AD-A276 256

IENTATION PAGE

Form Approved
OMB No 0704-0188

1 AGENCY USE ONLY *(Leave blank)*	2 REPORT DATE February 1994	3 REPORT TYPE AND DATES COVERED Professional Paper

4. TITLE AND SUBTITLE
TOWARDS SIMPLICITY: NOISE AND COOPERATION IN THE 'PERFECT INTEGRATOR'

5. FUNDING NUMBERS
In-house Funding

6. AUTHOR(S)
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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
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94–06720

19pgs

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Naval Command, Control and Ocean Surveillance Center (NCCOSC)
RDT&E Division
San Diego, CA 92152–5001

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

C
MAR 0 1 1994
D
E

12a. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution is unlimited.

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 words)*

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DTIC QUALITY INSPECTED

94 2 28 121

Published in *Proceedings of the Second Apalachian Conference on Behavioral Neurodynamics,* November 1993, 18 pages.

14. SUBJECT TERMS
nonlinear cooperative effects
Stochastic Resonance (SR)

15. NUMBER OF PAGES

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
UNCLASSIFIED	UNCLASSIFIED	UNCLASSIFIED	SAME AS REPORT

UNCLASSIFIED

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Towards Simplicity: Noise and Cooperation in the 'Perfect Integrator'

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I. INTRODUCTION

Neuroscientists have known for decades that sensory information is encoded in the intervals between the action potentials or "spikes" characterizing neural firing events. Statistical analyses of experimentally obtained spike trains have shown the existence of a significant random component in the inter-spike intervals. There has been speculation, of late, that the noise may actually facilitate the transmission of sensory information; certainly there exists evidence that noise in networks of neurons can dynamically alter the properties of the membrane potential and the time constants [37,66]. The recent rekindling of interest in the Stochastic Resonance phenomenon has lead to speculation that such nonlinear cooperative effects may occur naturally in living systems.

Stochastic resonance (SR) is a cooperative nonlinear phenomenon wherein the signal-to-noise ratio (SNR) at the output of a noisy nonlinear dynamic system driven by a weak deterministic modulation (which we shall take to be time-periodic), can actually be *enhanced* by increasing the noise. Given a bistable dynamic system, for example, information is transmitted through the system in the form of switching events between the stable states (attractors) of the potential function underlying the dynamics. Suppose a periodic signal is applied; its effect is to rock the potential, alternately raising and lowering the wells. However, should its amplitude be very low (compared to the height of the potential barrier), it will not be able to induce switching. In the presence of even small amounts of noise (assumed throughout this work to be Gaussian and delta-correlated) there will, however, always be a finite switching probability. Since the switching probability is greater when the system is in the 'elevated' well, which occurs when the signal is at its maximum, one realizes that the noise-induced switching events may acquire some degree of coherence with the deterministic signal as long as certain important system parameters (notably the potential barrier height and the locations of the fixed points) are appropriately adjusted. The power spectrum obtained from the time-series solution of this system shows a sharp signal, together with its weaker *odd* harmonics (for the case of a symmetric potential), superimposed on a Lorentzian-like noise background. Theoretically, the signal is represented as a δ-function spike; in practice, of course, the spike has a finite width and amplitude determined by the bandwidth of the measuring system [73,74]. Then, in order to compare theoretical results with experiments or simulations, one integrates over the line-shape of the signal function (at the fundamental frequency). If the signal feature is narrow and, in particular, falls entirely within one bin of the (discrete) experimental Fourier transform process, then one replaces the δ-function by $1/\Delta\omega$, the inverse of the width of a single frequency bin in the FFT. The area obtained by the integration represents the fraction of total switching events that are coherent with the stimulus. With increasing noise, the signal power spectral density, S (measured at the fundamental frequency ω), rises until, for a critical noise strength, the intra-well motion gives way to inter-well (or hopping) motion as the major contributor to the dynamics. At this point S decreases with noise; for very large noise strengths, the switching becomes noise-dominated and very rapid, with all coherence with the periodic signal being destroyed. For modulation frequencies comparable to the Kramers rate (the characteristic well-to-well switching rate in the noise-only case), the critical noise strength (at the maximum of the *signal-power* curve) corresponds to a matching between the modulation frequency and twice the Kramers rate, hence the somewhat misleading characterization of this effect as a 'resonance' in the physics literature. The noise power spectral density $N(\omega)$ is given by the background at the base of the signal feature and the SNR defined, in decibels, as $SNR \equiv 10 \log_{10}(S/(N \Delta\omega))$. A plot of SNR vs. noise strength demonstrates a bell-shaped profile similar to that of the signal power spectral density; in the limit of very low (compared to the unperturbed Kramers rate) drive frequency, this curve and the signal power spectral density peak at approximately the same critical noise strength [27,50]. In the literature (and in this review), the SNR vs. input noise variance profile is sometimes taken to be the hallmark of SR, although the classical definition of the resonance involves the above-mentioned behavior of the signal feature in the output, rather than the SNR. The physics literature is replete with theories and examples of SR with good reviews available in forthcoming articles by Moss [52] and Jung [36] as well as the proceedings of a recent NATO workshop on the subject [53]. From a biological perspective, the recent work on SR in globally coupled arrays of nonlinear switching elements [8,35,54] is particularly significant.

It is important to point out that stochastic resonance (as characterized by the bell-shaped curve of SNR vs. noise) has not yet been directly observed in living systems with *internal* noise. One of its prime ingredients, noise-induced switching, has however been demonstrated in biological experiments [16,24,25]. In all such experiments, it is common to assemble an ensemble of firing events and fit a histogram to the refractory or reset intervals occurring between the "spikes". Such Inter-Spike-Interval Histograms (ISIHs) are ubiquitous in the neurophysiological literature and, as we shall see below, can be simply and elegantly explained by simple models of neurons as bistable dynamic switching devices subject to noise. The results have lead a few bold individuals to speculate on the possible beneficial role of noise (in particular, cooperative stochastic processes such as described in the preceeding paragraph) in the processing of sensory neural information [7-11,44-48]. Other researchers have speculated [40,61,62] that the experimentally observable background noise may be a natural phenomenon rather than a laboratory curiosity. Statistical analyses of experimentally obtained spike trains --the ISIH is obtained from experimental data, by assembling an ensemble of quiescent intervals (that separate firing events) into a histogram-- have also shown the existence of a significant random component in the inter-spike-intervals. These observations have lead neuroscientists to ponder the role of noise in sensory information processing for decades, usually relying on experimentally obtained spike trains and their associated ISIHs (both of which are ubiquitous in the neuroscience literature). It is impossible to exhaustively cite this vast body of prior work, but it must be pointed out that our efforts complement and extend conventional treatments by examining the response of our model neuron to a time-periodic external stimulus that is too small to induce firing by itself; in this case, the background noise nudges the system past its firing threshold (which, as we shall see in the next section, may actually be a function of the noise). Hence the noise, in some sense, mediates the response of the model neuron to the stimulus, an idea that will turn out to be central to our treatment of the ISIH.

The results of an investigation into some aspects of the role of noise in periodically modulated nonlinear systems in a neurophysiological context, constitutes the subject of this article. Our previous work [for a review, see e.g. refs. 11,12] consisted of modelling the sensory neuron as a noisy bistable (describable by a dynamics predicated on a "soft" potential) switching element. Such a model has been derived [8-10] from a fully coupled model of a cell body interacting (at the axon hillock), via a weak nonlinear coupling, with a dendritic "bath", the dendrites being represented as quasi-linear elements which, in general, would also be capable of "firing". Of course, the idea of bistability in this context is not new; it dates back to the seminal work of Landahl, McCullough and Pitts [41] who considered the neuron as a discrete (i.e. two-state) noisy threshold device. Today, their model while generally viewed as an over-simplification of real neurons, has served as a convenient starting point for the class of "connectionist" models of neural networks [2,17,18,20,30,32,33,49]. Although our model yields acceptable fits to experimental data and can provide a very elegant explanation of the salient features of experimentally observed ISIHs (these are summarized in the following section) it has become evident, recently, that it raises almost as many questions as it answers. For instance, it is generally accepted that neurons show bistability, of the type described above, only in certain restrictive regimes of parameter space. Different classes of neurons (even sensory neurons) are thought to exhibit different types of bistability, e.g., bistability between a fixed point and limit cycle that characterizes excitable oscillators such as those considered by Winfree [73]; the Fitzhugh-Nagumo model of excitable cells [26] belongs to this class. Experiments show [24] that background noise produces qualitatively similar cooperative behavior in this class of bistable models as well. Bistability of various kinds has been quantified in simplified Hodgkins-Huxley-type models [23] and postulated via theoretical arguments [1,57,72]. However, in other simple quasi-linear neural models e.g,. the "perfect" integrate-fire models, the results can be ambiguous. Here, noise introduces effects, in the ISIH, that closely resemble those observed in bistable models; the explanation of these effects cannot, however, be based on the same nonlinear stochastic-dynamic effects that underlie the response of bistable models. Recent results for this class of models are described in section III. Our fundamental characterization of bistable model neurons as threshold devices (no firing in the absence of noise) raises the issue of information loss during signal processing since only the firing events, that occur when a threshold is crossed, are recorded, with dynamical details regarding the passage to threshold being ignored. Of course, this must be weighed against experimental studies that demonstrate the existence of cooperative stochastic effects (e.g. SR) that cannot be explained by any form of linear filtering theory.

A final caveat: our approach lacks detailed "neurophysiological rigor". As physicists, we take a reductionist view by attempting to describe the global response of a complex system in terms of the response of a very few degrees of freedom that characterize the gross properties of the system (the renormalization group approach and the enormous success that it has enjoyed in treating complex systems is a classic example of this idea). As will become evident, in the following sections, noise introduces qualitatively similar effects in different dynamical models of stimulated neurons. These effects are visible at the level of the ISIH and the SNR, both of which are statistical (i.e. averaged) characterizations of the response. In addition to these measurements, other quantities that characterize the response (e.g. the mean firing rate and its variance) can be obtained via simple averages computed with respect to the ISIH; these quantities can also be directly measured in repeated trials in an experiment. Our approach is, therefore, quite adequate for describing the coupling between the noise and modulation in the neural dynamics on a statistical or *coarse-grained* level, as well as the mechanism whereby noise might actually enhance the flow of information through the system.

II. NEURONS AS BISTABLE ELEMENTS CHARACTERIZED BY A 'SOFT' POTENTIAL; STATISTICAL ANALYSIS OF SPIKE TRAINS

Recent work by Longtin, Bulsara and Moss (LBM) [44,45,48] has demonstrated how experimental ISIHs measured, for example, on the auditory nerve fibers of squirrel monkey [60] could be explained via a new interpretation of noise-driven bistable dynamics. They have introduced a simple bistable neuron model, a two-state system controlled by a double-well potential with neural firing events corresponding to transitions over the potential barrier (whose height is set such that the deterministic stimulus alone cannot cause transitions). The cell dynamics are described via a variable $x(t)$, loosely denoting the membrane potential, and evolving according to

$$\dot{x}=f(x)+q\sin\omega t+F(t), \qquad (1)$$

where $f(x)$ is a hysteretic flow function (expressible as the gradient of a potential $U(x)$) and $F(t)$ is noise, taken to be Gaussian, delta-correlated, with zero mean. In the bistable description, the potential is taken to be the "soft" function $U(x)=ax^2/2-b\,ln(cosh\,x)$. The system (1) has been numerically integrated, with the residence time in each potential well (these times represent the firing and quiescent intervals in our model) assembled into a histogram (the residence times density function $P(t)$), which displays a sequence of peaks with a characteristic spacing. Two unique sequences of temporal measurements are possible: the first measures the residence times in only one of the states of the potential and the histogram consists of peaks located at $t=n\,T_0/2$, T_0 being the period of the deterministic modulation and n an odd integer. The second sequence encompasses measurements of the total time spent in both potential wells, i.e. it includes the active *and* reset intervals; in the presence of noise, the reset intervals are of largely stochastic duration. The histogram corresponding to this sequence consists of peaks at locations $t=n\,T_0$ where n is any integer. The sequence of peaks implies a form of phase locking of the neural dynamics to the stimulus. Starting from its quiescent state, the neuron attempts to fire at the first maximum of the stimulus cycle. If it fails, it will try again at the next maximum, and so on. The latter sequence is the only one observable in an experiment; the former sequence, which corresponds to the refractory events is elegantly elucidated by the LBM theory. In addition to the peak spacing in the ISIH, most of the other substantive features of experimental ISIHs are explainable [47] via the simple model (1):

(a). Decreasing the noise intensity (keeping all other parameters fixed) leads to more peaks in the histogram since the "skipping" referred to above becomes more likely. Conversely, increasing the noise intensity tends to concentrate most of the probability in the first few peaks of the histogram.

(b). In general, the probability density of residence times is well approximated by a Gamma-like distribution of the form $P(T)=(T/\langle T\rangle^2)\,exp(-T/\langle T\rangle)$, where $\langle T\rangle$ is the mean of the ISIH. It is apparent that $P(T)\to 0$ and $\exp(-T/\langle T\rangle)$ in the short and long time limits, respectively. For vanishingly small stimulus amplitude q, the distribution tends to a Gamma, conforming to experimental observations.

(c). Increasing the stimulus amplitude leads to an increase in the heights of the lower lying peaks in the ISIH.

(d). Memory effects (even within the framework of a description based on the theory of renewal processes) frequently occur, particularly at very low driving frequencies; they manifest themselves in deviations from an exponentially decaying envelope at low residence times (the first peak in the ISIH may not be the tallest one).

(e). The mean of the ISIH yields (through its inverse) the mean firing rate.

(f). The ISIH decay rate λ (the slope of the envelope on a semi-log scale) itself depends sensitively (exponentially) on the stimulus amplitude q for constant noise strength, and (again, exponentially) on the noise strength for fixed q.

Analog simulations of the dynamics yield an extremely good fit [44,48] to experimental data; the fit can be realized by changing only one parameter (the stimulus intensity or the noise intensity) and the results are almost independent of the functional form of the potential $U(x)$, depending critically on the ratio of barrier height to noise variance; this ratio determines the hopping rate between the basins of attraction in the absence of noise.

The LBM theory demonstrates that the peaks of the ISIH *cannot exist in the absence of noise*. In fact, one could speculate that, over a certain range of parameters, the noise and signal play interchangeable roles in determining the shape of the ISIH. All the stimulus and noise features are encoded in the ISIH, with the phase preference (we assume perfect phase locking to the stimulus throughout) encoded in the peak width, this assumptions seems to be consistent with experimental auditory nerve data at least. The noise may be used by the neuron to encode the stimulus features in the ISIH, while preserving a fine amplitude discrimination through the exponential dependence on λ. Other researchers [66] have shown that noise linearizes the mean firing rate-vs. current characteristic in neurons, producing a large dynamic range along with ISIH variations. This dynamic range is not found in noiseless Hodgkins-Huxley type models. Identifying the mean firing rate with the inverse of the mean of the ISIH seems to lead one naturally to this encoding. Although the LBM model provides an important first step in the understanding of the (possibly pivotal) role of noise in sensory information transfer, it is far from complete. The results do not appear to depend critically on the characteristics of the potential function $U(x)$ and the fundamental question: what aspects of the data are due to the statistical properties of noisy two-state systems as opposed to real (i.e. biological) properties of cells that transcend this simple description, has not been satisfactorily answered.

Bistable models of the type discussed above provide one of the simplest explanations of the possible mechanism underlying the processing and coding of sensory information in the nervous system. They elucidate the sequence of reset events that follow each neural firing, and noise is seen to play a pivotal role in the production of the ISIHs. The dynamics in a generic bistable system of the form (1) displays the N-shaped flow characteristic that is known to exist in exciteable cells [57]. In our derivation of the bistable model from the fully coupled neuro-dendritic model, the coefficients a and b in the potential function $U(x)$ are obtained in terms of the cell and bath parameters. Hence, the effect of the dendritic coupling is to modify the height of the potential barrier, thereby directly affecting the switching dynamics and the structure of the ISIH. The potential function for the system becomes bimodal above a critical value of b/a; this transition to bimodality is mediated by the noise in the dendritic bath; in fact, the theory introduces the concept of a noise-dependent firing threshold (defined as the barrier height). Stochastic resonance (as described in the preceeding section) is readily observable in these many-body models and the output SNR can be further enhanced (over its expected value for the isolated case) by the coupling to the dendritic bath. Since none of the cooperative effects that we have described here will occur in a monostable potential, the critical role of background noise is evident.

The physical model outlined above is striking for its simplicity and provides an elegant explanation for several features of experimentally computed ISIHs. Nonetheless, it can be criticized for lacking the neurophysiological rigor afforded by, say, the Hodgkins-Huxley equations and their derivants, including the class of "Integrate-and-Fire" models. We now consider some of the statistical properties of the simplest of these models.

III. THE 'PERFECT INTEGRATOR' REVISITED

In our work to date, we have confined our attention to nonlinear dynamic models of neuronal firing; the models rely on bistable firing characteristics to model the dynamics. However, the neurophysiological literature is replete with stochastic models of spontaneous and induced firing which are similar in spirit to the bistable models: firing takes place when the membrane voltage crosses a threshold. However, the models are not all characterized by hysteretic flow functions. The most ubiquitous of these models, the class of integrate-fire (IF) models, can be heuristically derived from single-neuron dynamics of the form (1), in the limit when the nonlinear term in the dynamics is very weak, so that the potential $U(x)$ is approximately parabolic, using stochastic linearization techniques [5,59]. In the most general case, the "leaky" integrator with threshold, one writes the dynamics in the form [65],

$$\dot{x} = \lambda (u_r - x) + \mu + F(t) + q \cos \omega t \, , \tag{2}$$

which represents an Ornstein-Uhlenbeck process [15,69,71] in which μ is the (positive) drift to a firing threshold a, and λ is a decay constant governing the decay of the voltage variable $x(t)$ to an equilibrium or resting level u_r. $F(t)$ is taken to be white noise having zero mean and variance D. Equation (2), in the absence of the periodic stimulus, has been extensively studied [3,14,19,21,31,34,39,42,43,55,56,63,67,68] in the theoretical neuroscience literature. In these studies, it is generally assumed that the noise term $F(t)$ represents the net contribution from all the synaptic inputs to the cell. Deterministic IF models have been studied by Keener et. al. [38].

We consider now a simplification of the above model due originally to Gerstein and Mandelbrot (GM) [29] in which the $q=0, \lambda=0$ case was considered, the so-called "perfect integrator". Assuming the underlying dynamics to be time-stationary, a random walk description of the neural firing dynamics has been invoked by GM, based on the cornerstone requirement of a stable distribution function for the probability density of first passage times corresponding to the dynamics. The state variable x is assumed to execute a biased random walk to an absorbing threshold at which point a firing event is designated to have occurred and the membrane potential x is then instantaneously reset to its starting value (the reset mechanism being purely deterministic). It is this reset which renders the 'global' dynamics nonlinear. The distance between the origin and the threshold is the "barrier height" a, analogous to the height U_0 of the potential barrier in our bistable model. Further, it is assumed that the motion in phase space occurs under the influence of a positive drift coefficient μ which was defined by GM as roughly the difference between the drift velocities corresponding to excitatory and inhibitory synaptic inputs (it is neurophysiologically reasonable to assume these velocities to be different). For this model, the Wiener process with drift, one readily writes down the associated Fokker Planck Equation (FPE) [28,58,70]:

$$\frac{\partial}{\partial t}P(x,t) = -\mu\frac{\partial P}{\partial x} + \frac{D}{2}\frac{\partial^2 P}{\partial x^2}, \tag{3}$$

whence the probability density function of first passage times is [22,29],

$$g_0(t) = \frac{a}{\sqrt{2\pi D t^3}}\exp\left\{-\frac{(a-a_0-\mu t)^2}{2Dt}\right\}, \tag{4}$$

a_0 being the starting point of the random walk. The density function $g_0(t)$, often referred to in the statistical literature as the 'Inverse Gaussian', reproduces many of the properties of experimentally observed ISIHs for the spontaneous firing case. The mean first passage time $(a-a_0)/\mu$ to the absorbing threshold is calculated as the first moment of $g_0(t)$, and its reciprocal yields an average firing rate. The variance of the first passage time is $D\,(a-a_0)/\mu^3$. The model reproduces the salient features of the ISIHs obtained from spontaneous firing events reasonably well, including the long (exponential) tail in the first passage time density function $g(t)$. It also has numerous limitations (which have been ennumerated by GM), the most fundamental one being the assumption that the membrane potential is reset following each spike, with the random walk to the threshold restarting; nevertheless, the model provides a simple vehicle to explain the dynamics (on a grossly simplified level) that arise from the coupling of the noise and the periodic stimulus. A more rigorous (from a neurophysiological standpoint) grounding of the FPE (3) has been given by Stevens [64]. In order to make even better contact with experimental results, it is necessary to provide reasonably good numerical values for the drift coefficient μ, the "barrier height" a and the background noise variance D in the above model. A first attempt to do so (while simultaneously providing a test of the goodness of fit of the model to neurophysiological data) was carried out by Berger et. al. [4]. They carried out an experiment aimed at recording the inter-spike-interval distribution from extra-cellular recordings on the cat visual cortex. Having obtained the experimental ISIHs, they were able to compute the equivalent model quantities μ and a via the mean and standard deviation of the experimentally obtained ISIHs, assuming a fixed background noise variance D. While we do not give any further details of the experiment, it is noteworthy that, once these "self-consistent" values of μ, a and D were substituted into the first passage time probability density function, an excellent fit of the model to the experimental ISIHs resulted.

We now consider the GM model in the presence of a deterministic periodic stimulus $q\cos\omega t$, assuming the initial condition $a_0=0$. Once again we assume the phase-locked case. One can then write down and solve [13] the FPE to yield the probability density function $P(x,t)$. The first passage times density function is then computed via the prescription [22]:

$$g(t)=-\frac{d}{dt}\int_{-\infty}^{a}P(x,t)\,dx\,,$$

which yields, after some calculation,

$$g(t)=\frac{1}{\sqrt{2\pi D}}\,\frac{a}{t^{3/2}}\,e^{-h_1(a,t)}+\frac{aq}{Dt^2}\left(t\cos\omega t-\frac{1}{\omega}\sin\omega t\right)\Phi_c(h_3(a,t))e^{h_2(t)}, \tag{5}$$

where $\Phi_c(x)\equiv 1-\frac{2}{\sqrt{\pi}}\int_0^x e^{-t^2}dt$ is the Complementary Error function and we have defined,

$$h_1(a,t)\equiv\frac{\left(a-\mu t-\frac{q}{\omega}\sin\omega t\right)^2}{2Dt}$$

$$h_2(t)\equiv\frac{2a}{Dt}\left(\mu t+\frac{q}{\omega}\sin\omega t\right)$$

$$h_3(a,t)\equiv\frac{\left(a+\mu t+\frac{q}{\omega}\sin\omega t\right)}{\sqrt{2Dt}}\,.$$

We now discuss briefly some of the properties of the density functions (4) and (5). A plot of (5) yields an ISIH with the peaks at locations nT_0 where n is an integer and T_0 the stimulus period. The hidden or reset mechanism in this model is instantaneous (and deterministic), in contrast to the bistable models. However, the model differs from the bistable models in another very important respect. In the absence of noise and the periodic stimulus, the state-point *will* reach the threshold, provided the drift μ is positive; the model admits of the possibility of deterministic 'switching' or firing. For the $q\ll\mu$ case, a first-order perturbation solution (for t) of the dynamic equation $a=\mu t+\frac{q}{\omega}\sin\omega t$ yields the deterministic passage time,

$$\bar{T}=t_0\left\{1-\frac{\frac{q}{a\omega}\sin\omega t_0}{1+\frac{q}{\mu}\cos\omega t_0}\right\}, \tag{6}$$

where $t_0\equiv a/\mu$ is the mean first passage time (MFPT) in the presence of noise alone. Note that $\bar{T}\rightarrow t_0$ at high drive frequencies ω, as should be expected. The deterministic passage time (6) is also the MFPT in the presence of the noise and the periodic stimulus. For a long-tailed distribution of the form (3) however, possibly the more important quantity is the most probable time, or the mode. For the $q=0$ case, this time is readily obtained by differentiation:

$$t_m=\frac{3D}{2\mu^2}\left\{\sqrt{1+\frac{4a^2\mu^2}{9D^2}}-1\right\}. \tag{7}$$

It is significant that the mode t_m depends on the noise. In experiments, firing times clustered about the mode are more probable. The mean of a large number of firing times may yield a MFPT t_0 which, depending on the physical characteristics of the density function (3) is close to the mode or far out in the tail. When analysing the properties of the ISIH the interplay of the three time-scales T_0, t_0, and t_m is crucial. With decreasing inhibition (represented as increasing drift μ for fixed excitation) or with decreasing noise strength (keeping the drift fixed), the ISIH approaches a more sharply peaked (Gaussian-like) density (in effect, the tail of the Gamma-like density (3) shrinks, with the mean

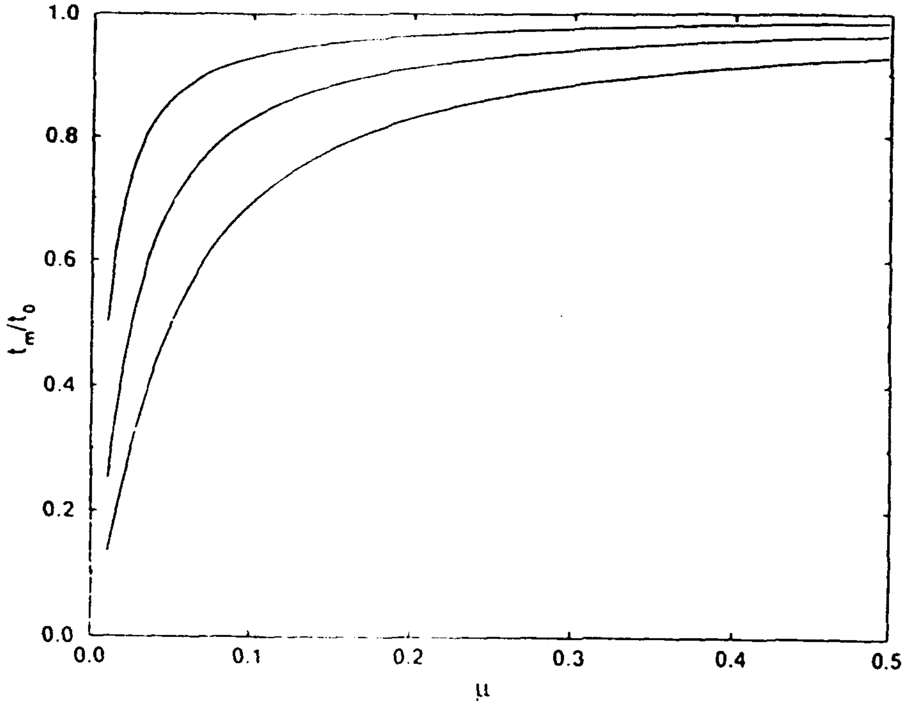

Fig 1. Mode of the noise-only density function (4), normalized to the mean, vs. the drift coefficient μ for a=20 and noise variance D = 0.1, 0.25, 0.5 (top to bottom curves).

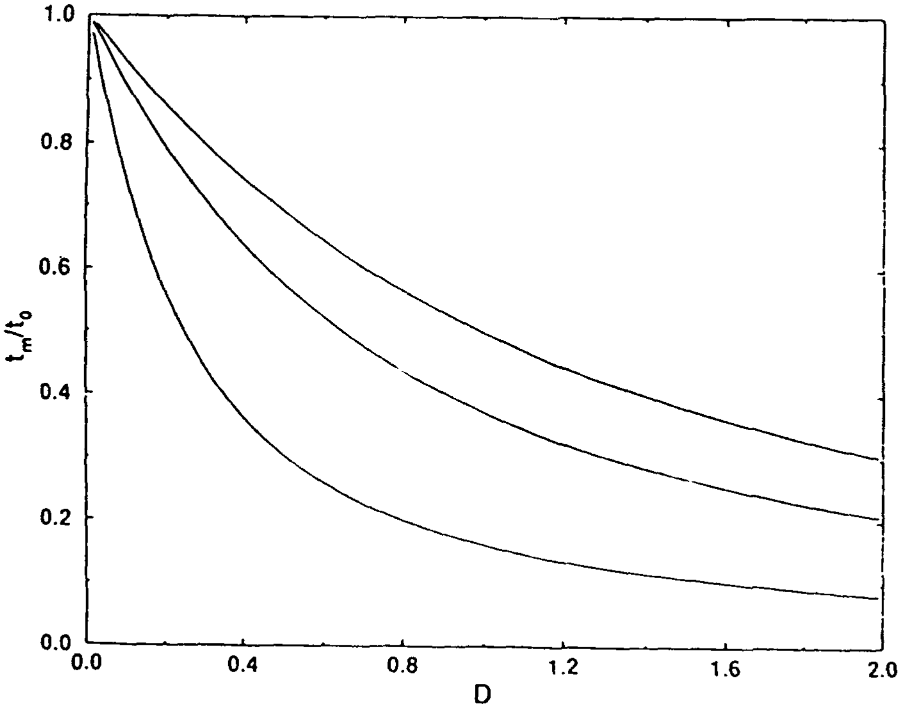

Fig 2. Mode of the noise only density function (4), normalized to the mean, vs. the noise variance D for a=20 and drift μ=0.1, 0.065, 0.025 (top to bottom curves).

approaching the mode). This may be demonstrated via a Gram-Charlier expansion of the density function (3) and is depicted in figures 1 and 2 in which we plot the ratio t_m/t_0 vs. the drift μ and the noise variance D respectively. Increasing the drift leads to a more sharply peaked distribution (characterized by the rate at which $t_m/t_0 \rightarrow 1$) for a given noise

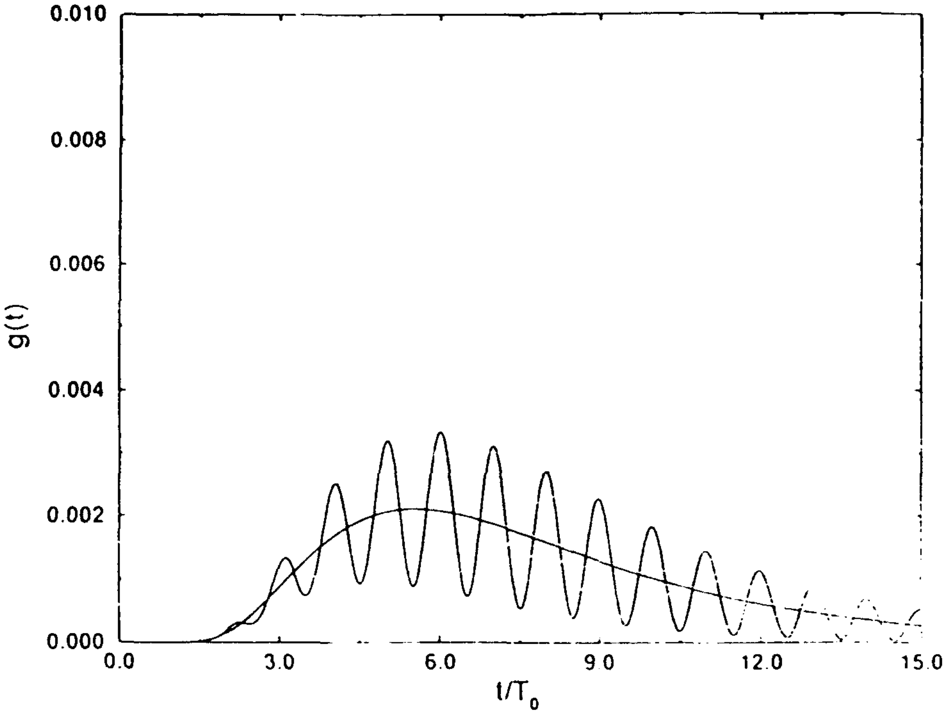

Fig 3. First passage time density function (5) and its $q=0$ counterpart (4) for $(a, \mu, q, \omega, D) \equiv (20, .04, .03, .1, .2)$.

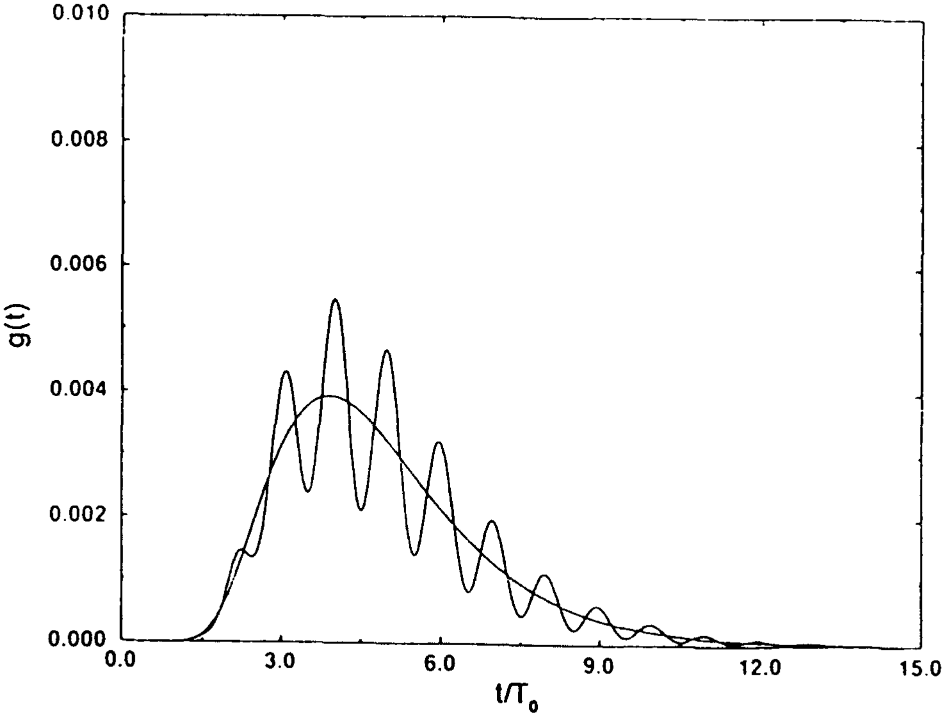

Fig 4. Same as figure 3 with $\mu=0.065$.

variance; the approach to a very sharply peaked distribution is more rapid at lower noise strengths as seen in both figures. Figures 3-5 show the effect of increasing the drift μ on the ISIH; in these figures, the smooth curves represent the $q=0$ density function (3). Note that if we introduced a phase ϕ into the argument of the periodic stimulus and then defined a phase-averaged ISIH (the averaging being performed over a uniform distribution on $[0,2\pi]$), the two curves in each of the figures 3-5 would coincide; for the phase-locked case, one obtains an ISIH that is qualitatively similar to those observed for the bistable models. The mean, variance, and mode of the ISIH (for small q) are seen to be extremely close to the corresponding quantities for the $q=0$ ISIH, as predicted above. It should be evident that if we adjust the stimulus and/or system parameters such that

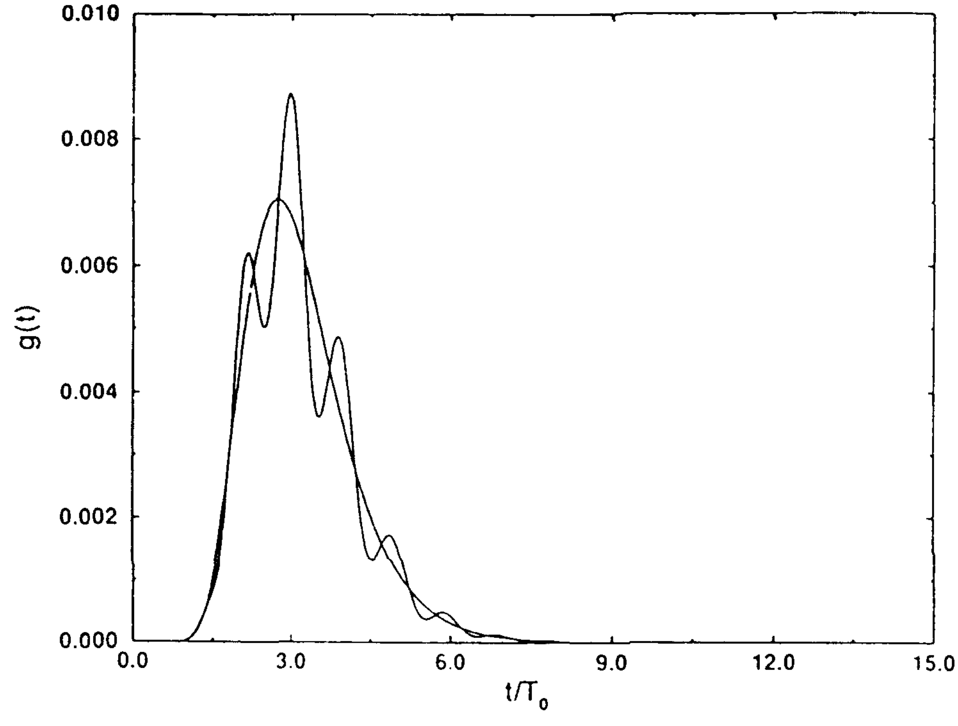

Fig 5. Same as figure 3 with $\mu=0.1$.

$$t_m = nT_0, \tag{8}$$

then the n^{th} peak in the ISIH will be the highest one.

The interesting feature about the ISIH (5) is that the peak heights go through maxima as functions of the noise variance D, all other parameters being held constant. This is demonstrated in figure 6 for a particular set of system and modulation parameters. One can calculate from (5) the critical noise D_c at which the n^{th} peak passes through its maximum. Note that the peaks in (5) occur at times $t=nT_0$. Hence, the amplitude of the n^{th} peak is given by

$$g_n = g_0 + g_1, \tag{9}$$

where

$$g_0 = \frac{a}{\sqrt{2\pi D t_n^3}} \exp\left[-(a-\mu t_n)^2/2Dt_n\right], \tag{10a}$$

$$g_1 = \frac{aq}{Dt_n} e^{2a\mu/D} \Phi_c\left[\frac{a+\mu t_n}{\sqrt{2Dt_n}}\right], \tag{10b}$$

are the contributions from the $q=0$ and $q>0$ parts of the density function (7) (we set $t_n=nT_0=2n\pi/\omega$). Writing $D_c=D_{c0}+\delta$ where D_{c0} is the noise variance at which the expression (10a) is maximized and δ is the (much smaller) contribution from (10b), we easily find

$$D_{c0}=(a-\mu t_n)^2/t_n\,. \tag{13}$$

The remaining contribution δ is found by setting the derivative of (9) equal to zero and then expanding to $O(\delta)$. This contribution is, however, much smaller than D_{c0} and can be neglected for the present. In figure 7, we focus our attention for a particular peak ($n=4$). We set $\mu\equiv\mu_c=0.159$ where, for this case, μ_c is found by setting $nT_0=t_0$. For a fixed noise variance D, this value of μ_c maximizes the height of this peak, although this does *not* imply that the peak in question is the highest one in the ISIH. Now, the noise variance is further decreased. This has the effect of moving the mode t_m such that the n^{th} peak coincides with the mode ($t_m\simeq nT_0$) and this peak becomes the highest one. Decreasing the noise further causes the peak to get taller and narrower; it becomes delta-function-like and attains its maximum height in the $t_m\to t_0\simeq nT_0$ limit as discussed earlier.

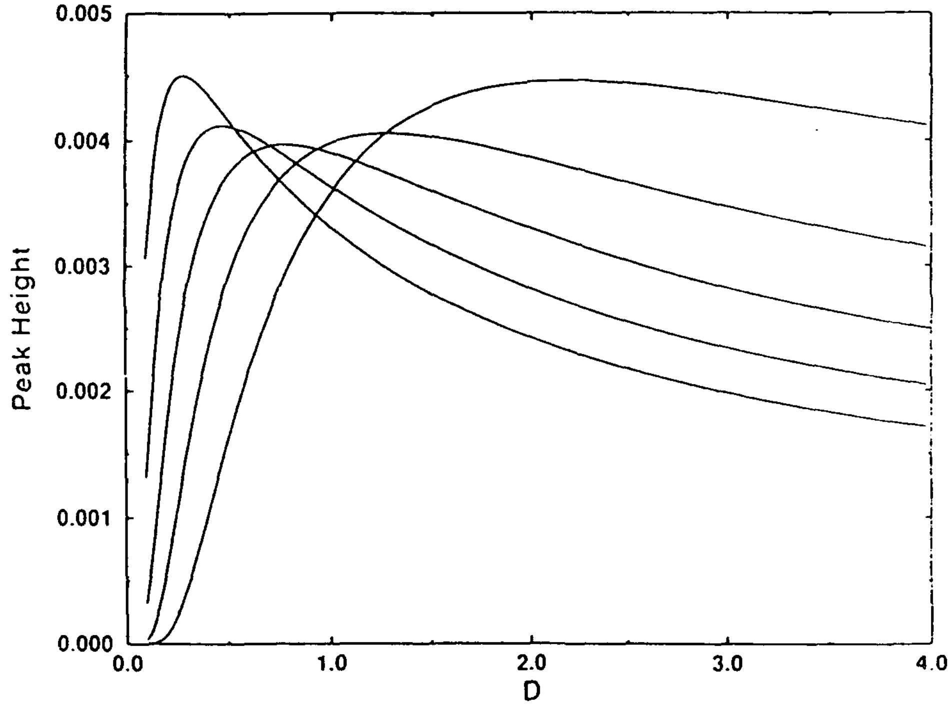

Fig 6. Peak heights vs. noise variance D for the density function (5) with $(a,\mu,q,\omega)\equiv(20,.055,.0475)$. Curves correspond to (reading from left to right) peak numbers $n=7,6,5,4,3$.

IV. DISCUSSION, CONCLUSIONS AND SPECULATION

It seems fitting to conclude this article with a question and some speculation. Clearly the question to be answered is: "Can the neuron indeed be characterized by a noisy nonlinear switching element, describeable by a bistable dynamics of the form (1) (with, say, a 'soft' potential $U(x)$) or a far simpler switching element described by the dynamics (2)?" Certainly, there is ample evidence that noise plays a critical role in the transmission and coding of information in the nervous system; most reasonable models of neural firing invoke some kind of diffusion process representation of the system on a statistical or coarse-grained level (in which the system is described via a probability density function rather than an individual trajectory solution). It seems reasonable then, that there should exist a form of self-regulatory mechanism such that the internal parameters of the system (these parameters control, for instance, the height U_0 of the potential barrier) can be adjusted in response to the stimulus and noise characteristics. In our previous

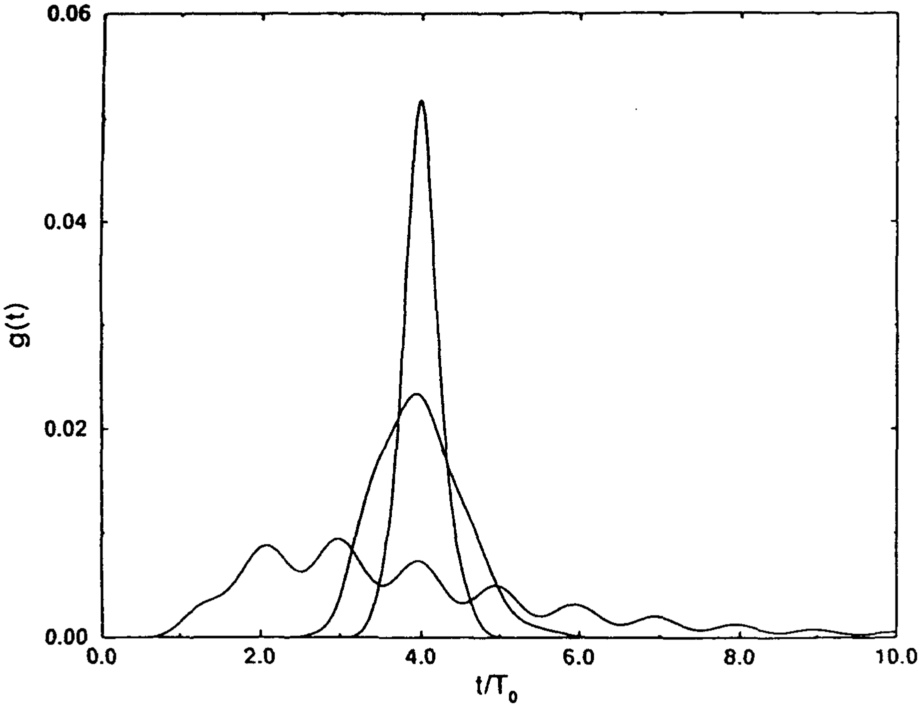

Fig 7. Height of peak no. 4 with $(a, q, \omega) \equiv (20, .0475, .2)$ and $\mu=0.159$ (critical value...see text). Top curve: D=0.012, middle curve: D=0.06, bottom curve: D=1.0.

work [8,9], in fact, we have been lead, in a simple way to the concept of a noise-dependent firing threshold. This is important because, for given stimulus and noise, one obtains well-defined histograms for only a small range of U_0. One may speculate further that the neuron (or the network) then *uses the background noise so that its response* (measured via the SNR or, equivalently, through the ISIH) *is optimized.* This implies that, for configurations that admit of stochastic resonance, the neuron (or network) operates close to the maximum of the stochastic resonance curve (SNR vs. noise variance) while simultaneously obtaining other information (e.g. amplitude, frequency, and phase) about the deterministic stimulus, via the ISIH. In effect, our construction and interpretation of the ISIH (together with the remarkable ability to explain most of the features of experimentally obtained ISIHs) as a natural outcome of our modelling the neuron as a noisy bistable switching element (in the LBM theory) or even via the extremely simple model of section III implies that *sensory neurons may measure the stimulus intensity by comparing it to the background noise, using the (internally adjusted) potential barrier height to mediate and optimize the measurement* [F. Moss 1992; private discussions]. In the perfect integrator model, the firing threshold is equivalent to a 'barrier' in the jargon of bistable dynamics; such models may be, in fact, derivable from more complex models such as those considered in the LBM studies. Our studies of collective behavior in large networks show that the coupling to other elements can enhance or degrade the SNR depending on the magnitudes *and* signs of the coupling coefficients, i.e., the excitatory or inhibitory nature of the interactions is critical. In the perfect integrator, the drift μ is controlled by the inhibition which, therefore, plays a critical role in even this simplest of descriptions of neural dynamics. What should be amply clear from this study and our previous work is that there is no single model that describes the dynamics of neurons everywhere in the nervous system; even the very simple model of section III has its drawbacks, but it serves to provide a simple description of the role of noise and inhibition in the firing dynamics of a single cell. In fact, a generalization of this model, the so-called 'leaky' integrator characterized by the full dynamics (2) may well provide a good model of the bursting that is so ubiquitous a feature of axonal firing.

The Inter-Spike-Interval Histograms are not, by themselves, necessarily an indicator of the presence of stochastic resonance as an underlying cooperative effect in neurophysiology. For bistable models having the general form (1) they are, however, a product of correlated (between the noise and deterministic modulation) switching and, as we have indicated in section I, there is some evidence that such switching processes do occur in neurophysiology (although the form of the bistability may be different from the potential systems defined by dynamics such as (1)). Various features of these histograms can, however, lend themselves to explanations based on stochastic resonance. Perhaps the most important of these features is that the heights of successive peaks pass through a maximum as a function of the noise strength. This has been demonstrated in section III for the simple 'perfect' integrator model and is also known to occur in bistable systems of the form (1) [47,76]. So far, attempts to quantify this "resonance" as a matching of two characteristic rates have been inconclusive, for the bistable case, largely because of the difficulty of (numerically) producing good ISIHs with low noise. For the simple IF model of section III, however, this connection (or lack of it) might be possible to establish, due to the analytical tractability of the problem; this is an area currently being actively investigated. Since these models admit of a deterministic switching (or firing) mechanism, in contrast with the fundamental precept of no deterministic switching that underlies the bistable models, the mechanism for the observed "resonances" of figure 6 may well differ from the corresponding mechanism in the bistable case.

What should be clear from this paper is that effects that, qualitatively at least, appear to be similar can occur in systems that are quite different. A simple observation of the ISIH or the resonance in the peak heights as a function of noise is not sufficient to establish a model for the underlying dynamics. In different terms, it is probable that simple models of the type discussed in section III may provide a good fit to experimental ISIHs just as we have seen [24,44,45,48] in various forms of bistable descriptions. In fact, we have shown that, for the bistable case, a good fit to experimental data is obtained using dynamics of the form (1) with different flow functions $f(x)$; the data shed no light on the precise form of the dynamics. This is a characteristic of our coarse-grained description of the dynamics in terms of probabilities and power spectra. In most theories of stochastic resonance in bistable systems, the quantity that critically mediates the dynamics is the ratio of the barrier height to the noise variance. This ratio, in fact, determines, as outlined in section II, the number and sizes of the peaks in the ISIH. So, one must end this review with the (by now) somewhat obvious question: "Which features of the ISIHs are due to underlying neurophysiological processes and which features are influenced by the statistics of the detection/measurement process or the statistics of the simple models such as (1) and (2) which have been invoked to explain the features of the ISIHs?"

ACKNOWLEDGEMENTS

It is a pleasure to acknowledge energizing conversations with Professor Karl Pribram (Radford Univ.) and Drs. Andre Longtin (Univ. of Ottawa), Frank Moss (Univ. of Missouri, St. Louis), Dante Chialvo and A. Vania Apkarian (Univ. of Syracuse), Stephen Schiff (Childrens' Hospital, Washington DC), Alianna Maren (Accurate Automation, Chattanooga, TN), Donatella Petracchi (Univ. of Pisa) and Bill Jacobs, Gabor Schmera and Mario Inchiosa (NCCOSC, San Diego). Support from the Physics and Life Sciences

Divisions of the Office of Naval Research is also gratefully acknowledged.

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