

Coefficient of variation vs. mean interspike interval curves: What do they tell us about the brain?

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Abstract

A number of models have been produced recently to explain the high variability of natural spike trains (Softky and Koch, J. Neurosci. 13 (1) (1993) 334). These models use a range of different biological mechanisms including partial somatic reset, concurrent inhibition and excitation, correlated inputs and network dynamics effects. In this paper we examine which model is more likely to reflect the mechanisms used in the brain and we evaluate the ability of each model to reproduce the experimental coefficient of variation (CV) vs. mean interspike interval (ISI) curves ($CV = \text{standard deviation}/\text{mean ISI}$). The results show that the partial somatic reset mechanism is the most likely candidate to reflect the mechanism used in the brain for reproducing irregular firing. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

The available experimental data indicating the degree of irregularity of neuronal firing is intrinsically noisy. The best analysis of such data has been performed by Softky and Koch [18], who demonstrated that real neural firing at high firing rates is consistent with a Poisson process and plotted the experimental curve of the coefficient of variation (CV) vs. mean interspike interval (ISI) (Fig. 9 in [18]; the CV is a measure

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of spike train irregularity defined as the standard deviation divided by the mean interspike interval). Analysis of experimental data has also been performed by Shadlen and Newsome [15] who plotted the experimental ISI histogram distribution (recorded from the area MT of an alert monkey, see Fig. 1C in [15]), which can be fitted to an exponential probability density function, pointing to an underlying generating process of Poisson type. Poisson-type firing is verified if the interspike intervals are both exponentially distributed and independent [21]. Although independence has not been verified experimentally, we will postulate that neuronal firing in cortical cells is of Poisson type. Apart from the work mentioned above [15,18], other earlier experimental studies have shown that cortical neuron firing is highly irregular; Smith and Smith [17] investigated the spontaneous cortical activity in the biologically isolated forebrain of a cat and pointed out that trains of action potentials in this preparation sometimes represent a series of events that is almost random with respect to time. They showed that there is a large range of intervals over which the probability of occurrence of any chosen interval can often be predicted from the Poisson distribution. Similarly, Burns and Webb [5], have observed that nerve cells in the cerebral cortex of an unanesthetized mammal appear to exhibit spontaneous activity. In other words, they discharge in an irregular fashion at times which often bear no obvious relation to the events in the animal's environment. In this paper we evaluate current models of production of irregular spike trains in terms of their ability to reproduce a typical Poisson firing (limited by the refractory time). It has to be pointed out that measurements with models have been taken by selecting a long time window in a spike train produced by a simulated stationary process. In real firing spike trains, however, there is no stationary data for sufficiently long time and one needs to devise a special technique for measuring statistical properties in dynamically changing firing patterns (as done in [18]).

The aim of the work presented in this paper is primarily to identify the determinants of the highly variable firing that has been observed in neurons. Secondly, the paper aims to precisely clarify the firing mechanism of individual spikes, which might give us an insight to the controversial issue of the 'neural code'. The neural code controversy refers to the two conflicting interpretations given to the highly irregular timing of successive action potentials. The first supports that this irregularity reflects noise and does not convey information suggesting that the neuron carries information by a mean firing rate obtained by temporarily integrating input signals [14,15]. The second one, on the other hand, supports that this irregular timing does convey information suggesting that the neuron operates by precise processing of coincident input signals [2,11,18].

2. Candidate mechanisms for producing high firing variability

2.1. *Partial somatic reset*

In an attempt to model high irregularity, we have demonstrated, using a simple leaky integrator model with *partial reset* on the somatic membrane potential, that

irregular firing can be produced at high firing rates resulting from current fluctuation detection [4], despite long somatic temporal integration times. We have also showed that partial somatic reset is a powerful parameter to control the gain of the neuron. A partial reset model (V_{reset} being 6 mV below threshold) was also used by Troyer and Miller [20] who produced high firing variability by stressing the fact that the *high gain* of their model is responsible for this behaviour. The high gain is in fact a result of the partial reset, as we showed in [4]. The CV values that Troyer and Miller [20] achieved however, fall only in the lower half of the 0.5–1 physiological range reported by Softky and Koch [18].

Examination of the CV vs. mean ISI curve we produced with the partial somatic reset mechanism (Fig. 1) shows a close similarity with the experimental one, when the somatic reset parameter is $\alpha = 0.91$. The solid line in Fig. 1 shows the theoretical curve for a random spike train with discrete time steps and a refractory time t_R given by $CV = \sqrt{(\Delta t_M - t_R)/\Delta t_M}$, where Δt_M is the mean ISI [3,4]. Fig. 2 shows the ISI histogram distributions for the three reset parameters for mean ISIs $\Delta t_M = 15$ ms. As it can be seen, with the somatic reset parameter set to 0.91, the firing ISIs are exponentially distributed. Fig. 3 shows the autocorrelation graph of the firing ISIs indicating that they are independent. Thus, the partial reset mechanism produces Poissonian firing (since the firing ISIs are both exponentially distributed and independent), postulated for the experimental spike trains, making this mechanism a strong candidate for the one used by the brain.

2.2. Concurrent excitation and inhibition

We have also demonstrated [7] that with concurrent excitation and inhibition (with inhibition being at a level of approx. 80% of excitation), firing is nearly consistent with

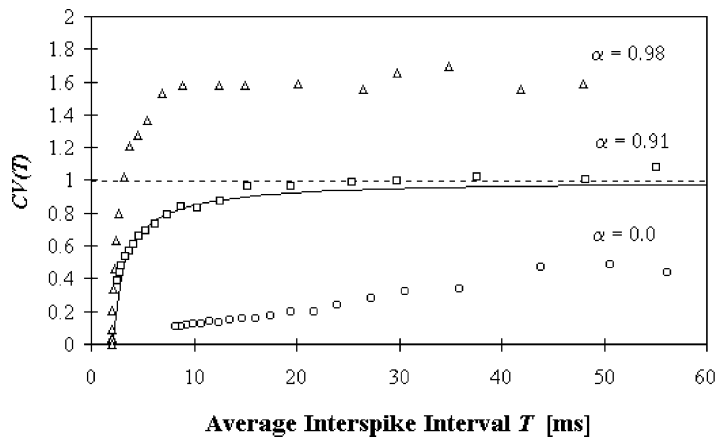


Fig. 1. CV vs. mean ISI produced with the partial somatic reset mechanism. The CVs obtained with $\alpha = 0.91$ (somatic reset parameter) are very similar to those observed in cortical neurons (Fig. 9 in [18]). The solid line shows the theoretical curve for a random spike train with discrete time steps (see [3,4]).

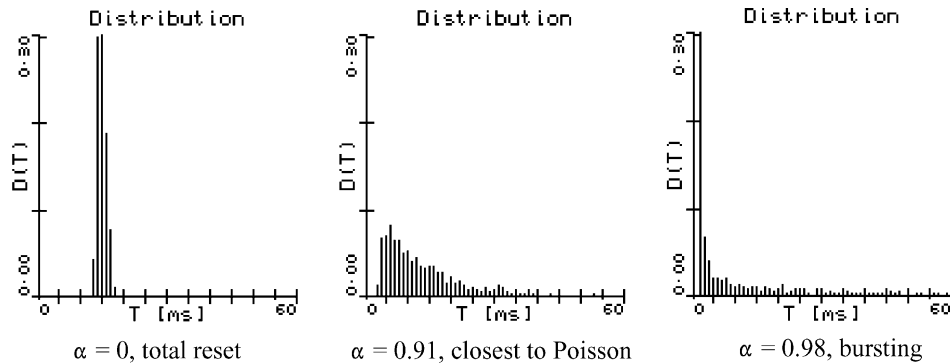


Fig. 2. ISI histogram distributions for $\Delta t_M = 15$ ms for different levels of somatic reset.

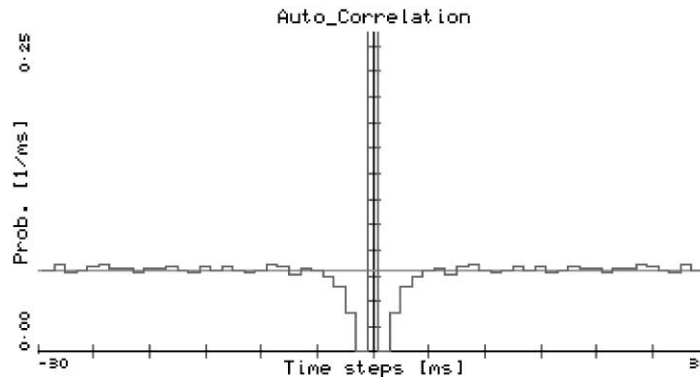


Fig. 3. Autocorrelogram for the leaky I&F neuron with partial reset. Apart from a small depletion in intervals close to the refractory time, the curve is flat, indicating independence of the interspike intervals. Simulation details: time step: 1 ms; refractory time: 2 ms; reset to 91% of threshold value; mean interspike interval: 15.4 ms; CV = 0.85. Other details in [4].

a Poisson-type variability observed in cortical neurons at high firing rates as reported in [18]. However, the CV vs. mean ISI curve though obtained (Fig. 4) does not match in a convincing way the experimental one. In addition, we have shown that the mechanism by which inhibition increases the CV values with this method is by introducing more short intervals in the firing pattern. This is indicated by the small initial hump at the beginning of the ISI histogram distributions (see Fig. 5). This tendency to produce short clusters of spikes is also revealed in the autocorrelogram of Fig. 6.

The effect of concurrent inhibition and excitation was also examined by Feng and Brown [8,9] who showed that the CV is an increasing function of the length of the distribution of the input inter-arrival times and the degree of balance between excitation and inhibition (r). They also showed that there is a range of values of r that CV values between 0.5 and 1 can be achieved (which is considered to be the

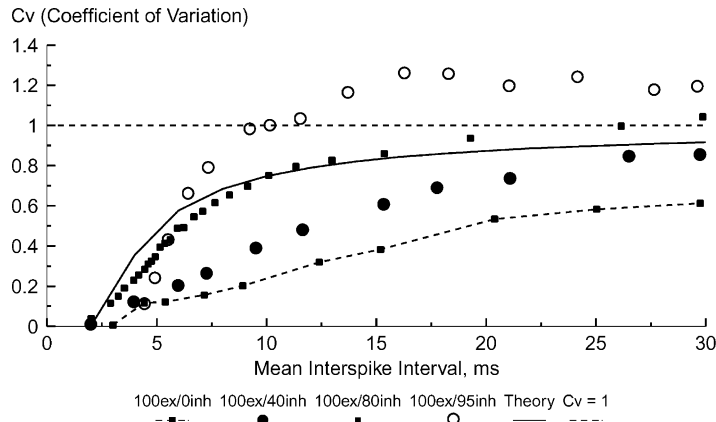


Fig. 4. CV vs. mean ISI showing the firing variability different levels of inhibition. The CV values with 80% inhibition are the closest to the ones observed experimentally. Simulation details: time step = 1 ms; refractory period = 2 ms; time constant = 10 ms (see [7] for the rest of the details and parameter values).

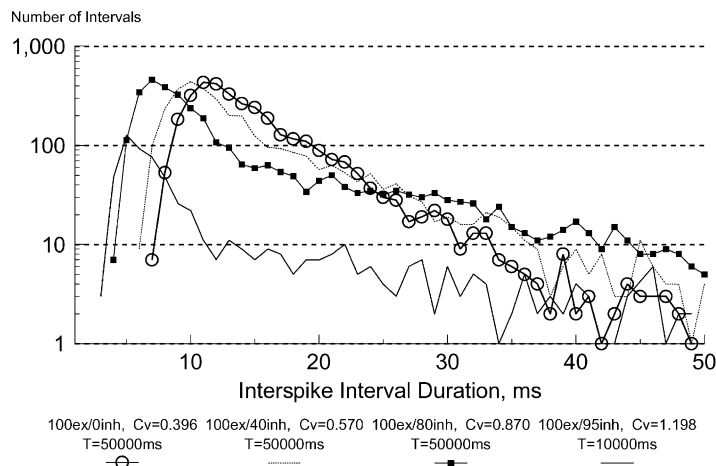


Fig. 5. Interspike interval histogram distributions for $\Delta t_M = 15$ ms for different inhibition levels. T indicates the total time the system was left to operate. Rest of the parameter details as in Fig. 4 and in [7].

physiological range) and this range excludes exact balancing between excitation and inhibition. The results of Feng and Brown [8,9] do not answer the problem posed by Softky and Koch [18] for two reasons: (i) as they do not show a CV vs. mean ISI curves, it is not clear whether the CV values they obtained hold also for high firing rates and (ii) they only used the CV statistic for assessing high variability which on its own is not a reliable indicator, since CV values $\in [0.5, 1]$ are not equivalent with Poisson statistics. The effect of inhibition was also examined by Shadlen and

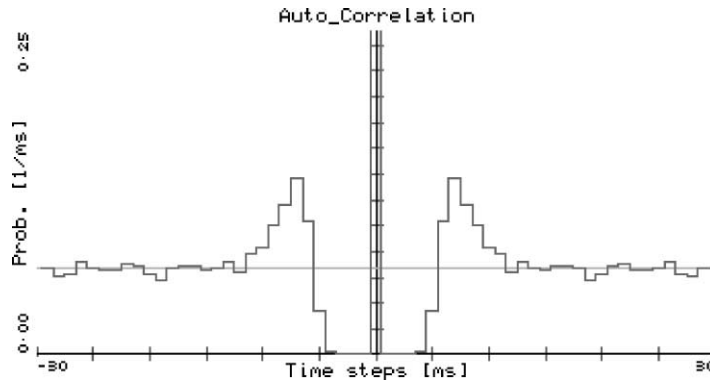


Fig. 6. Autocorrelogram for the leaky I&F neuron with concurrent excitation and inhibition (with inhibition at 80% of excitation). The curve shows a tendency for the model to produce pairs of spikes with intervals of typically 7 ms. These short bursts contribute to the high value of the CV. Simulation details: time step: 1 ms; refractory time: 2 ms; mean interspike interval: 15 ms; CV = 0.87. Other details as in Fig. 5 (and in [7]).

Newsome [14], who used a random walk model and by appropriate balancing of concurrent excitation and inhibition on a single cell, they produced highly irregular firing. Their results were disputed though by König et al. [11] who questioned in particular the biological realism of their assumptions, namely that there is an exact balance between excitatory and inhibitory inputs and the high rate of input signals. The assumption of how balanced excitation and inhibition is brought about naturally in model networks has also been studied in [1,23,24]. In a new paper, Shadlen and Newsome [15] reiterate their previous findings by reinforcing both of their questionable assumptions with experimental evidence. All models based on concurrent excitation and inhibition have so far failed to produce appropriate CV vs. mean ISI curves for comparison.

2.3. Precise stochastic coupling in a network of I&F neurons

In contrast, CV vs. mean ISI curves fitting the experimental ones, have been reproduced by Lin et al. [12] (see Fig. 3 of their paper) by using precise stochastic coupling in a network of integrate and fire neurons arranged in a one-dimensional ring topology. This work shows that dynamic network effects can indeed produce high CVs. However, when these network effects are examined in more realistic neural networks like the one by Usher et al. [22], they do not produce high variability in the high frequency range as showed by Softky and Koch [18].

2.4. Correlated inputs

Stevens and Zador [19] illustrated experimentally that uncorrelated inputs to neurons do not account for the high firing variability but temporarily correlated ones

do. This was also confirmed by modelling by Sakai et al. [13] and analytically and numerically by Feng and Brown [10]. Stevens and Zador [19], Sakai et al. [13] and Feng and Brown [10] have not produced any CV vs. mean ISI curves. For these results to be widely accepted, more experimental studies should be conducted to prove the validity of the assumption that the inputs to cortical neurons are temporarily correlated (or synchronous) rather than independent (Poisson-distributed as assumed by Softky and Koch, [18]). For non-cortical neurons, the correlation hypothesis may be valid, as illustrated for example in the auditory nerve fibres where correlated inputs have been observed due to cochlear vibrations [6,16].

3. Conclusions

It was pointed out in Section 2.2 that the mere statement that CV values $\in [0.5, 1]$ neither implies that the CV vs. mean ISI curve will follow the experimental one, nor indicates that firing is Poissonian. For proving that ISIs are Poissonian, it is necessary to show that they are both exponentially distributed and independent. Poissonian spike trains will produce CV vs. mean ISI curves with the characteristic shape as in the theoretical curves in Figs. 1 and 4, but that shape alone is not a sufficient proof of Poissonian firing. In this paper we accepted experimental evidence for a Poissonian firing of cortical cells, and considered that a model of irregular firing which is able to produce Poissonian spike trains is likely to reflect firing mechanisms in real cortical cells.

From the above study, only the partial somatic reset mechanism can so far reproduce the experimental CV vs. mean ISI curve and firing which is consistent with a Poisson process (as suggested by experimental studies, [15,18]). Therefore, partial somatic reset is a good candidate to reflect the mechanism used in the brain for reproducing irregular firing. Further it has been shown [4] that with partial somatic reset individual spikes are produced by groups of coincident input spikes supporting the view that individual spikes carry significant information.

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