^2 - \langle \xi_i^2\rangle}{(\langle m_i^2\rangle - \langle m_i\rangle^2)T^2 + 2\langle \xi_i^2\rangle}\,. \tag{1}$$

These correlations can be estimated from the data in Fig. 1 (the period T is normalized to one), since m represents the nearest integer to a given ISI: $\langle \xi^2\rangle = 0.00461$, $\langle m_{i+1}m_i\rangle = 24.86$, $\langle m_i^2\rangle = 26.78$, and $\langle m_i\rangle^2 = 25.39$, yielding an serial correlation of -0.381. This is close to the actual value of -0.351, which justifies our assumption about the t_i. Another justification comes from inspection of the ISIH; an ISI can be written as $I_i = m_i T + \eta_i$. The η_i govern the ISIH peak widths and satisfy $\langle \eta_{i+1}\eta_i\rangle / \langle \eta_i^2\rangle = -0.5$. This second serial correlation, which our data exhibits (not shown) and which explains the negatively sloped elongation of each cluster in the ISI return map (Fig. 1b), results from phase locking: when a firing leads (lags) the mean EOD phase at which firings occur, the next firing will lag (lead) on average, so that firings keep in step with the EOD.

The dominant serial correlation, due to $\langle m_{i+1}m_i\rangle$, implies that long skips tend to be followed by shorter skips, and vice versa. Thus, there is memory extending beyond one ISI, as expected from refractory effects at such firing rates [13,14,16]. Our model builds on the leaky integrate-and-fire (LIF) model [13,14,17] to account for this memory as well as noisy phase locking to periodic input. Firing occurs when membrane voltage reaches threshold, after which voltage is reset to zero. In contrast with the standard LIF model, this threshold is a dynamical variable (see, e.g.,[14,16]). Resetting the threshold to the same higher value after each spike [14], or to a random value (see, e.g.,[18]), wipes out memory, as voltage resetting does. Rather, here the threshold carries the memory of previous spikes. After a spike, a fixed amount Δw is simply added to the threshold value just prior to firing. After staying at this new value for an absolute refractory period T_r, the threshold decays exponentially towards w_0 until the next firing. Alternative schemes in which the voltage carries the memory and which involve noise and synaptic input have been studied (without periodic input) in [16]. There are a number of plausible mechanisms for threshold-based refractory effects which increase the voltage-threshold distance after a spike. Examples include slow sodium cumulative inactivation [19] , synaptic desensitization [20], or other slow negative adaptation currents [21].

These refractory dynamics are here driven by stochastic and periodic input. Let $A\sin(2\pi f t)$ be the transdermal potential due to the EOD of amplitude A and frequency f. The P-unit's nerve is driven by a steady state synaptic current I_{syn} from its receptor cells [22]:

$$I_{\text{syn}} = \gamma A[1 + \xi(t)]\sin(2\pi f t) H[\sin(2\pi f t)] + \eta(t)\,, \tag{2}$$

where γ is a constant, $\xi(t)$ is a zero-mean Gaussian "synaptic" noise of variance σ^2 that is fixed over one EOD cycle, and $H(t)$ is the Heaviside function that accounts for the fact that many receptors rectify a periodic forcing [18,23]. An Ornstein-Uhlenbeck process $\eta(t)$ with correlation time τ_η and variance D/τ_η mimics other noise sources [13,14,16] and further increases ISIH peak widths. These choices are biophysically plausible, but our results do not depend on the specifics of these choices. The equations for voltage v and threshold w between the last firing time t_{last} and the next one t_{next}, i.e., until $v(t_{\text{next}}) = w(t_{\text{next}})$, are

$$\dot{v} = -\frac{v}{\tau_v} + I_{\text{syn}}\,, \tag{3}$$

$$\dot{w} = H(t - t_{\text{last}} - T_r)\left(\frac{w_0 - w}{\tau_w}\right) + \Delta w\,\delta(t - t_{\text{last}})\,, \tag{4}$$

where δ is the delta function. Spike train properties, shown in Fig. 2, closely match those in Fig. 1. Without noise, 5:1 periodic firing occurs, i.e., the stimulus is suprathreshold. The ISI serial correlation at lag one is -0.372, very close to that in Fig. 1 [24]. We have verified that such correlation is not present in the FitzHugh-Nagumo [9] or the Hodgkin-Huxley models with standard parameters. Further, subthreshold periodic forcing produced interval histograms that were too broad or asymmetric. Note that, while this correlation is a deterministic property, it appears in Fig. 1 only when noise perturbs the 5:1 limit cycle. Finally, our model also reproduces tuning curve data [11] (not shown).

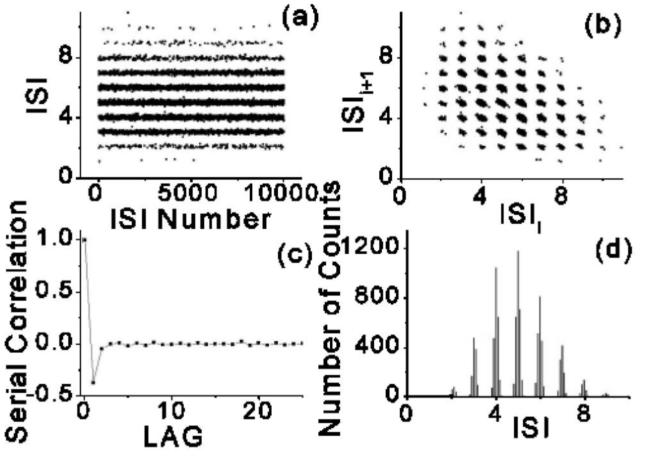

FIG. 2. Analysis of 10 000 ISI's generated by the model of Eq. (4). Time is in EOD cycles. (a) Raster plot, (b) return map, (c) serial correlation, and (d) histogram. Parameters are: $f = 1000$ Hz, $T_r = 1$ ms, $A = 0.3$ mV, $\gamma = 0.87$, $w_0 = 0.03$ mV, $\Delta w = 0.05$ mV, $\tau_v = 1$ ms, $\tau_w = 7.75$ ms, $\sigma^2 = 0.0256$, $\tau_\eta = 0.075$ ms, and $D = 1.758 \times 10^{-4}$.

This model now finally allows us to make predictions on the ability of P-units to encode AM's. Increasing the EOD amplitude increases P. Yet, without intrinsic noise and AM's, and due to the model's deterministic phase locking structure, two EOD's of neighboring amplitudes may produce the same firing pattern, thus being indistinguishable for higher brain centers. This occurs when amplitudes fall within the same plateau in a plot of P (proportional to firing rate) versus forcing amplitude A, as shown in Fig. 3 (see also [8] for the LIF model). Interestingly, Fig. 3 exhibits only small plateaus in the operating range around $P = 0.2$. Thus, our model suggests the interesting property that, even without noise, the P-unit in Fig. 1 has an almost invertible relationship between amplitude and firing rate despite nonlinear phase lockings, i.e., it has an intrinsic almost-smooth stimulus-response characteristic.

Figure 3 also shows that intrinsic noise in the P-unit further smoothes out the small steps of the "devil's staircase": the noise breaks up phase locking patterns (see also [15,23]). The implication for our model is that this intrinsic noise induces a skipping pattern whose mean frequency (averaged over a few EOD cycles) can always track the slower fluctuations of an AM. However, such smoothing also results from AM's alone, since they induce transitions between neighboring (in parameter space) deterministic firing patterns. For example, the ISIH in Fig. 2 can also be obtained by turning off the noise sources and turning on a random AM of a certain variance. Thus, it is not clear whether P-unit noise enhances or degrades the encoding. To address this point, we used the stimulus reconstruction technique [25] in the implementation of [6,18] to quantify information transfer from bandlimited random AM's to the spike train. This method constructs from the data an optimal response filter which, when convolved with the spike train, produces a "reconstructed stimulus" that is closest, in the mean square sense, to the actual stimulus.

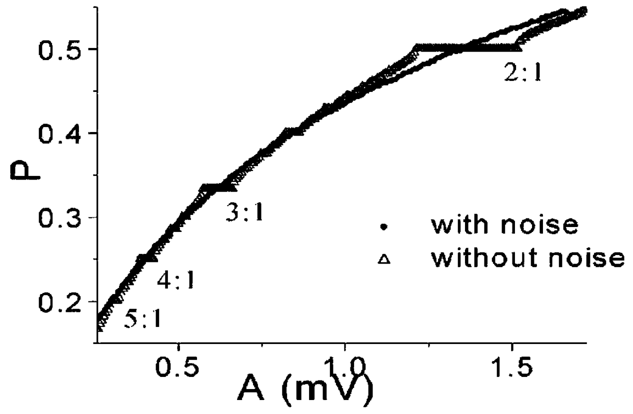

FIG. 3. Mean frequency of firing versus amplitude of the forcing in Eq. (4), without (hollow) and with (solid) P-unit noise. A devil's staircase structure is seen in the noiseless case; steps are "rounded" by noise. Each value is obtained from the mean firing rate of a 500 ms simulation.

Figure 4 shows the novel result that the information transfer increases or decreases with increasing P-unit noise [ξ in Eq. (2)] in this suprathreshold case (η was set to zero for simplicity). For small P, although increased information transfer is expected from the linearization of plateaus

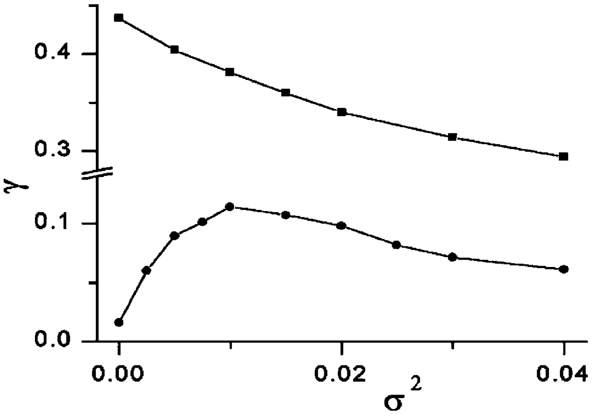

FIG. 4. Coding fraction γ vs synaptic noise variance σ^2 on a small plateau (5:1, upper curve) and a large plateau (2:1, lower curve) of Fig. 3. The AFM signal $S(t)$ is a lowpass-filtered Gaussian noise of variance $\sigma^2_{\rm sig}$ (fourth-order pole with cutoff frequency f_c equal to one-tenth of the EOD frequency [6]). This signal modulates the amplitude of the carrier, i.e., $A(t) = A[1 + \xi(t) + S(t)]$. An optimal Wiener filter $h(t)$ was obtained [6] by minimizing the mean square error $\epsilon = [\int_{-f_c}^{f_c} S_{nn}(f)\,df]^{1/2}$, where $S_{nn}(f)$ is the power spectrum of $n(t) = S(t) - S_{\rm est}(t)$; here $S_{\rm est}(t)$ is an estimated signal resulting from the convolution of the spike train with $h(t)$. The coding fraction is $\gamma = 1 - \epsilon/\sigma_{\rm sig}$, the quality of encoding being best for $\gamma = 1$. The signal variances were 0.15 (5:1) and 0.04 (2:1), yielding lower values of γ for the latter case. Parameters other than σ are the same as in Fig. 2, except for $A = 1.38$ mV in the 2:1 case and $D = 0$ in both cases.

(Fig. 3), the noise actually introduces more randomness into the spike train. On the other hand, P-units with a large P [5] sense a larger effective EOD amplitude. Their deterministic dynamics may then fall on a large plateau such as the one for the 2:1 firing pattern in Fig. 3 (i.e., $P = 0.5$). This pattern would therefore not change with small AM's. Thus, no coding could occur, unless perhaps P-unit noise smooths out such a plateau as in Fig. 3. Information transfer in this case now increases with increasing noise (Fig. 4). The information transfer is again degraded at larger noise as more spikes occur at irrelevant times. Note that this is not a stochastic resonance effect [4], since the forcing here is suprathreshold.

In summary, our analysis of ISI correlations in P-type electroreceptors has led us to a simple generic excitable model based on suprathreshold forcing, memory, and dynamical noise. Its phase locking structure suggests that low-P P-units naturally have smooth responses to random carrier AM's. Furthermore, despite suprathreshold dynamics, receptor noise can help certain high-"P" P-units encode small AM's by perturbing periodic phase locked patterns.

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