Reply

Is there a signal in the noise?

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Introduction

The irregular pattern of neural discharge has captured the interest and imagination of neuroscientists since Lord Adrian [1]. To comprehend the nature of information transmission in cerebral cortex, we must determine whether constellations of action potentials — their intervals, coincidences, and precise timing relationships — convey information or whether they arise capriciously. Do specific conditions cause the neuron to spike in one millisecond and not another, or are such variations the random instantiations of a desired discharge rate? Do synchronized spikes from two neurons encode the precise occurrence of some event, or do such spikes arise merely as manifestations of shared connectivity, bearing no special significance for information transmission?

Whether the irregular spike discharge from cortical neurons reflects noise or information clearly depends on the rules governing the conversion of synaptic input to spike output. In our recent review for *Current Opinion in Neurobiology* [2], entitled 'Noise, neural codes and cortical organization', we suggested that cortical neurons fire irregularly because they are inundated with synaptic input [2]. Therefore, to achieve a graded, dynamic range of spike rates, the cortical neuron might balance excitation and inhibition. The statistics of this process would lead to an irregular interspike interval, effectively randomizing the spike output. If this is the case, then the precise pattern of spikes from a neuron is no more likely to convey specific information than the pattern of tea leaves at the bottom of a cup. One can only infer whether the neural response, like tea, is stronger or weaker. Likewise the cerebral cortex must be organized to transmit and detect rate changes through noisy elements, necessitating redundancy and weak correlation.

A contrasting viewpoint is presented in the preceding paper (see pp 239–247, in this issue), in which William Softky makes an interesting case for precise temporal signaling capacities in cortical neurons. Softky suggests that present knowledge of synaptic integration does not preclude a precise temporal coding scheme, and he has constructed a hand-tuned neuronal model that could implement such a scheme. Softky's model incorporates active dendritic conductances balanced by strong inhibition, together permitting only precise coincidences of synaptic excitation to propagate from the dendrite to the axon hillock. Were this the case, the neuron could signal the occurrence of certain combinations of presynaptic events with a temporal fidelity on the order of a millisecond or less (i.e. well under the average interspike interval). An action potential arises only from synaptic activity in the preceding millisecond, whereas inputs that fail to produce a spike in the subsequent millisecond are effectively erased. This notion appears fanciful to us because it extrapolates so far beyond existing data, but it remains a logical possibility, and we agree that it would permit the neuron to propagate a coincidence code. In fact, Softky's hand-tuned model is an excellent example of the sort of mechanism required of any scheme in which downstream neurons attach significance to synchronous spikes [3–7].

The random walk model is a poor coincidence detector

While fascinated by Softky's hand-tuned model, we strongly disagree with his inference that even a simple integrate-and-fire mechanism can act as a precise coincidence detector when it balances excitation with inhibition. In such a model, the membrane voltage follows a random walk between resting potential and spike threshold. EPSPs drive the membrane toward spike threshold and IPSPs drive the membrane toward resting potential (E_{Cl}). A crude version of the model was illustrated in Figure 1c of [2]. We cited many of the originators of this model, and its more sophisticated implementations, therefore, we will not reiterate this here.

The model is somewhat counterintuitive because instead of increasing neural discharge by adding excitation over inhibition, both excitation and inhibition are modulated together. The membrane voltage reaches spike threshold for the same reason that a particle in Brownian motion ultimately diffuses out of the one open window in a room. The rate of spikes, like the rate of diffusion, depends on the frequency of the steps and their relative size. Turning up the input spike rate is like adding heat to the room. The process allows the neuron to integrate a plethora of synaptic inputs with reasonable time constant (7–20 ms) and yet to spike at a reasonable rate. We pointed out that the result of the random walk is a nearly random interspike interval and suggested that the output spike train contains information in its rate only.

Abbreviations

EPSP—excitatory postsynaptic potential; **IPSP**—inhibitory postsynaptic potential.

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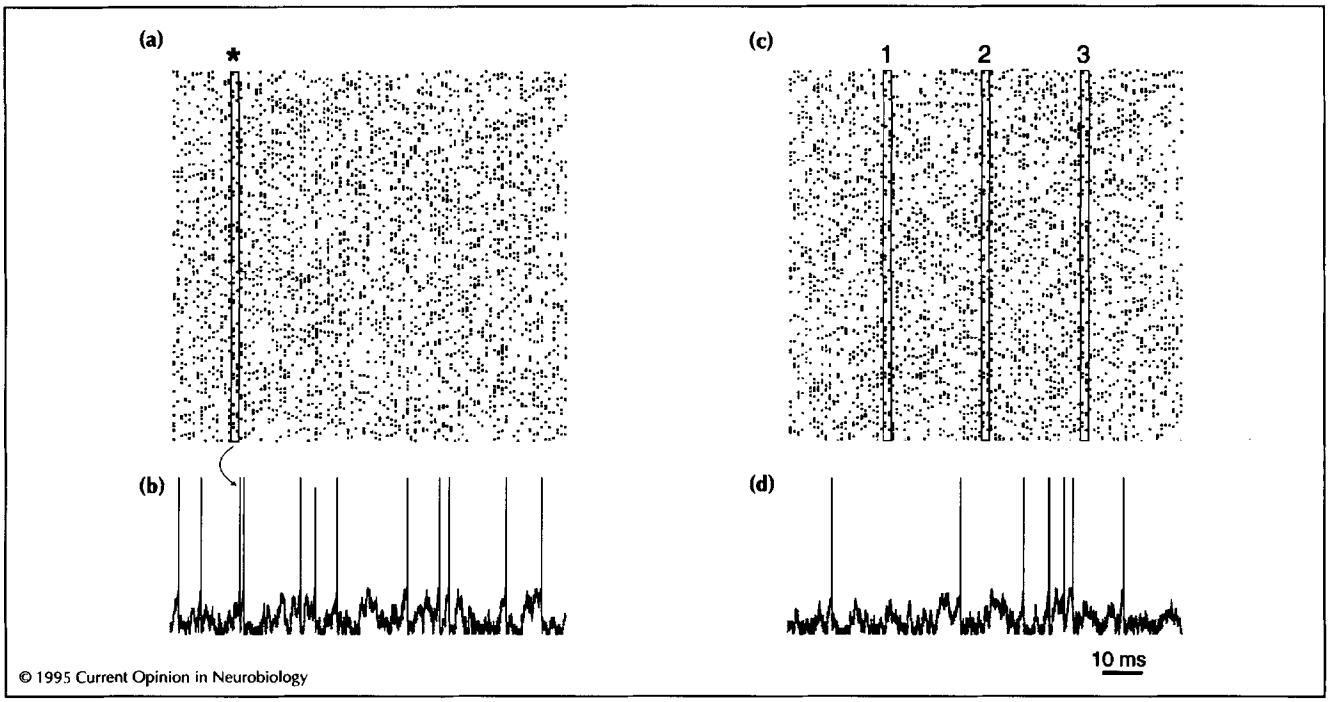

Fig. 1. A random walk model of synaptic integration with balanced excitation and inhibition. **(a)** and **(c)** Raster representation of 300 excitatory inputs. Each row represents the spike train from a single neuron. The average input discharges 10 times in the 100 ms epoch shown. **(b)** Simulated membrane potential resulting from synaptic integration of the excitatory inputs in (a) and 150 inhibitory inputs (not shown). **(d)** Simulated membrane potential from integration of the excitatory inputs in (c) and 150 inhibitory inputs. Spike trains in (a) and (c) are unrelated except where indicated by boxes. The box marked with an * in (a) identifies the set of inputs preceding the third spike in (b), identified by the arrow. Identical inputs are shown in each of the boxes numbered 1–3 in (c), and are also provided at corresponding times in the inhibitory spike trains (not shown). Notice that the same inputs fail to produce a spike at times marked 1 and 3, and produce a spike prematurely at 2. It would be misleading to conclude that the third spike in (b) was caused by the inputs that immediately preceded it. (See text for a more detailed explanation.)

In contrast, Softky suggests that the random walk model is, in fact, sensitive to the fine temporal structure of its inputs and, moreover, that it performs a kind of statistical coincidence-detection on its inputs. This conclusion is based largely on an analysis of spike-triggered average EPSPs and IPSPs, shown in his Figure 1 (see pp 239–247, in this issue). This analysis demonstrates simply that spikes arise just after EPSPs, and less probably after IPSPs. This point is obvious and was explicitly incorporated in the design of the model. Softky's Figure 1 simply restates that the random walk model is deterministic; the process of generating a spike does not include magic. This is hardly an argument for temporal precision or coincidence detection. Softky has confused the precise deterministic mechanics of the random walk with an illusory capacity for temporal encoding.

For the issue of temporal coding, the critical question is whether a postsynaptic spike indicates that some pattern of inputs occurred within the preceding millisecond or two (i.e. a temporal regime well below the average interspike interval). At a minimum, we would expect the synaptic activity preceding a spike to cause another spike, if only we could replay these events to the neuron. In Softky's hand-tuned model, this must be so — nothing before the preceding millisecond affects the neuron. For the random walk, however, there is no guarantee that the synaptic activity preceding a given spike would cause another spike, were it to recur. This point is illustrated in Figure 1.

We used the same simple random walk model portrayed in Figure 1c of [2] to produce 100 ms worth of spikes from 300 excitatory inputs (Fig. 1a). Each of these inputs spikes at a nominal rate of 100 impulses per second and there are 150 inhibitory inputs (not shown) that would look indistinguishable. The membrane undergoes depolarization along a lattice of voltages, from −70 mV to −55 mV. Each EPSP causes the membrane to depolarize by a twenty-fifth of the necessary excursion to spike threshold, whereas each IPSP causes twice this amount of hyperpolarization. There are no voltage dependencies outside the elastic barrier at −70 mV, beyond which hyperpolarization is precluded. After a spike, the membrane resets to −70 mV. As in our previous article [2], we do not intend this as a serious biophysical model. It is only a heuristic device. To reiterate, the parameters of the model were chosen to allow the neuron to spike at a nominal rate that is similar to any one of its inputs — that is, we use the random walk to achieve a proper dynamic range.

Figure 1b shows the simulated membrane voltage and spikes resulting from the bombardment of input shown in Figure 1a. We identified the synaptic activity immediately preceding the third spike (arrow, Fig. 1b). These events are shown in the box marked with an asterisk

in Figure 1a. According to Softky, these inputs caused the spike at the 16 ms point (arrow, Fig. 1b). This idea can be examined directly. We simply generated a new set of excitatory inputs (Fig. 1c) and inhibitory inputs (not shown), and ran the same random walk algorithm to produce the spike output in Figure 1d. At three times during the 100 ms epoch, we introduced the pattern of synaptic inputs we identified as causing the third spike in Figure 1b. These are shown by the boxes marked 1 through 3 in Figure 1c. In each of these two millisecond epochs, we used the exact same excitatory and inhibitory inputs that preceded the third spike in Figure 1b. The result is rather disappointing for coincidence detection. The first and third arrivals (boxes marked 1 and 3; Fig. 1c) produced no spike whatsoever. The second (box 2; Fig. 1c) was associated with a spike, but it occurred too early (less than 0.1 ms into the two millisecond epoch). The arrival of the first few EPSPs happened to drive the membrane to threshold. This spike cannot plausibly reflect the precise time of inputs that we hypothesized were responsible for the third spike in Fig. 1b. For purposes of coincidence detection, this spike ought to reflect events falling in a millisecond window to the left of box 2 in Figure 1c.

Using Monte Carlo methods, we confirmed that the synaptic activity immediately preceding a spike in the random walk model fails to produce a spike 70–80% of the time, were such activity to recur. Even this figure is overly generous, however, because it presumes no fluctuation in the amplitude of an EPSP or IPSP. A more realistic model (with variation in the amplitude of the postsynaptic potential) indicates that a spike is no more likely to occur after such identified causal input than by chance. Thus, were we to identify a group of inputs that immediately precede any given spike (by 1–2 ms), repetition of this exact pattern of inputs would not guarantee another postsynaptic spike.

For a coincidence code to propagate information, an action potential must indicate that a subset of the neuron's inputs were active within the preceding millisecond or two. Proponents of such a code do not require that the same inputs give rise to each and every spike — in fact, the notion that the neuron's spikes help to encode many different items of information is touted as appealing. It is critical, however, that inputs which cause a spike, do so somewhat reliably; otherwise it would be impossible to decode the coincidences. As indicated in the preceding paragraph, the nearly random relationship between inputs and spikes would preclude reliable coding of coincident inputs. Of course, an overwhelming excitatory barrage would lead invariably to a precisely timed spike, but it is wrong to conclude that the action potentials in Figure 1 reflect precise coincidences. They do not.

As we stated in our earlier paper [2], a simple balance of excitation and inhibition (i.e. the random walk model) provides an adequate explanation for the irregularity of cortical spike discharge without appealing to coincidence detection. Due to other inputs on the neuron, almost any group of inputs would exhibit nearly random correlation with postsynaptic spikes. This is intuitive. Whereas the exact bumps and wiggles of the membrane voltage may reflect exact sequences and combinations of inputs, the spike output cannot possible convey such complexity.

Concluding remarks

Whether cortical neurons express a noisy rate code or a precise temporal code — whether the interspike interval is a random instantiation of the average synaptic activity or a time stamp for some specific occurrence of inputs — affects our conception of cortical organization and information transmission. The information encoding properties of a coincidence code are certainly appealing. Synchronous spikes have been proposed to mediate information transmission [3], to store memories [8], to distinguish figure from ground [6], and even to elevate the representation of visual data to consciousness [7]. By comparison, modulation of a noisy rate code seems rather dull. Yet, no evidence presently indicates that the cortex can propagate a code based on synchrony, and we do not find Softky's appeal to evolution compelling. As argued previously, a balance of excitation and inhibition allows the neuron to maintain a reasonable dynamic range in the face of massive synaptic input. We suppose that noisy interval statistics are a small price to pay for the computational power endowed by large numbers of inputs.

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References

1. Adrian ED: *The physical background of perception.* Oxford: Clarendon Press; 1946.
2. Shadlen M, Newsome W: **Noise, neural codes and cortical organization.** *Curr Opin Neurobiol* 1994, **4**:569–579.
3. Abeles M: *Corticonics. Neural circuits of the cerebral cortex..* Cambridge, UK: Cambridge University Press; 1991.
4. Aertsen A, Arndt M: **Response synchronization in the visual cortex.** *Curr Opin Neurobiol* 1993, **3**:586–594.
5. Engel A, Konig P, Kreiter A, Schillen T, Singer W: **Temporal coding in the visual cortex: new vistas on integration in the nervous system.** *Trends Neurosci* 1992, **15**:218–226.
6. Singer W: **Putative functions of temporal correlations in neocortical processing.** In *Large-scale neuronal theories of the brain.* Edited by Koch C, Davis J. Cambridge, Massachusetts: MIT Press; 1994.
7. Crick F, Koch C: **The problem of consciousness.** *Sci Am* 1992, **267**:153–159.
8. Lisman J, Idiart M: **Storage of 7±2 short-term memories in oscillatory subcycles.** *Science* 1995, **267**:1512–1515.

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