Competition model for aperiodic stochastic resonance in a Fitzhugh-Nagumo model of cardiac sensory neurons

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Regional cardiac control depends upon feedback of the status of the heart from afferent neurons responding to chemical and mechanical stimuli as transduced by an array of sensory neurites. Emerging experimental evidence shows that neural control in the heart may be partially exerted using subthreshold inputs that are amplified by noisy mechanical fluctuations. This amplification is known as aperiodic stochastic resonance (ASR). Neural control in the noisy, subthreshold regime is difficult to see since there is a near absence of any correlation between input and the output, the latter being the average firing (spiking) rate of the neuron. This lack of correlation is unresolved by traditional energy models of ASR since these models are unsuitable for identifying ''cause and effect'' between such inputs and outputs. In this paper, the ''competition between averages'' model is used to determine what portion of a noisy, subthreshold input is responsible, on average, for the output of sensory neurons as represented by the Fitzhugh-Nagumo equations. A physiologically relevant conclusion of this analysis is that a nearly constant amount of input is responsible for a spike, on average, and this amount is approximately *independent* of the firing rate. Hence, correlation measures are generally reduced as the firing rate is lowered even though neural control under this model is actually unaffected.

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I. INTRODUCTION

Thresholded biological systems such as sensory neurons and hysteretic neural populations, are exposed to a host of time varying stimuli *in vivo* that can be represented by an aperiodic input with superimposed noisy variations. Aperiodic stochastic resonance (ASR) is the study of how noise in such systems is able to provoke a response to slowly varying, subthreshold, aperiodic inputs. As such inputs are involved in neural cardiac regulation [1,2] the study of ASR is important to provide insight into noise enhancement of cardiac control.

A feature commonly used to measure ASR in sensory neurons is the correlation between noisy, slowly varying, subthreshold aperiodic inputs and the average activity level generated by such neurons [3–9]. In this paper, the term ''activity level'' is also variously referred to as a ''firing rate'' or ''spiking rate.'' Concerning sensory neurons subjected to *periodic* inputs [stochastic resonance (SR)], it is the relationship between the power spectrum of a noisy periodic input and that of the average firing rate that is thought to characterize the control [10–13]. Analytic expressions for the correlation between input and neuronal firing rate have been found based on the canonical Fitzhugh-Nagumo (FHN) equations [3,4]. The FHN equations describe the resettable firing dynamics of a sensory neuron and allow for the approximation of an action potential as the escape from a potential well followed by a recovery period within which no activity can be generated (absolute refractory period) [4]. The average firing rate of a neuron in the presence of noise then follows Kramer's escape rate [14] from which the correlation between the noisy input and firing rate is directly constructed.

The potential-well description defines an energy level that must be surmounted in order for a neuron to fire. Since this energy is accumulated from all inputs after the generation of a previous spike, the energy description is capable of predicting *when*, but not *how* a spike occurs in the presence of noisy subthreshold inputs. That is, energy formulations are unsuitable in identifying the input factors responsible for a spike.

The aim of this paper is to replace potential theory with a competition model that is capable of assessing the expected time to fire (*when*) as well as cause and effect (*how*) between the noisy subthreshold aperiodic inputs and the average firing rate generated by a neuron (output). For analytic simplicity, the FHN equations, which approximate the physiologically based Hodgkins-Huxley (HH) equations, are chosen as a model for the firing of a sensory neuron. This choice is further justified by the experimental observation [2] (and others referenced in Ref. [2]) that any model of a cardiac sensory neuron must include the response of sensory neurites to mechanical and chemical stimuli. Until such a model is constructed and verified with experimental data, there is little physical preference in this work for either the FHN or HH equations. However, the conclusions drawn in this paper, based upon the FHN equations, must be regarded as being physiologically qualitative. The method of analysis in this study (a detailed description appears in Ref. [15]) is applicable to more complex neural models such as the HH equations [5].

If $R(t)$ is an external forcing (input), $v(t)$ is the neural voltage, $w(t)$ is a slow recovery variable, and $f(v)=v(a-v)(v-1)$, where a is a parameter, then

$$\epsilon\dot{v}(t)=f(v)-w(t)+R(t),$$

$$\dot{w}(t)=v(t)-w(t)-b. \tag{1}$$

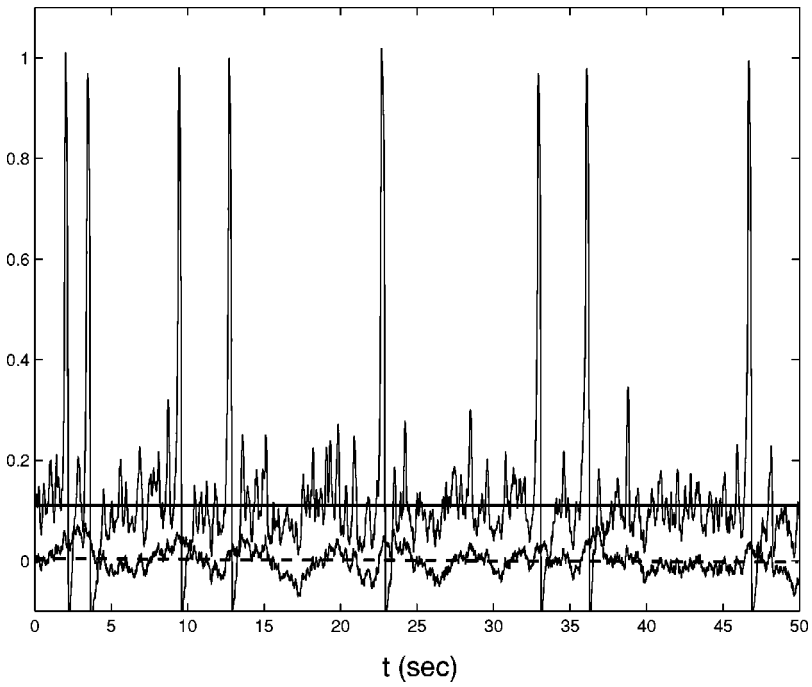

FIG. 1. The numerical solution of the FHN model (1) is shown along with the inputs $R(t)$. In the absence of firing, the voltage variable $v(t)$ is close to the stable fixed point shown as the heavier solid line. The inputs $R(t)$, are near the zero expected value $[\mu(t)=0]$ shown as the heavier dashed line. All variations around the heavier dashed line are the fast, red noise, fluctuations. There is little correlation between inputs and outputs [average firing rate of $v(t)$].

is the FHN neural model, where $a=0.5$ and $b=0.15$ are parameters, while the parameter ϵ is taken to be 0.008 (this is same order of magnitude as that chosen in Ref. [3]). To determine cause and effect between the noisy inputs and the average firing rate of $v(t)$, it is necessary to eliminate the recovery variable $w(t)$ from Eq. (1) so that the dependence of $v(t)$ on the inputs $R(t)$ is explicit. Since the FHN equations are linear in the recovery, variable $w(t)$ is conveniently eliminated to give

$$\epsilon\ddot{v}(t)+[\epsilon-f'(v)]\dot{v}(t)+v(t)-f(v)-b=R(t)+\dot{R}(t). \quad (2)$$

The elimination of the recovery variable could have been performed by linearizing around the stable fixed point. This latter approach is necessary when there is a nonlinear dependence on the recovery variable(s), such as occurs in the HH equations.

In this form, it is clear that the recovery variable $w(t)$ feeds back the rate of change of inputs $\dot{R}(t)$, to $v(t)$ and is therefore of primary importance in generating a spike in the presence of noisy subthreshold inputs (high-frequency noise has large derivatives). This point is further demonstrated in Fig. 1. The solution of Eq. (1) is shown along with a noisy forcing $R(t)$, taken from the solution of $R(t)+\dot{R}(t)=\mu(t)+\sigma S(t)$, where $\mu(t)$ is the process mean (this is the control signal), σ is the noise standard deviation, and $S(t)$ is a stationary Gaussian random process with zero mean, unit variance, and exponentially decaying correlation function $\rho(\tau)=\exp\{-2|\tau|/\theta\}$ (this form of forcing is also considered in Ref. [12]). The correlation scale of fluctuation [16] θ, is chosen here to equal the firing time constant $\epsilon=0.008$ s. At this θ value, the fluctuations $S(t)$ are ''almost'' white noises and will not be confused with the slowly varying ''essential'' or control input $\mu(t)$. The ''almost'' means that the noise variance is restricted to a finite value, essentially by band limiting its spectral density.

The solution of $R(t)+\dot{R}(t)=\mu(t)+\sigma S(t)$, is a Gaussian random noise with a ''red'' spectral density function (decreasing power at higher frequencies) and is referred to here as ''red noise.'' In Fig. 1, $\mu(t)=0$ and $\sigma=0.6$. There is little pointwise (in time) correlation between the input $R(t)$, and the output [average firing rate of $v(t)$]. Hence, a question arises: *how* are the fast fluctuations in the input causing firing?

The cause and effect description of the FHN equations, in the noisy subthreshold forcing regime developed here, is also used to describe a possible role for noisy mechanical fluctuations in inputs to cardiac afferent neurons. Developing a better understanding of the effects of noise in the cardiac neural regulatory system is important because this system utilizes feedback and feedforward mechanisms involving spatially localized domains. Control within such a system must deal with the effects of noise, ideally using noise to its advantage [15,17].

The inputs to a cardiac afferent neuron are represented as the sum of two components. First, there is a slowly varying component, which varies at a $1-10$ second time scale and mainly represents chemical stimuli. Second, there is a fast fluctuation component that has amplitude fluctuations of duration $0.01-0.1$ s that derive from noisy mechanical stimuli representing local muscle strain as transduced by sensory neurites (see Ref. [2] for a literature review and detailed description). The fast fluctuations are still an order of magnitude more slowly varying than a cardiac afferent action potential and this relationship is the basis for the focus in this paper on red noise fluctuations (Fig. 1). Furthermore, the firing rate of a cardiac afferent neuron under noisy subthreshold inputs is typically on the order of 10 Hz [2]. This order

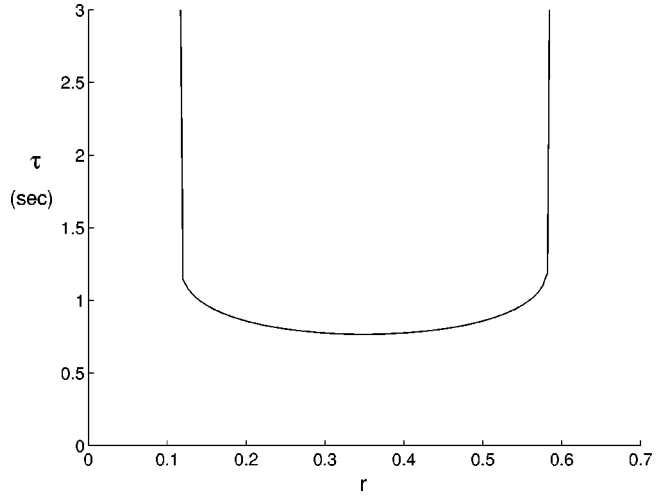

FIG. 2. Time to fire (interspike interval) for a constant input r.

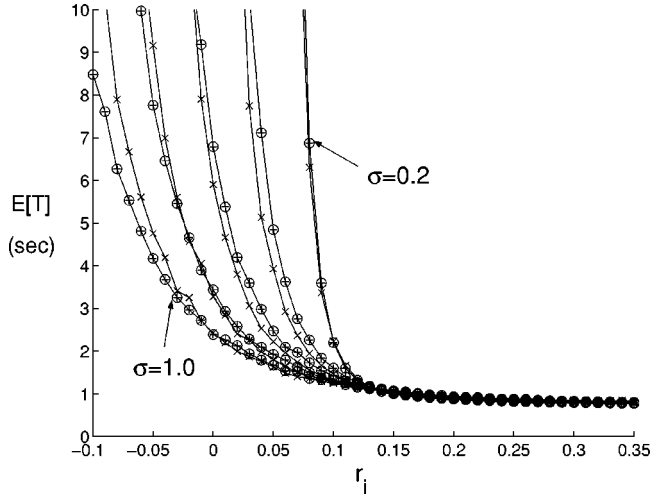

FIG. 3. The expected time to fire, $E[T]$, is shown for curves of constant σ ranging from $\sigma=0.2$ to $\sigma=1.0$ with steps of $\sigma=0.2$. $E[T]$ found from the differential equations (2) (solid lines with ''x'' symbols), is compared to that using the competition between averages model developed in Sec. III (solid lines with ''o'' symbols).

of magnitude reduction in activity level, due to a possible reliance on noisy subthreshold inputs, from a maximal activity of $100-150$ Hz in the presence of superthreshold inputs, agrees with that derived from the FHN equations (Fig. 1).

A main difficulty in understanding cardiac control is the ability to envision how a large noisy component in afferent neural activity, arising from local muscle strains, could be useful to cardiac neural regulation. Hence, understanding *how* noisy inputs cause firing in the FHN equations allows an understanding of the role of fast mechanical fluctuations in cardiac control.

II. NOISY APERIODIC INPUTS AND NEURAL CONTROL

Cardiac afferent neurons provide feedback in closed-loop control of regional cardiac function through variations in their average activity. The investigation of firing in the presence of noise will be performed by first looking at the noise-free problem where the noisy input $R(t)$ is replaced by a constant input r. In the FHN model, (1 or 2) the time between spikes τ for a *noise-free* constant input r in the range $0.11<r<r^*$, is $\tau(r)>\tau^*$ ($r^*\approx 0.35$ and $\tau^*\approx 0.8$). This is depicted in Fig. 2. Note that $r>r^*$ results in a monotonic *increase* in τ. The competition model is described using a threshold definition of the time between spikes taken from the inverse, $r(\tau)$, of $\tau(r)$. If a threshold $r(\tau)$ is defined, then an input of $r(\tau)$ ensures that within a time τ another spike will occur. For $r<r^*$, the lower branch of the inverse of $\tau(r)$ is taken ($\tau(r)$ increases for $r>r^*$) and as τ is decreased to τ^* from above, the threshold $r(\tau)$ monotonically increases to $r(\tau^*)=r^*$ from below. For $\tau<\tau^*$ it is necessary, for consistency, to set the threshold to $r(\tau)=\infty$.

The assumption adopted in Sec. I, that randomized inputs satisfy $R(t)+\dot{R}(t)=\mu(t)+\sigma S(t)$, is arbitrary. To investigate the affect of the noise spectral density shape on the neural response, the noise model may be more generally parametrized as

$$R(t)+\beta\dot{R}(t)=\mu(t)+\sigma S(t). \tag{3}$$

Choosing $\beta=1$ yields a red noise $R(t)$ while the lower limit $\beta=0$ gives an $R(t)$ with an almost white spectral density. The effect of variations in β is followed up in the conclusions and it is hereafter assumed that $\beta=1$. The slowly varying input component, $\mu(t)$, is approximated as being piecewise constant

$$\mu(t)=\sum_{i=0}^{\infty} r_i[U(t-t_i)-U(t-t_{i+1})], \tag{4}$$

where $U(t)=0, t<0$, and $U(t)=1, t\geqslant 0$, is the Heaviside step function, and $\mu(t)=r_i$ over $t=t_i$ to $t=t_{i+1}$.

For $\sigma>0$, $\tau(r_i)$ generalizes to the expected time to fire $E[T]$ that is dependent on both the mean input r_i, and the noise variance σ^2. The piecewise constant model for essential control inputs is useful to present a simple constraint for neural control in the presence of noisy, subthreshold inputs; the duration of a level r_i should be long enough to allow the average firing interarrival time, $E[T]$, to be established and the input r_i to have the desired effect (at least, $t_{i+1}-t_i \gg E[T]$). Lone spikes, which may occur at transitions between levels r_i and r_{i+1}, will have a negligible effect on the expected time to fire.

Expected firing times $E[T]$ from Eq. 2 are depicted in Fig. 3, as the solid curves with ''x'' symbols, for various levels r_i and fluctuation levels σ, where $\sigma=0$ (not shown) is the same result as Fig. 2 for noiseless $r(t)=r_i<r^*$. All of the expected time to fire curves in Fig. 3 are estimated from 1000 interspike intervals and numerical solutions are obtained using a fourth-order Runge-Kutta scheme. The solid curves with ''o'' symbols are the expected times to fire predicted from the competition between averages described below.

III. COMPETITION BETWEEN AVERAGES

A cause and effect relationship between the noisy inputs and average firing rate is found by backwards local averages (see Ref. 15) of Eq. (2) over the time interval from t to $t-W$ (where W is the averaging window width). If $v(t)$ is near the stable fixed point (not firing, see Fig. 1), then $f_W(v) \approx f(v_W)$ (the subscript W denotes the width of the backwards moving average) and, to first order,

$$\epsilon \ddot{v}_W(t) + [\epsilon - f'(v_W)]\dot{v}_W(t) + v_W(t) - f(v_W) - b = [R(t) + \dot{R}(t)]_W, \tag{5}$$

for all $t > W$.

A local average taken over a finite window will not generally equal its expectation. However, the averaging does reduce the overall variance of the local average by a factor of $\gamma(W)$, (see Ref. [15]) where at zero window width $\gamma = 1$ and at large window width, where $W \gg \theta$, γ approaches θ/W. All averaging of Eq. (2) for a level r_i is taken over the time interval $(t_i, t_{i+1}]$.

The hypothesis here is the same as that for a hysteretic population of neurons [15]: the expected time to fire under noisy external forcing can be expressed in terms of the time to fire $\tau(r_i)$, in the *absence* of noise, as discussed above. In the presence of noise, firing will occur at time t if *any* of the backward local averages from time t to time $t-W$ exceeds $r(W)$ [$0 < W < t$ and $r(W)$ is the input threshold, which leads to a first spike after time W]. Hence, each instant in time has a range of local averaging windows, $0 < W < t$, from which to draw a ''winning'' threshold exceedance, $R_W(t) > r(W)$. This is the competition between averages.

A further assumption is made concerning the barrier $r(W)$: The time to fire, $\tau(r)$, (Fig. 2) is modeled as the sum of a variable activation time when the external forcing is actively causing a spike, and an absolute refractory time, τ_r, during which no spiking is possible (a recovery takes place). The minimum time to fire is $\tau^* = \tau_a + \tau_r$, where τ_a is a minimum activation time. Therefore, the absolute refractory time τ_r is removed from the time to fire $\tau(r)$ in Fig. 2 by shifting this curve downwards by τ_r. The minimum of the shifted $\tau(r)$ curve is equal to the minimum activation time τ_a. The inverse of this curve $r(\tau)$ now forms the variable barrier $r(W)$. Unless explicitly stated it is now assumed that $\tau(r)$ and $r(W)$ are the appropriately shifted curves.

The above hypothesis and assumption are clearly verified in Fig. 3. Monte Carlo simulation of the expected time to fire, found from the FHN differential equation (2), is compared to the same found from the competition model (using a different generator seed). The absolute refractory time is chosen as $\tau_r \approx 0.3$ giving a minimum activation time $\tau_a \approx 0.5$. The differential equation is forced with almost white noise ($\theta = 0.008$) superimposed on r_i.

The description of cause and effect arising from the competition model is rooted in the averaging window W since this tells how much of the recent past has been responsible for a spike. This description is best clarified by a semianalytical model of the expected times to fire and is based upon the following restatement of the competition between averages (details are in Ref. [15]).

A local average of width W moving forward in time, has a known upcrossing (firing) rate over a threshold $d = r(W) - r_i$ given by $\nu(W)$ (see Ref. [15]), where $W \gg \theta$. For a Gaussian noise process with threshold $d > 0$, upcrossings will approximately follow a Poisson point process (the approximation improves as d increases). The time T to the *first* upcrossing of the threshold d by the local average process $[R(t) + \dot{R}(t)]_W$, is given by

$$E[T|W] = \tau_r + W + \frac{1}{\nu(W)}. \tag{6}$$

This conditional expectation is a function of the (random) averaging window width W of inputs responsible for a spike. Taking expectations with respect to W yields

$$E[T] = E[E[T|W]] \approx \tau_r + E[W] + E\left[\frac{1}{\nu(W)}\right] = \tau_r + \int_0^\infty w H(w)\, dw + \int_0^\infty \left(\frac{1}{\nu(w)}\right) H(w)\, dw, \tag{7}$$

where $H(w) = H(w; r_i, \sigma)$ is the probability density function of W, the averaging window width associated with a spike. Although the lower limits are zero in Eq. (7), there is no contribution to these integrals below $w = \tau_a$, since $H = 0$ when $0 < w < \tau_a$; the window width cannot go below the minimum activation time. This is a restatement of the competition between averages. It means that the likelihood a particular average of the inputs over a window width w, $[R(t) + \dot{R}(t)]_w$, causes a spike, is given by $H(w)$. Therefore, cause and effect resides in the probability density function of W, $H(w)$, which characterizes the amount of past input responsible for a spike.

A numerical description of H (no analytical results are available) is used to describe its properties in the subthreshold range $r_i < 0.11$, where the noise levels σ are associated with low firing rates ($E[T] \gg 1$). Simulation for subthreshold inputs shows that H is approximately lognormal, but is truncated to $w \geqslant \tau_a \approx 0.5$. The fitted lognormal distribution and the numerically derived normalized histogram are shown in Fig. 4. It is also clear that H has a complicated, but weak dependence upon r_i and σ. The weak dependence of H upon r_i and the noise level σ implies that the window width of noisy subthreshold inputs responsible for the average firing rate is approximately *independent* of the average firing rate (Sec. IV). The semianalytical formulation (7) and the competition between averages are compared in Fig. 5 for subthreshold inputs.

For superthreshold inputs, $r_i > 0.11$, H is strongly dependent on r_i and σ. However, in this case it tends to be normally distributed to first order around $\tau(r_i)$, and so a reasonable approximation (not shown) of the expected time to fire is $E[T] = \tau(r_i)$, taken from Fig. 2. This approximation is anticipated by the first-order independence of $E[T]$, at superthreshold inputs, on σ.

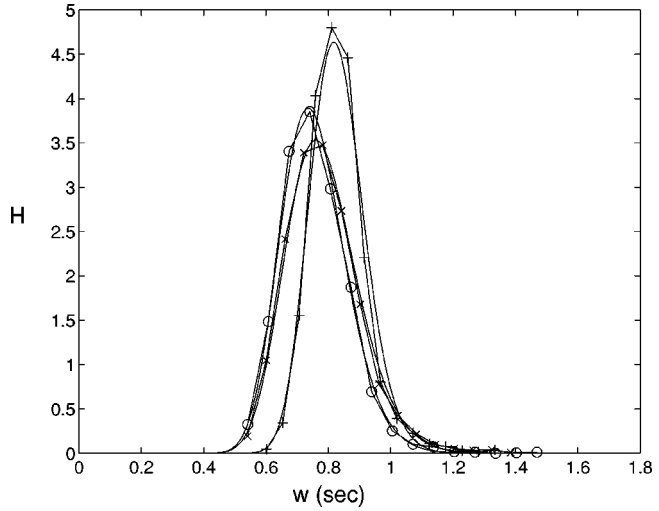

FIG. 4. The normalized histogram of the averaging window distribution $H(w;r_i,\sigma)$ is shown for three sets of r_i and σ: $H(w;0.03,0.6)$ as solid lines with ''x'' symbols, $H(w;0.04,0.4)$ as solid lines with ''+'' symbols, $H(w;-0.05,0.8)$ as solid lines with ''o'' symbols. The respective expected times to fire are $E[T] \approx 3.5$, $E[T] \approx 7$, and $E[T] \approx 8$. A fitted lognormal distribution is also shown as a solid line nearly superimposed upon each of the numerically derived $H(w;r_i,\sigma)$. There is little variation in $H(w;r_i,\sigma)$ despite large changes in the expected time to fire, $E[T]$, and the dependence of H upon r_i and σ is weak.

IV. SUMMARY AND CONCLUSIONS

The competition model presented here has been used to provide an understanding of cause and effect between inputs and the average firing rate, within the noisy, subthreshold input regime for the FHN equations. (Note, the FHN equations approximate the more physiologically accurate HH equations, and to this extent the conclusions drawn here regarding cause and effect are physiologically qualitative.) The connection between cause and effect in this regime is crucial to understanding how neural control can be meaningfully exerted in spite of a near absence of any (pointwise) correlation between the inputs and the average firing rate. Use of the competition model allows the drawing of the following, physiologically relevant conclusions:

(i) An approximately *constant* amount of input, is responsible, on average and at lower firing rates, for a spike (Sec. III). This feature of the FHN equations (which may not be true for other neural models), is due to the approximate independence of the probability density function H from the essential inputs r_i and the noise level σ as demonstrated in the previous section (Fig. 4).

(ii) Given (i), correlation between the input and average firing rate (output) is generally unsuitable to measure neural control. At lower firing rates (i) implies that, on average, the fraction of inputs responsible for a spike is inversely proportional to the time to fire and this forces a reduction in any correlation measure as the expected time to fire increases. This reduction is an artifact because neural control continues to be exerted through an approximately constant length of input per spike. Hence, the tuning or modulation of input noise levels to increase correlation levels with the intention of improving control performance [6], may be unnecessary. This last observation is important since it allows the extension of ASR-based control to situations, such as cardiac neural control, where noise modulation has not been observed and little correlation is observed between inputs and average firing rate.

(iii) The *recovery variable* $w(t)$, is predicted as being primarily responsible for neural firing in the regime of noisy, subthreshold inputs. The recovery variable does this by feeding back the input derivative to the voltage $v(t)$ [Sec. I, Eq. (2)]. This property of the FHN equations arises due to the wide separation of the slow (recovery) and the fast (firing) time scales and may differ in the HH equations where these time scales are less separated [5].

(iv) Given (iii), this sensitivity of the voltage $v(t)$ to the input derivative, seen in Eq. (2), also implies that forcing of the FHN equations by almost ''white'' Gaussian noise is

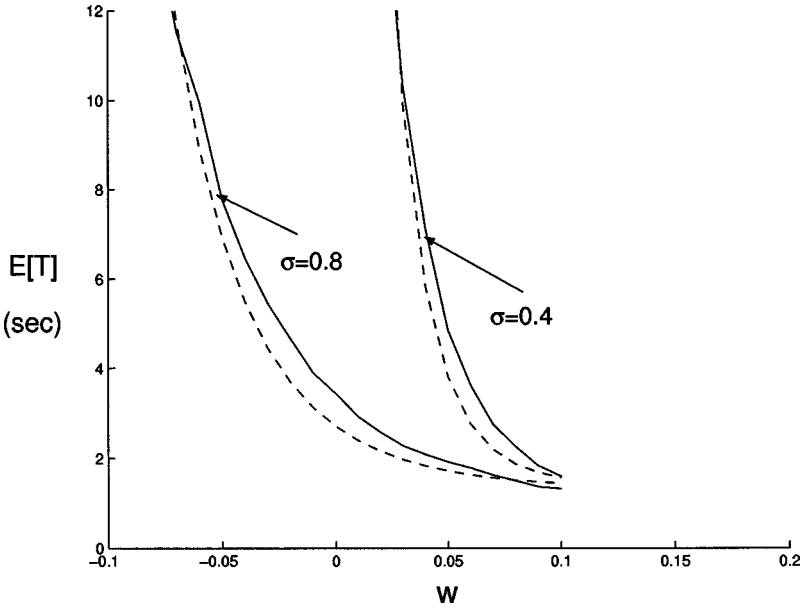

FIG. 5. The expected time to fire, $E[T]$ from the competition between averages (solid lines) is compared to the same predicted from the semianalytic model (7) (dashed lines) for two values of σ. The fitted log-normal distributions, $H(w;0.04,0.4)$ and $H(w;-0.05,0.8)$ (see Fig. 4), are, respectively, used in the evaluation of $E[T]$ (7) for $\sigma=0.4$ and $\sigma=0.8$. The dependence of H on r_i is neglected in computing $E[T]$. The closer agreement between the semianalytical model and the competition, near $r_i=-0.05$ and $r_i=0.04$, is due to the use of the corresponding $H(w;r_i,\sigma)$ at those locations.

likely to be less physical since it greatly increases the gradient of the expected time to fire with respect to the noise level. Specifically, with respect to Eq. (2), the standard deviation of white-noise forcing, $\beta=0$, is a factor of $\sqrt{1+2\pi/\theta^2}$ [16] greater than the red noise forcing found when $\beta=1$. In addition, this noise magnification factor is typically large and unknown since the correlation scale is $\theta \ll 1$ (taken to be the firing time constant $\epsilon=0.008$ here) and difficult to estimate. It is felt that such a white-noise model runs counter to control performance requirements and so seems unlikely to be implemented in the actual biological model.

Given (i)–(iv), it is clear that a useful feature of the competition model is the capability to form much more precise, physiologically based, comparisons between neural models such as the Hodgkins-Huxley and the Fitzhugh-Nagumo equations; their treatment of cause and effect in the noisy subthreshold regime can now be directly evaluated. For example, the possibility, that neural models may behave differently in the noisy subthreshold regime, has recently begun to be investigated [18,19].

Understanding of cardiac regional control has been obscured by the fact that most afferent neural activity, basic to feedback information for cardiac neural regulation, has a large noisy component arising from sensory neurites responding to fast fluctuations in local muscle strains [1,2]. However, when considered in light of ASR-based control, the model considered here suggests that noisy fluctuations could well serve to amplify subthreshold essential control inputs, derived mainly from chemical stimuli operating at longer time scales. Such extension of cardiac neural control to subthreshold input levels would certainly be useful in improving cardiac control performance. The understanding of these points will aid the design of experiments to uncover the details of cardiac regional control.

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[1] J.A. Armour, M.H. Huang, A. Pelleg, and C. Sylven, Cardiovasc. Res. **28**, 1218 (1994).
[2] R.D. Foreman, R.W. Blair, H.R. Holmes, and J.A. Armour, Am. J. Physiol. **276**, 980 (1999).
[3] J.J. Collins, C.C. Chow, and T.T. Imhoff, Phys. Rev. E **52**, 3321 (1995).
[4] J.J. Collins, C.C. Chow, and T.T. Imhoff, Nature (London) **376**, 236 (1995).
[5] J.J. Collins, C.C. Chow, A.C. Capela, and T.T. Imhoff, Phys. Rev. E **54**, 5575 (1996).
[6] C.C. Chow, T.T. Imhoff, and J.J. Collins, Chaos **8**, 616 (1998).
[7] C. Heneghan, C.C. Chow, J.J. Collins, T.T. Imhoff, S.B. Lowen, and M.C. Teich, Phys. Rev. E **54**, 2228 (1996).
[8] A. Capurro, K. Pakdaman, T. Nomura, and S. Sato, Phys. Rev. E **58**, 4820 (1998).
[9] D.R. Chialvo, A. Longtin, and J. Muller-Gerking, Phys. Rev. E **55**, 1798 (1997).
[10] A. Longtin, J. Stat. Phys. **70**, 309 (1993).
[11] M. Franaszek and E. Simiu, Phys. Rev. E **57**, 5870 (1998).
[12] B. Lindner and L. Schimansky-Geier, Phys. Rev. E **60**, 7270 (1999).
[13] S.R. Massanes and C.J.P. Vicente, Phys. Rev. E **59**, 4490 (1999).
[14] H.A. Kramers, Physica **7**, 284 (1940).
[15] G.C. Kember, G.A. Fenton, K. Collier, and J.A. Armour, Phys. Rev. E **61**, 1816 (2000).
[16] E. Vanmarcke, *Random Fields* (The MIT Press, Massachusetts, 1984).
[17] J.A. Armour, K. Collier, G. Kember, and J.L. Ardell, Am. J. Physiol. **274**, 939 (1998).
[18] D. Brown, J. Feng, and S. Feerick, Phys. Rev. Lett. **82**, 4731 (1999).
[19] J.R. Clay and A. Shrier, J. Theor. Biol. **197**, 207 (1999).