Neural mechanisms to improve timing

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Abstract

We use probabilistic techniques to study neural systems which improve the timing accuracy of action potential firing. A striking example of such accuracy was discovered in the columnar region of the VNLL by Covey and Casseday (J. Neurosci. 11 (1991) 3456). In response to sound stimulation, these VNLL cells fire an action potential whose latency under repeated trials has a standard deviation of approximately 100 µs. This is remarkable because the typical standard deviation in the auditory nerve is 1 ms. In simple systems, we show how the improvement in timing depends on the number of incoming fibers and the number of hits required in a small time window.

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1. Introduction

A fundamental problem in neurobiology is to understand how the central nervous system (CNS) performs accurate calculations with components whose properties vary in time and from cell to cell and which give variable responses under repeated trials. Local noise would compromise the information processing capabilities of successive levels of the CNS unless strong compensatory mechanisms were in place. Therefore, situations in which experimental evidence shows that information is sharpened as it progresses inward from the periphery to the CNS are particularly interesting for they may provide clues about such compensatory mechanisms.

A particularly striking example of increasing accuracy as one proceeds into the CNS from the periphery in the auditory system was discovered by Covey and Casseday [2]. Neurons in the auditory nerve (AN) synapse on cells in the cochlear nucleus (CN) and

certain cells in the CN, notably octopus cells, send projections to cells in the columnar region of the ventral nucleus of the lateral lemniscus (VNLLc). Covey and Casseday discovered that in bats these VNLLc cells fire a single action potential in response to sound stimulation with a precise latency; the standard deviation of this latency under repeated trials is typically about 100 μs and in some cases as low as 30 μs. This is remarkable because in the AN of mammals typical standard deviations for latency under repeated trials in a single fiber are approximately 1 ms. Oertel and co-workers [3,7] have proposed that much of this improvement in accuracy is created by coincidence detection by octopus cells of incoming signals from converging AN fibers.

For many years, synchronous firing of groups of neurons has been proposed as the mechanism by which sensory patterns are represented in the cortex. One mechanism by which stable patterns of synchronous firing could be created is the synfire chain model introduced by Abeles [1] and further developed by Aertsen, Diesmann, and others. These investigators have shown that if the number of firing neurons is large enough and the initial standard deviation of firing times is small enough, then stable propagation is possible. Our research explores the improvement of the standard deviation of spike timing at a single target neuron which receives convergent input. Thus we are continuing the line of investigation by Marsalek et al. [4]. Detailed understanding of the improvement of the standard deviation for firing times at single neurons will be of value for understanding the properties of synfire chains using less restrictive hypotheses.

Our report describes the mathematical properties of coincidence detection in a highly simplified neural system [8]. Consider the network shown in Fig. 1. There are n identical input neurons stimulated at the same time. Each responds by sending a single
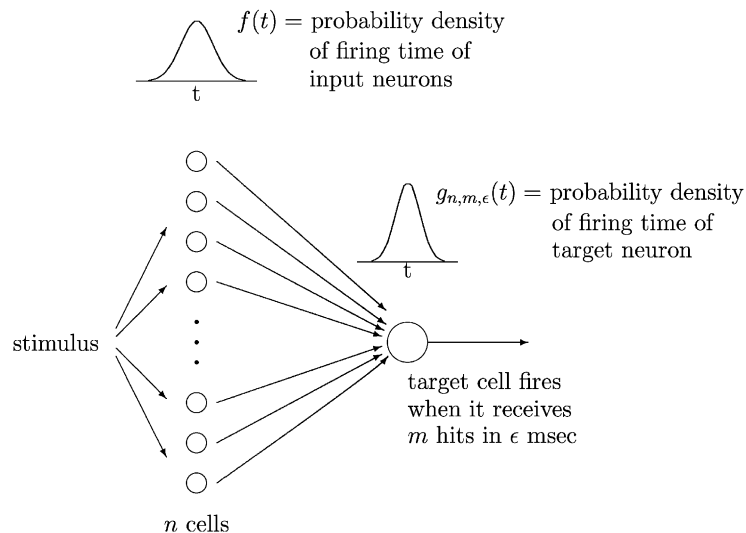

Fig. 1. The connectional pattern. n input neurons, whose stochastic times of firing are selected from the probability density, f, project to a target cell. The probability density for the firing time of the target cell is $g_{n,m,\varepsilon}(t)$. (Taken with permission from [8].)

spike to the target neuron at a random time t selected from a distribution f with standard deviation σ. We assume that the target neuron fires one spike (if it fires at all) the first time it receives m spikes in the preceeding ε milliseconds. Let $\sigma_{n,m,\varepsilon}$ denote the standard deviation of the time of firing of the target cell. If $\sigma_{n,m,\varepsilon}$ is smaller than σ, then the accuracy of the time of firing of the target cell has improved compared to the accuracy of its inputs. We report in this study the behavior of $\sigma_{n,m,\varepsilon}$ as a function of n, m, and ε.

Unfortunately, even in this highly simplified biological situation, one cannot compute explicit formulas for $\sigma_{n,m,\varepsilon}$ in terms of n, m, ε, and f, except in special cases.

One millisecond which is reasonable since the standard deviation under repeated trials in auditory nerve fibers is of this magnitude. One can show that for any value of σ, the parameters can be rescaled so that the probability density of the output is simply a rescaling of the output for the $\sigma = 1$ case. Therefore, we fix $\sigma = 1$ ms, which is the typical standard deviation under repeated trials in auditory nerve fibers. We begin by examining the behavior of $\sigma_{n,m,\varepsilon}$ for two special cases, $\varepsilon = 0$ and ∞. Then we investigate the general behavior of $\sigma_{n,m,\varepsilon}$ as a function of ε and as a function of m.

2. The case $\varepsilon \to 0$

Under appropriate hypotheses on the properties of f, one can prove mathematically that

$$g_{n,m,\varepsilon}(t) \to \frac{f(t)^m}{\int_{-\infty}^{\infty} f(t)^m \, dt}, \tag{1}$$

as $\varepsilon \to 0$ [5]. Intuitively, taking the mth power of a continuous density f and renormalizing will emphasize the region near the peak and de-emphasize the regions away from the peak. One can show that for m large the standard deviation, $\sigma_{n,m,0}$, will be of order $1/m$ for input densities, f, which have non-zero first derivative at their maximum (e.g. the exponential) and order $1/\sqrt{m}$ or larger for input densities which have a first derivative of zero at their maximum (e.g. the normal) [6]. Clearly, the improvement in timing will depend strongly on the specific input density chosen.

3. The case $\varepsilon \to \infty$

As ε gets large the time window restriction has less effect. Thus, in the limit when $\varepsilon \to \infty$, the target neuron will fire when the mth action potential arrives (this is equivalent to the simplest integrate and fire model considered by Marsalek et al. [4]). The mth largest of n selections from a density f is called an order statistic and this random variable has probability density:

$$g_{n,m,\infty}(t) = \frac{n!}{(m-1)!(n-m)!} F(t)^{m-1}(1 - F(t))^{n-m} f(t), \tag{2}$$

where $F(t)$ is the cumulative distribution function of $f(t)$, that is $F(t) = \int_{-\infty}^{t} f(s) \, ds$.

4. Dependence on ε and *m*

We now consider the effect of the size of the time window, ε, and the number of hits required, *m*. In this case the bulk of our investigation was done by Monte Carlo simulation. One would expect that as ε increases, the timing would become less accurate, i.e. $\sigma_{n,m,\varepsilon}$ would increase. In some cases, this is exactly what happens (e.g. $n = 10$, $m = 2$, f is exponential). On the other hand, there are also cases where exactly the opposite occurs (e.g. $n = 10$, $m = 8$, f is exponential). There are even cases where $\sigma_{n,m,\varepsilon}$ has a peak at some intermediate value of ε (e.g. $n = 10$, $m = 5$, f is exponential)! Similarly, one would expect that as *m* increases, more convergence of inputs would cause a decrease in $\sigma_{n,m,\varepsilon}$. In fact, our Monte Carlo simulations showed that in most cases $\sigma_{n,m,\varepsilon}$ is a non-monotone function of *m*! From these examples, we see that the dependence of $\sigma_{n,m,\varepsilon}$ on ε and *m* is complex and often counter-intuitive.

In conclusion, the complexity of the behavior that we have found suggests that determining the relationship between structure and function in the nervous system may be very difficult. In some circumstances, one could get improvement in timing either by increasing or by decreasing *m*. Similarly, one could get improvement either by increasing or by decreasing ε. The degree to which timing is improved depends in a complicated and interesting way on the input density f, the number of input neurons, *n*, the number of hits required, *m* and the duration of the time window, ε.

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