

Correlation Detection and Resonance in Neural Systems with Distributed Noise Sources

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We investigated the resonance behavior in model neurons receiving a large number of random synaptic inputs, whose distributed nature permits one to introduce correlations between them and investigate its effect on cellular responsiveness. A change in the strength of this background led to enhanced responsiveness, consistent with stochastic resonance. Altering the correlation revealed a type of resonance behavior in which the neuron is sensitive to statistical properties rather than the strength of the noise. Remarkably, the neuron could detect weak correlations among the distributed inputs within millisecond time scales.

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Phenomena such as the amplification of weak signals or the improvement of information transfer capacity in nonlinear dynamical systems in the presence of noise, originally proposed as a possible explanation for the periodicity of Earth's ice ages [1] and now well established under the term *stochastic resonance* (SR) [2], have been shown to be inherent properties of many physical, chemical, and biological systems (see [3] for a comprehensive review). Especially neural systems, whose excitable dynamical properties, highly nonlinear responses, and noisy environments provide one of the most natural system that could display SR, are subject to an increasing number of theoretical [4,5] and experimental [6,7] investigations. However, although these studies indicate that stochastic mechanisms could play an essential role in sensory and peripheral nervous systems, due to experimental difficulties, the presence of SR in more central neural systems, such as the cerebral cortex, remains only poorly characterized [8].

Neocortical pyramidal cells are embedded in a very dense network and receive several thousand synaptic inputs from other neurons [9]. Given that, on average, cortical neurons fire tonically at frequencies up to 20 Hz in awake animals [10], these neurons are subject to a tremendous synaptic background activity [11,12]. The release characteristics at each synapse (frequency, conductance, random nature) during background activity were estimated from a combination of intracellular recordings with models of reconstructed cortical neurons [13]. These models established that background activity could be reproduced by distributed random inputs, in which all synapses release randomly according to Poisson processes with an average frequency of 1 and 5.5 Hz for excitatory and inhibitory synapses, respectively.

Because this background activity is omnipresent in cortical neurons, a natural question to ask is whether this activity could induce effects comparable to SR, and therefore could play a similar role as the external noise in sensory neural systems. We have investigated this possibility by using detailed biophysical models of neocortical

neurons with spatially extended dendrites, subject to distributed random inputs. In contrast to previous studies [8], this extended dendritic structure allows one to modulate different aspects of the noise applied to the system. The membrane equation was described by the standard cable equation (e.g., [14]), voltage-dependent currents for generating action potentials were described by Hodgkin-Huxley equations [15], and synaptic currents were described by kinetic equations of transmitter-receptor interactions [16] (see Appendix and [13]). These models successfully reflect experimental measurements obtained in living biological systems and, thus, can be viewed as realistic models of the neuronal biophysics in active states.

We first investigated the presence of classical SR [2] in this system. The signal to be detected, a subthreshold periodic stimulation, was added by introducing a supplementary set of excitatory synapses uniformly distributed in the dendrites and firing with a constant period of 100 ms (see details in [17]). To quantify the response to this additional stimulus, we made use of a special coherence measure based upon the statistical properties of spike trains, defined by $COS = N_{ISI} / N_{spikes}$, where N_{ISI} denotes the number of interspike intervals of length equal to the stimulus period, and N_{spikes} denotes the total number of spikes within a fixed time interval [6]. In contrast to other well-known measures like the signal-to-noise ratio or the synchronization index [18], this coherence measure reflects in a direct way the threshold nature of the response and, thus, is well suited to capture the response behavior of spiking systems with simple stimulation patterns.

To vary the strength of the noise in this distributed system, the release frequency of excitatory synapses generating the background activity was changed within a range of 50%–200% around the optimal value of 1 Hz established previously [13]. This frequency change directly impacted on the amplitude of the internal membrane voltage fluctuations (Fig. 1A). The response coherence showed a resonance peak when depicted as a function of the background strength or the resulting internal noise level

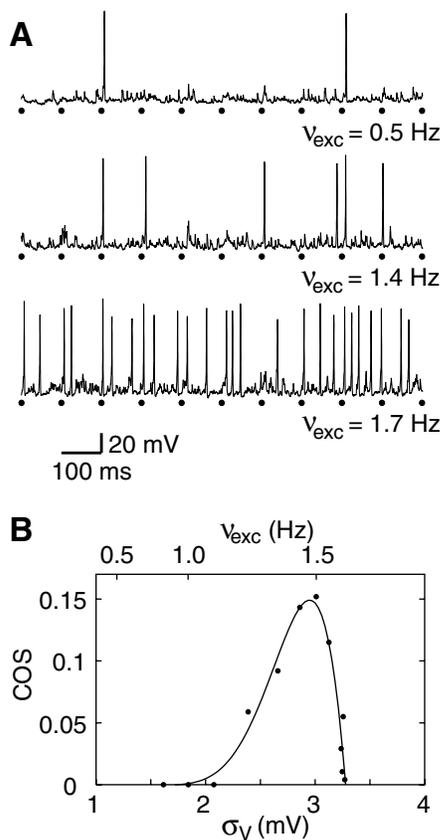


FIG. 1. Classical stochastic resonance behavior in model pyramidal neurons. The strength of the synaptic background activity (“noise”) was changed by varying the average release frequency at excitatory synapses ν_{exc} , which directly impacts on the membrane voltage fluctuations (σ_V) and the firing activity of the cell (A). Evaluating the response of the cell to a subthreshold periodic signal [dots in (A)] by the coherence measure COS reveals a resonance peak (B), showing that the detection of this signal is enhanced in a narrow range of fluctuation amplitudes ($\sigma_V \sim 2\text{--}3.3$ mV).

(Fig. 1B). Qualitatively similar results were obtained in simulations where the noise strength was altered by changing the conductance of individual synapses (data not shown). In both cases, maximal coherence was reached for comparable amplitudes of membrane voltage fluctuations, namely $3 \leq \sigma_V \leq 4$ mV. Remarkably, this range is covered by the amplitude of fluctuations measured experimentally *in vivo* ($\sigma_V = 4.0 \pm 2.0$ mV in [13]). Qualitatively similar results were obtained for different binsizes of the interspike-interval histogram underlying the COS measure, as well as for different measures of coherence, such as the computationally more expensive signal-to-noise ratio (not shown). At this point we therefore conclude that, for neurons with distributed noise sources, noise strength is capable of inducing resonance comparable to classical SR paradigms.

We next investigated the influence of the statistics of the synaptic background activity rather than its strength. To this end, we took advantage of the distributed nature of noise sources to introduce a redundancy in the Poisson-

distributed events assigned to the presynaptic compartments, labeled by a correlation parameter c ($0 \leq c \leq 1$). N_0 Poisson-distributed events were generated, where $N_0 = N + \sqrt{c}(1 - N)$, and, at each integration time step, randomly distributed among the N synaptic channels of the model. The redundancy results from $N_0 < N$, in which case each individual synapse still releases randomly according to the same Poisson distribution, but with a probability for releasing together with several other synapses. Note that in this way the average correlation for every pair of synapses is the same, irrespective of their location in the dendritic tree. Moreover, the procedure allows one to control the correlation of the background independently, by changing N_0 , without affecting the average release frequency at each synapse and, thus, the overall conductance due to the background activity.

Within this framework we investigated the behavior of the coherence measure as a function of the correlation. Increasing the correlation led to large-amplitude membrane voltage fluctuations as well as an increased rate of spontaneous firing (Fig. 2A). Similar to the classic SR illustrated above (Fig. 1B), we obtained a clear resonance peak in the COS measure as a function of the correlation parameter c or the resulting internal noise level σ_V (Fig. 2B). This indicates the existence of an optimal temporal statistics of the distributed noise sources to evoke coherent responses in the cell. The optimal value of the correlation depended on the overall excitability of the cell (as defined by the density of Na^+ channels), and was shifted to larger values for low excitability (not shown). Interestingly, the peak coherence was again reached at $\sigma_V \sim 4$ mV for an excitability that corresponded to the Na^+ channel densities found experimentally in adult hippocampal pyramidal neurons [19].

To further probe the ability of the neuron to detect correlations, we submitted the model to transient changes in c (Fig. 3A). Step changes in the correlation were chosen based on values corresponding to the foot and top of the resonance peaks of Fig. 2B. These changes affected both the level of membrane voltage fluctuations and the average firing frequency. A qualitatively similar result was obtained by changing the noise strength (Fig. 3B), which was obtained by step changes in the background frequency based on analog positions of the resonance peaks in Fig. 1B. The correlation-induced changes occurred with no major impact on the average membrane voltage (Fig. 3A, top), whereas there were significant voltage changes associated with changes in the noise strength (Fig. 3B, top). In both cases we observed a clear change in the spiking behavior of the cell (Figs. 3A and 3B, middle traces).

As Fig. 3A shows, the neuron reacts relatively fast to correlation changes. This aspect was further investigated by submitting the model to brief changes in correlation using steps of short duration (Fig. 4). Remarkably, not only these brief correlation changes were detected, but the model was able to resolve steps down to 2 ms, which is comparable to the time scale of single action potentials.

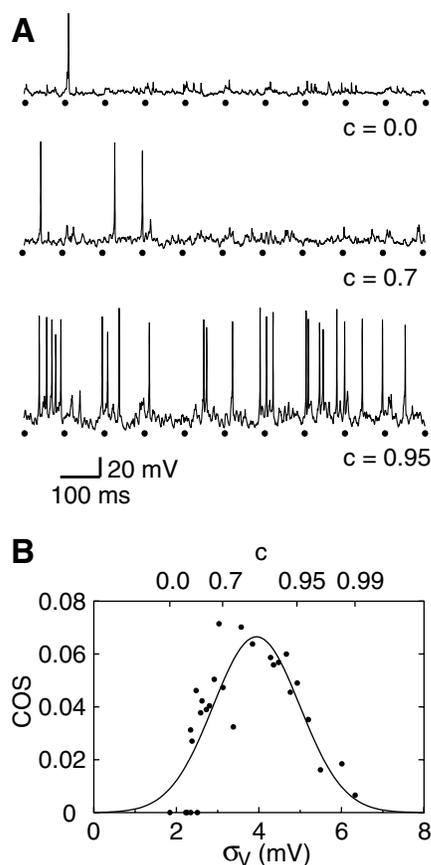


FIG. 2. Resonance behavior as a function of the correlation c between distributed random inputs. Increasing levels of correlation led to higher levels of membrane voltage fluctuation and a spontaneous firing rate of the cell (A). The response to subthreshold stimuli (dots) was evaluated using the coherence measure COS. A resonance peak can be observed for a range of fluctuation values of $\sigma_V \sim 2\text{--}6$ mV (B). Optimal detection was achieved for weakly correlated distributed random inputs ($c \sim 0.7$; Pearson correlation coefficient of ~ 0.0005).

The response always occurred within 5 ms after the correlation onset, which is a result of the spatial extension of the dendritic structure (not shown). These results indicate that the neuron is able to monitor very brief changes in the correlation among the distributed noise sources, with no major change in its average membrane potential.

In conclusion, we found that neurons with distributed noise sources display a resonance behavior comparable to SR, but with respect to a different form of modulation, namely noise statistics rather than noise strength. These findings refer to previous studies which also outlined that correlated noise can lead to SR in simple neuron models (e.g., [5]), but without investigating further the effects of the correlation itself. Our data show that the neuron was optimally responsive when the different noise sources were weakly correlated ($c \sim 0.7$, corresponding to a Pearson correlation coefficient of ~ 0.0005), consistent with the weak correlation found between pairs of neurons in monkey cerebral cortex [20]. Experiments indicate that pairs of cortical neurons can respond to external stimuli through

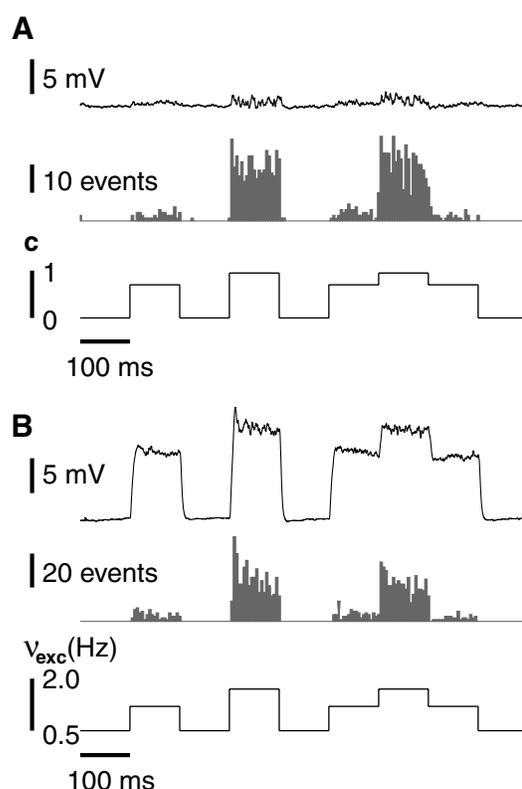


FIG. 3. Comparison of the effects of noise amplitude and correlation on the membrane voltage and the spiking behavior of the investigated cell. Steplike changes of correlation [(A), bottom trace] induced immediate changes in firing activity (middle trace) while the effect on average membrane potential was minimal (top trace). Steplike changes in the amplitude of the background activity, caused by altering the excitatory frequency ν_{exc} [(B), bottom trace], led to changes in firing activity (middle trace) but, in contrast to the correlation case, to a significant effect on the average membrane voltage (top trace).

a change in their correlated firing rather than a change in their firing rate [21]. The present findings suggest that cortical neurons are particularly efficient in detecting such correlations among populations of neurons. How this property is exploited at the network level constitutes an interesting challenge for future studies.

Appendix.—The cell was divided into isopotential compartments, each of which was described by the following cable equation (e.g., [14]):

$$C_m \dot{V}_i = -g_L(V_i - E_L) - \sum_j I_{ji}^{\text{int}} - \sum_k I_{ki}^{\text{syn}} - \sum_l \frac{1}{r_{li}}(V_i - V_l),$$

where V_i is the membrane potential in compartment i , $C_m = 1 \mu\text{F}/\text{cm}^2$ is the specific capacity of the membrane, g_L is the leak conductance, and E_L is the leak reversal potential. Intrinsic voltage-dependent currents and synaptic currents are, respectively, represented by I_{ji}^{int} and I_{ki}^{syn} (see below). The last term represents axial currents flowing

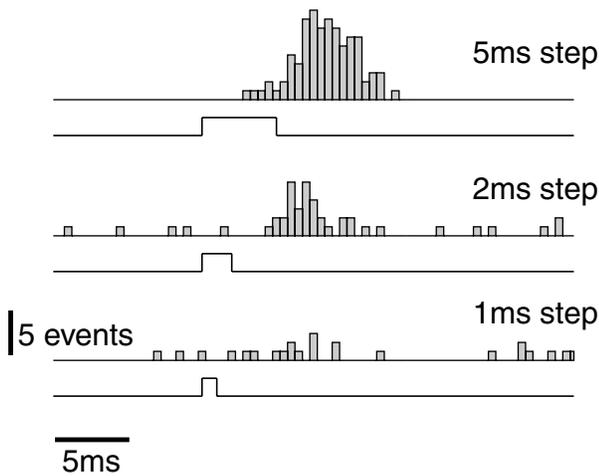
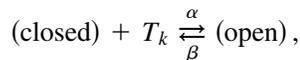


FIG. 4. Correlation detection can occur within time scales comparable to action potentials. Brief changes in correlation (between $c = 0.0$ and $c = 0.7$) were applied by using steps of different durations. Although these steps caused negligible changes in the membrane potential (see the first step in Fig. 3A), they led to a clear increase in the number of fired spikes down to steps of 2 ms duration. In all cases the response started within 5 ms after the onset of the step.

from neighboring compartments, where r_{li} denotes the axial resistance between compartments l and i .

Intrinsic voltage-dependent currents were described by the generic form $I_{ji}^{\text{int}} = \bar{g}_j m_j^M h_j^N (V_i - E_j)$, where the current is expressed as the product of, respectively, the maximal conductance \bar{g}_j , activation (m_j), and inactivation variables (h_j), and the difference between the membrane potential V_i and the reversal potential E_j . Activation and inactivation gates follow the kinetic scheme introduced by Hodgkin and Huxley [15].

Synaptic currents were described by [16] $I_{ki}^{\text{syn}} = \bar{g}_{ki} m_{ki} (V_i - E_{ki})$, where ki indicates the k th synaptic contact converging to compartment i , \bar{g}_{ki} is the maximal conductance, and E_{ki} is the reversal potential. m_{ki} denotes the fraction of open receptors according to the simple two-state kinetic scheme:



where T_k is the concentration of transmitter in the synaptic cleft. When a release event occurs at synapse ki , T_k is set to 1 mM during 1 ms, leading to the transient activation of the current which matches experimental measurements [16].

These equations were implemented in a pyramidal neuron model with 197 compartments, in which the soma and dendrites had voltage-dependent sodium and potassium currents as well as excitatory and inhibitory synapses. The kinetics and densities of these currents were matched to experimental data (see details in [13]).

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