Noise induced tuned decrease in firing in neural models: inverse stochastic resonance

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ABSTRACT

Neurons in the central nervous system are influenced by complex and noisy signals due to fluctuations in their cellular environment and in the inputs they receive from many other cells [1,2]. Such noise often increases the probability that a neuron will send out a signal to its target cells [2-5]. In stochastic resonance, which occurs in many physical and biological systems, an optimal response is found at a particular noise amplitude [6-8]. Remarkably, in classical neuronal models [9,10] and experimentally [11,12] it has also been found that noise can subdue or turn off repetitive neuronal activity. Surprisingly, we find that in some cases there is a noise level at which the quenching is at a maximum and the cells response is at a minimum. We call this tuning phenomenon *inverse stochastic resonance* and argue that it requires hysteresis between a stable rest point and a limit cycle.

KEY WORDS

1. Introduction

In the central nervous system, neurons are embedded in complex neuronal and glial networks [13,14]. They receive input signals from many other neurons through thousands of excitatory and inhibitory synapses at unpredictable or random times [15,16]. In order for a neuron to send out an action potential, [17] it must receive sufficient net excitation (over inhibition) in a small enough time interval. Technically this means that the current or voltage distribution in the cell must pass through some threshold condition. Once the threshold is reached, self-exciting processes lead to the emission of an action potential.

The neuronal responses to input currents, whether injected or synaptic, have been much investigated experimentally and theoretically [18,19]. It had long been realized that noise tends to increase neuronal activity [2-5]. This increase may depend on the properties of the noise, such as amplitude, and as been called Stochastic Resonance [6,7,9]. The *stochastic resonance*, in which a measure of response (e.g. the signal to noise ratio) rises to a maximum and then decreases as the noise amplitude is increased, has been argued to be to be universal and naturally occurring in noise modulated threshold systems of which neurons are an example

In stark contrast to these previous results, recent studies [9,10] have found that noise, especially of small amplitude, can decrease firing rates and even stop neuronal activity altogether, a finding which has been recently confirmed experimentally [11,12]. Hence we have found that the opposite of *stochastic resonance* behavior can occur; that is, as the noise increases the response undergoes a minimum. Since the behavior is the reverse of that in stochastic resonance this new phenomenon is called *inverse stochastic resonance*.

2. Main Results

To study neuronal response to signals with noise we use the classical Hodgkin-Huxley model [20] capable of reproducing spiking properties which are similar to those of real neurons. We employ a model for the input to the cell which is described as "current-driven" and represents current injection by microelectrode in the laboratory. (While a “conductance-driven” model for the inputs [16,21] would reflect a situation closer to the *in vivo* situation we found similar results as for the former input model. Hence the results are not shown). The input is such that the mean level causes the neuron to fire repetitively if stimulated by a further transient “kindling” input. Noise added to the mean input then modulates the firing properties of the cell.

Figure 1 shows the voltage responses of the model neuron with various noise levels. The incoming signal has a mean of strength μ and a noisy component of amplitude σ. Without noise (top left record) there is, for this value of the steady input, μ=6.6, a repetitive stream of output spikes, (8 spikes in 150 msec shown). Adding noise makes the output sequence irregular. Extremely weak noise naturally has little effect but slightly larger amounts can yield significant inter-spike interval variability. Surprisingly, rather moderate strength noise can actually stop the spiking permanently. Yet a larger level of noise actually promotes spiking (increasing the firing rate). In the examples shown, a noise level of σ =0.2 can halt the firing of action potentials after 5 spikes and a somewhat

larger noise level of σ =0.5 here stops the spiking after just one spike. When the noise level is turned up to σ = 2, more spikes are emitted, there being 10 in the trial shown.

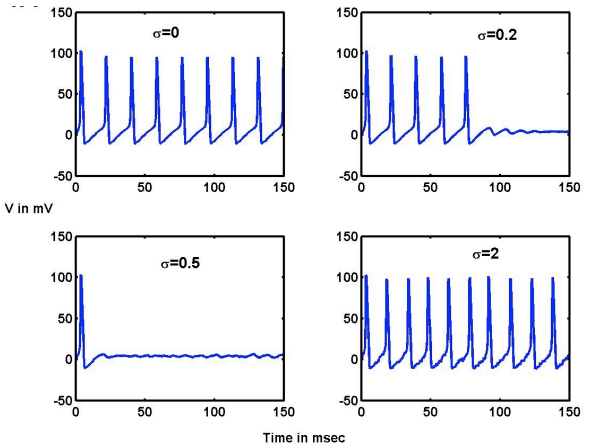

Figure 1. Showing voltage trajectories with spikes for a "current-driven" Hodgkin-Huxley model neuron. The mean input current density is 6.6 $\mu A/cm^2$ and the effects of noise of various magnitudes , σ ($\mu A/cm^2$), are shown.

We explored how varying the mean of the input and its noise level affects the spiking activity. In Figure 2, the results are shown. The number of action potentials, N, emitted over a 150 msec period (as typified by the records in Figure 1) is plotted as a function of the noise level σ for various values of the mean current μ. For each data point with noise, 500 trials were performed. Without noise (σ =0) there is a critical value of $\mu=\mu_c$, approximately 6.44, at which sustained repetitive firing occurs. When μ=5.5, below the critical value, there is only one spike without noise. As the noise level increases so does the number of spikes. However, when μ=6.8, not far above the critical value (there are 9 spikes without noise) increasing the noise level causes the number of spikes to drop dramatically - and even more so if a longer time period is examined. There is a pronounced minimum at about σ =0.5. Thereafter the mean number of spikes increases approximately linearly as the noise level increases.

The minimum in the response as the noise level increases through a certain value illustrates the phenomenon of *inverse stochastic resonance*. This is in direct opposition to the standard phenomenon defined as a maximum in any response variable as the noise level increases and called *stochastic resonance*. (Note that it does not have to be a maximum in a signal to noise ratio as often reported). We believe this novel finding to be generic and fundamental to a wide class of neuronal dynamical systems. Below we discuss the conditions for this phenomenon.

Our investigations of the silencing effects of noise on Hodgkin-Huxley neurons were motivated by our studies of pairs of coupled neurons of a different type [10] where a similar phenomenon was observed, namely that noise could cause the cessation of repetitive activity. We have also investigated the effects of noise on repetitively firing pairs of coupled Hodgkin-Huxley neurons and obtained similar results. Simulation of more complex nerve models and larger networks has yielded the same kind of behavior, indicating that these phenomenon are quite general.

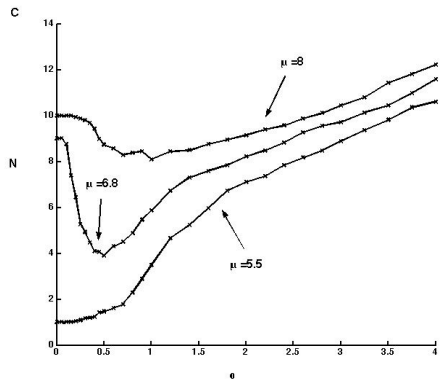

Figure 2. Inverse stochastic resonance in the "current-driven" Hodgkin-Huxley model. The mean number of spikes N over a 150 msec period is shown as the noise intensity increases for three values of the mean input current μ. A minimum in the output is clearly seen as σ increases when μ is near the critical value μ_c. For the larger value μ=8 of the mean input current, there is a noticeable, yet less pronounced, minimum in the number of spikes when σ is approximately equal to 1.

The effects of noise reported above can be explained in terms of the basic dynamical structure of the neuronal excitability. In particular, by the behavior of the voltage and other variables on what are called stable limit cycles [22,23] which occur when, for example, a neuron fires repetitively at the same frequency or a heart pacemaker beats continually [24]. Such a stable limit cycle in a dynamical system often appears by a bifurcation mechanism [22] when a parameter, like the mean input current strength in the Hodgkin-Huxley model varies continuously and crosses some critical value. Just above that critical value, the basin of attraction of the limit cycle, that is, the region from which it is approached, is rather narrow. Here the stable limit cycle may coexist then with one or more other attractors. In the Hodgkin-Huxley model, which undergoes the sub-critical Hopf bifurcation, the only other attractor is a stable quiescent or resting state. Noise can make the solutions leave the basin of attraction of the limit cycle for that of the quiescent state so that spiking ceases. When the noise is small, the solution will then typically stay quiescent for a very long time, but for larger noise there is then a considerable probability that the solutions get kicked back up to threshold so that spiking may resume. This may be followed by a period of relative silence and so on. We note that the key to this effect is bistability and hysteresis, although noise may lead to a similar effect near a weakly unstable focus and a stable limit cycle (B. Doiron, personal communication). A formal

characterization of such noise driven transitions and their characteristics remains under active investigation.

In the recent experiments on squid axon with noise [10], the effect of small noise has been likened to a switch. Thus, the functional significance of these effects of noise on rhythmic activity is that a very small disturbance can lead to a drastic change in system behavior. In the brain, electrical activity is often broadly rhythmic, involving limit-cycles in both normal and epileptic activity [24, 25]. If such oscillations arise near a bifurcation point implying hysteresis, then a small noisy signal could lead to the cessation of, or a sharp modification of, rhythmic activity. In a population of cells, those which are weakly responding and operating near the bifurcation point could be silenced easily by noisy inputs whereas cells firing at higher levels would have their activity augmented by noise, giving noise induced tuning to the population responses. This in fact may represent a different, noise induced, mechanism for sharpening of sensory neural responses.

3. Conclusion

Since stable limit cycles occur in dynamical systems in diverse fields, we expect to find that the phenomena of suppression of cyclic, repetitive or rhythmic activity by noise and inverse stochastic resonance will have widespread occurrence. For example, limit cycle activity is found in circadian rhythms [26], cardiology [27], cell kinetics and tumor growth [28,29] and oscillating neural networks [24,25] as well as in climatology, ecology and astrophysics. We thus predict that the ISR should be universal to systems showing hysteresis.

Although the phenomena we have described are of interest in themselves, as indeed is stochastic resonance, their functional significance in neurobiological and other dynamical systems remains to be fully explored. Similar findings were reported in a heuristic nonlinear stochastic model of affective disorders [30]. It seems that these effects could sometimes arise as pathologies rather than normal conditions, as for example if cardiac pacemaker activity was affected adversely by noise leading to an abnormal heart rhythm.

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