

Synchronization of Noise-Induced Bursts in Noncoupled Sensory Neurons

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We report experimental observation of phase synchronization in an array of nonidentical noncoupled noisy neuronal oscillators, due to stimulation with external noise. The synchronization derives from a noise-induced qualitative change in the firing pattern of single neurons, which changes from a quasiperiodic to a bursting mode. We show that at a certain noise intensity the onsets of bursts in different neurons become synchronized, even though the number of spikes inside the bursts may vary for different neurons. We demonstrate this effect both experimentally for the electroreceptor afferents of paddlefish, and numerically for a canonical phase model, and characterize it in terms of stochastic synchronization.

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Arrays of oscillators are ubiquitous in biological systems, e.g., in sensory nervous systems [1]. Neuronal oscillators commonly undergo “bursting” discharge patterns [2]. Synchronization of different oscillators, i.e., adjustment of their characteristic time scales to a single rhythm, is a fundamental nonlinear phenomenon in oscillator arrays [3]. Bursting and synchronization are both affected by noise, present in any natural system [4]. Bursting induced by noise has been simulated numerically [5,6]. Bursts in different neurons can readily be synchronized if the neurons are *coupled*, e.g., via synapses, as analyzed theoretically [2,7] and experimentally [8]. But what if the oscillators in an array are not coupled? Noise can play a positive role in some cases, enhancing [9] or even inducing synchronization, as can occur when a population of *identical* noncoupled oscillators is subjected to a common noisy field, studied theoretically by Pikovsky [10] and recently in [11]. However, in many cases the oscillators of an array are not identical, and instead have widely distributed natural frequencies. Also, there could be statistically independent internal noises present in the different oscillators of an array, tending to prevent synchronization. Under these unfavorable conditions, how can synchronization occur among noncoupled nonidentical noisy oscillators?

In this Letter, we show that synchronization of nonidentical neuronal oscillators which are *not coupled* can still be achieved via a specific mechanism of noise-induced slow dynamics. Experimental results are presented from the electrosensory system of paddlefish, using external noise stimulation. We show that synchronization between different electroreceptors occurs due to a noise-induced transition in the electroreceptor firing pattern, changing qualitatively from a quasiperiodic mode to a bursting mode in which rapid firing alternates with periods of quiescence. Synchronization of bursts in different receptors occurs because the receptors exhibit common slow dynamics, when driven by noise, even though they may have quite different mean firing rates. To our knowledge, this is the first experimental demonstration of noise-induced synchronization among pairs of noncoupled sensory neurons.

Electrosense in paddlefish (*Polyodon spathula*) represents a “passive radar” system, optimized by nature during 65×10^6 years of evolution. Thousands of electroreceptors are organized into linear arrays on the elongated rostrum, which acts as an antenna for detecting electrical signals from plankton prey [12,13]. A remarkable property of electroreceptors is that they are spontaneously active [14] and undergo biperiodic noisy self-sustained oscillations [15]. We can therefore hypothesize that synchronization among electroreceptors due to the (external) electrical signals from planktonic prey may be an important sensory mechanism for the detection and location of prey. An “electroreceptor” consists of a cluster of 3–35 skin pores, each leading into a short canal [16], which ends in a sensory epithelium containing ≈ 400 hair cells. All the hair cells of a cluster synaptically excite the terminals of a few primary afferents (sensory neurons), whose axons project to the brain. A given afferent shows a nearly constant mean frequency of background firing, but the mean rate in different afferents can vary over a wide range of 30–80 Hz. The instantaneous firing frequency of an afferent can vary threefold, with coefficients of variation (CV) of interspike intervals ranging from 0.1 to 0.3 in different afferents. There is no morphological or physiological evidence for coupling between receptors [14,16], which gives us a well-defined system for studying correlations between different sensory neurons due solely to external stimuli.

We simultaneously recorded the single-unit spikes from pairs of electroreceptor afferents *in vivo*, using metal microelectrodes (see [12,15] for experimental details). One receptive field was on the left side of the rostrum, the other on the right side. Their locations on opposite sides of the rostrum, which are innervated by separate nerves, guaranteed that the pairs of afferent neurons were not coupled [16]. We used uniform-field stimulation of all the electroreceptors: stimulus currents were passed between 15×5 cm silver plate electrodes at the ends of the experimental chamber. A computer-generated zero-mean Ornstein-Uhlenbeck (OU) Gaussian noise was used. The correlation time was set to be 0.002 sec, corresponding to

a 500 Hz bandwidth, much smaller than the mean firing period of afferents (0.013–0.033 sec), in order to study the general response properties of electroreceptors [17]. We generated a sequence of 30 segments of OU noise with incrementing intensities. Each noise segment was 180 sec long, and segments were separated by 5 sec of no stimulus. Approximately 10^4 afferent spikes occurred during each segment [18]. For comparison, we also used noise from a General Radio model 1390B generator, which was low-pass filtered by an eight-pole Bessel filter set to 50 Hz. This same noise was used in a previous study on electrosensory stochastic resonance [13]; its probability density was Gaussian, with a broad peak at 20 Hz in the power spectrum (see Fig. 1d in [13]). Data were from 9 pairs of afferents, from 4 animals.

Figure 1 shows representative data from two different afferent pairs, from different animals, using two different types of noise stimulation (panels A, B). In the absence of stimulation, the individual spikes of the afferent pairs were not correlated or synchronized. For instance, in Fig. 1B, afferent No. 1 fired slower than afferent No. 2, with mean firing rates of 33.4 and 45.1 Hz, respectively. Stimulation with weak noise ($<2.5 \mu\text{V}/\text{cm}$ rms) did not change the firing pattern, but rather led to the well-known effect of widening the power spectrum peak at the mean frequency of the afferent [15]. When noise of a certain intensity ($>2.5 \mu\text{V}/\text{cm}$ rms) was applied, the firing patterns of the afferents changed drastically such that both afferents of a pair produced bursts [18]. For larger noise ($>5\text{--}6 \mu\text{V}/\text{cm}$ rms), each burst started almost simultaneously in the two neurons of a pair, after stimulation (noise) was switched on, even though the number of spikes inside a burst was different for each neuron. The small constant time delay

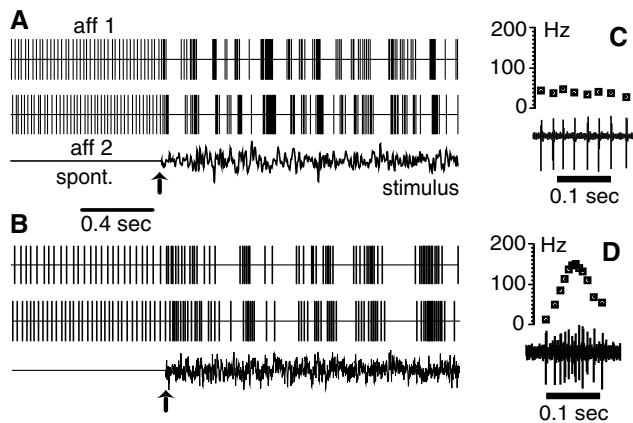


FIG. 1. Examples of simultaneous recordings of spike trains from pairs of electroreceptor afferents, for two different types of noise stimulation. Spikes are marked by vertical lines. A: stimulation with noise from a vacuum tube generator, of $20 \mu\text{V}/\text{cm}$ rms amplitude; B: stimulation with computer-generated OU noise of $16.8 \mu\text{V}/\text{cm}$ rms amplitude. The onset of stimulation is marked by the arrows. C and D: instantaneous firing rate during spontaneous activity (C) and noise-induced parabolic bursting (D).

between the burst onsets in the two neurons was probably due to different lengths of their axons. The interspike intervals within a burst decreased towards the center of the burst (Fig. 1D); such a pattern is termed “parabolic bursting” [19].

The 500 Hz bandwidth of the OU noise was significantly larger than any of the characteristic frequencies of the receptor system, and therefore burst initiation cannot be explained simply by slow changes in the stimulus. Indeed, bursts could also be induced by other types of stimuli (sine wave, impulselike, etc.), as well as by noise having different statistical properties, as in Fig. 1A. Similar results were also obtained using OU noise which was high-pass filtered at 20 Hz to remove the low frequencies.

As the noise intensity was increased from zero, the distribution of interspike intervals (Fig. 2A) changed smoothly from unimodal (curve 1, without stimulation) to a bimodal distribution during bursting, while the frequency of bursts increased progressively. The two peaks of the bimodal distribution correspond to the slow inter- and fast intraburst dynamics, resembling results from other noise-induced transitions [20]. The change from uni- to bimodal was quantitated by plotting the mean interburst interval $\langle\tau_b\rangle$ as a function of increasing noise intensity (Fig. 2B), which showed exponential falloff. The experimental results were well fitted by the Arrhenius law, $\langle\tau_b\rangle = \nu \exp(\Delta/\sigma^2)$ with $\nu = 0.23$ sec and $\Delta = 7.1 (\mu\text{V}/\text{cm})^2$; σ is the noise rms amplitude. This implies that burst generation is excitable and has a well-defined threshold [21], $2.7 \mu\text{V}/\text{cm}$ in this example, comparable to threshold estimates from behavioral experiments ($0.5\text{--}1 \mu\text{V}/\text{cm}$; [13]). In sum, the noise-induced transition to bursting involves a new characteristic slow time scale, reflected in the quiescent epochs between bursts. The slow time scale is distinct and well separated from the dynamics of fast spiking during bursts. Further experiments are needed to define the cellular mechanisms of the bursting; it probably arises from slow ionic currents in the afferent terminals, as in thermoreceptors [6].

To characterize the coincidence of bursts in pairs of neurons, we used the phase $\phi(t)$ of burst trains in each neuron,

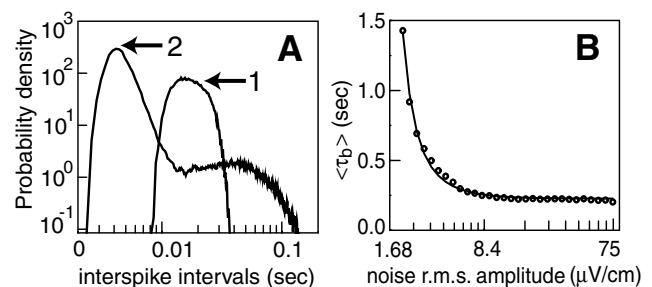


FIG. 2. A: Probability density of interspike intervals in the absence of noise (curve 1), or during stimulation with $16.8 \mu\text{V}/\text{cm}$ rms OU noise (curve 2). B: Mean interburst interval versus the rms amplitude of the stimulus OU noise (circles), and its fit by the Arrhenius law (solid line).

which increases by 2π every time a burst occurs, and interpolates linearly between two sequential bursts. When stochastic synchronization occurs, constant segments of the phase difference $\Delta\phi(t) = \phi_1(t) - \phi_2(t)$ (phase locking) are interrupted by abrupt 2π changes (phase slips) [4]. The probability density of the phase difference, $P(\Delta\phi)$, characterizes the degree of synchronization: a well-expressed peak in $P(\Delta\phi)$ indicates synchronization, while a uniform distribution indicates the absence of synchronization. For small noise (Fig. 3A), the bursts in the two afferents of a pair have different frequencies (see also Fig. 4B) and are not synchronized, indicated by a monotonic increase of the phase difference, and the uniform distribution of $P(\Delta\phi)$. In contrast, during burst synchronization induced by strong noise, the phases of the two afferents are locked for epochs lasting several seconds (inset, Fig. 3B), and there is a sharp peak in the probability density of the phase difference (Fig. 3B). This can be further quantified by calculating the synchronization index as $\gamma^2 = \langle \cos\Delta\phi \rangle^2 + \langle \sin\Delta\phi \rangle^2$, where the brackets denote the average over time [22]. The synchronization index increases with the noise intensity, indicating more complete noise-induced burst synchronization (Fig. 4A). This occurs because of frequency locking, in which the mean interburst intervals of the two afferents converge (Fig. 4B). This convergence implies that the two electroreceptors share similar slow dynamics. Since we were able to synchronize all the neuron pairs studied, it appears that all the electroreceptors have similar slow dynamics. Thus the transition to synchronization occurs in two steps: (i) common noise induces bursts in neurons, but since their burst thresholds may be slightly different the frequencies of bursts are different and thus the burst onsets are not synchronized; (ii) further increase of common noise leads to entrainment of slow dynamics in the two neurons and thus to burst synchronization.

We can narrow the choice of a model for our data based on a crucial property of the observed bursting, namely its parabolic character (see Fig. 1D). Parabolic bursting can be described in the most general way by a canonical model proposed by Ermentrout and Kopell [19]. The canonical model involves two subsystems, fast and slow. The fast subsystem describes the fast dynamics of a vari-

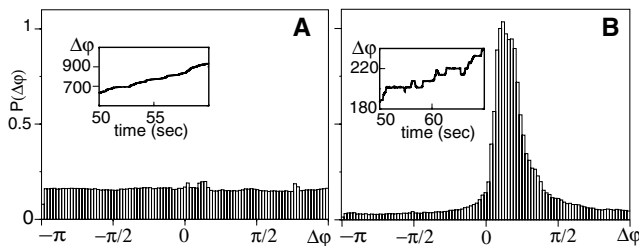


FIG. 3. Phase differences of burst trains in a pair of afferents (insets), and their probability densities. A: weak OU noise of $3 \mu\text{V}/\text{cm}$ rms amplitude. B: OU noise of $16.8 \mu\text{V}/\text{cm}$ rms amplitude.

able θ which refers to a phase along a limit cycle: $\dot{\theta} = (1 - \cos\theta) + (1 + \cos\theta)r$. The fast subsystem operates in the vicinity of saddle-node bifurcation which is controlled by the parameter r : for $r > 0$ the “neuron” fires periodically with the angular frequency $2\sqrt{r}$, while for $r < 0$ the fast system is excitable, with two equilibria $\theta^\pm = \pm \cos^{-1}[(1+r)/(1-r)]$, unstable and stable, respectively [2]. The slow subsystem mimics the contribution of slow ionic currents, and operates on a much slower time scale, modulating the parameter r of the fast subsystem [23]. In our model, external broadband noise excites the slow subsystem, which in turn modulates the parameter r of the fast subsystem, producing parabolic bursts:

$$\begin{aligned} \dot{\theta} &= (1 - \cos\theta) + (1 + \cos\theta)r \cos\psi + w(t), \\ \tau_s \dot{\psi} &= 1 - \epsilon \sin\psi + s(t), \end{aligned} \quad (1)$$

where ψ represents the excitable slow subsystem, $\tau_s \gg 1$ is a scaling factor, $w(t)$ is Gaussian white noise of intensity W , $\langle w(t)w(t+\tau) \rangle = 2W\delta(\tau)$, mimicking internal fluctuations, and $s(t)$ is the external stimulus [24]. The parameter ϵ determines the excitability of the slow subsystem. In the absence of any stimulus, [$s(t) = 0$] for $\epsilon < 1$, the slow subsystem resides at a stable equilibrium $\psi_s = \sin^{-1}(1/\epsilon)$. The unstable equilibrium, $\psi_u = \pi - \sin^{-1}(1/\epsilon)$, represents a threshold which should be overcome to induce a single rotation and thus a burst in the fast subsystem. The slow dynamics of ψ can also be interpreted as Brownian motion in a tilted periodic potential $U(\psi) = -\psi - \epsilon \cos\psi$. For the case of a white Gaussian noise stimulus, the escape rate from the potential well can be calculated analytically and follows the Arrhenius law [4]. We note that direct application to the fast subsystem of a rapid stimulus, fluctuating on a time scale comparable to the oscillation period of the fast subsystem, will not induce the long quiescent intervals we observe between bursts.

If we now consider two noncoupled systems described by Eqs. (1), with significantly different parameters r , slightly different parameters ϵ , and the same scaling factor τ_s , along with statistically independent internal noises $w(t)$, but receiving common external noisy input $s(t)$, then

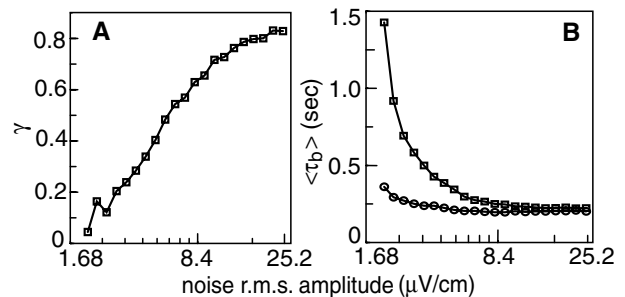


FIG. 4. The synchronization index γ (A) and the mean interburst interval $\langle \tau_b \rangle$ (B) as a function of external OU noise rms amplitude, for a pair of simultaneously recorded electroreceptor afferents.

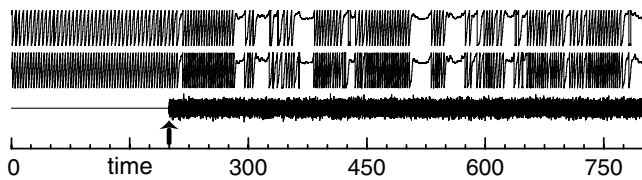


FIG. 5. Numerical simulation of two oscillators described by Eq. (1). The “membrane potentials” $\theta_{1,2} \bmod 2\pi$ are plotted in time (first two traces), along with the Gaussian white noise stimulus $s(t)$ of intensity 0.05 (third trace), which started at the arrow. Subscripts indicate oscillator No. 1 (upper trace) and No. 2 (lower trace). Parameter r of the fast subsystem was 1.0 and 2.0 for oscillators No. 1 and No. 2, respectively. Other parameters were $\epsilon_1 = 1.1$, $\epsilon_2 = 1.12$, $\tau_c = 20$, and $W = 0.005$.

synchronization of bursts is observed. This is illustrated in Fig. 5, where the frequencies of the fast subsystems for the two units differed twofold.

Synchronous burst responses of a population of sensory neurons may be a neural mechanism for coincidence detection, and may substantially simplify the neural operations that a fish’s brain must perform to detect prey and to calculate their position and velocity. Thus, the rostrum of the paddlefish, with its thousands of electroreceptors, can be considered as a preprocessor of input information, akin to the retina or olfactory bulb. The impulselike electrical signal emitted by an individual planktonic prey (e.g., *Daphnia*) moving along the rostrum [25], or the exponentially correlated Gaussian electrical noise generated by swarms of *Daphnia* [26], may be adequate stimuli for evoking synchronized bursting of different electroreceptors during feeding behavior. Further experimental study is needed to verify this hypothesis.

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- [1] W. Singer, *Neuron* **24**, 49 (1999).
- [2] E. M. Izhikevich, *Int. J. Bifurcation Chaos Appl. Sci. Eng.* **10**, 1171 (2000).
- [3] A. S. Pikovsky, M. G. Rosenblum, and J. Kurths, *Synchronization: A Universal Concept in Nonlinear Sciences* (Cambridge University Press, Cambridge, MA, 2001).
- [4] R. L. Stratonovich, *Topics in the Theory of Random Noise* (Gordon and Breach, New York, 1967), Vol. 2.

- [5] A. Longtin and K. Hinzer, *Neural. Comput.* **8**, 215 (1996); B. Hu and C. Zhou, *Phys. Rev. E* **63**, 026201 (2001).
- [6] H. A. Braun *et al.*, *Int. J. Bifurcation Chaos Appl. Sci. Eng.* **8**, 881 (1998).
- [7] F. C. Hoppensteadt and E. M. Izhikevich, *Weakly Connected Neural Networks* (Springer, New York, 1997); E. M. Izhikevich, *SIAM Rev.* **43**, 315 (2001).
- [8] E. A. Stern, D. Jaeger, and C. J. Wilson, *Nature (London)* **394**, 475 (1998); R. C. Elson *et al.*, *Phys. Rev. Lett.* **81**, 5692 (1998); R. Segev, Y. Shapira, M. Beneveniste, and E. Ben-Jacob, *Phys. Rev. E* **64**, 011920 (2001).
- [9] A. Neiman *et al.*, *Phys. Rev. E* **58**, 7118 (1998).
- [10] A. S. Pikovsky, *Radiophys. Quantum Electron.* **27**, 576 (1984).
- [11] C. Zhou, J. Kurths, I. Kiss, and J. Hudson, *Phys. Rev. Lett.* (to be published).
- [12] L. A. Wilkens, D. F. Russell, X. Pei, and C. Gurgens, *Proc. R. Soc. London B* **264**, 1722 (1997).
- [13] D. F. Russell, L. A. Wilkens, and F. Moss, *Nature (London)* **402**, 291–294 (1999).
- [14] A. Neiman *et al.*, *Phys. Rev. Lett.* **82**, 660 (1999).
- [15] A. Neiman and D. F. Russell, *Phys. Rev. Lett.* **15**, 3443 (2001).
- [16] J. M. Jørgensen, Å. Flock, and J. Wersäll, *Z. Zellforsch.* **130**, 362–377 (1972).
- [17] P. Z. Marmarelis and V. Z. Marmarelis, *Analysis of Physiological Systems: The White-Noise Approach* (Plenum Press, New York, 1978); H. L. Bryant and J. P. Segundo, *J. Physiol. (London)* **260**, 279 (1976); Z. F. Mainen and T. J. Sejnowski, *Science* **268**, 9 (1995).
- [18] Spike times were identified offline with 5 μ sec interpolated temporal resolution using Spike2™ software from Cambridge Electronic Devices (U.K.). Bursts were identified using the same software by imposing the following conditions: (i) a burst had to include at least 3 spikes, and (ii) the maximal time between two spikes in a burst was set to 0.01 sec.
- [19] G. B. Ermentrout and N. Kopell, *SIAM J. Appl. Math.* **46**, 233 (1986).
- [20] W. Horsthemke and R. Lefever, *Noise-Induced Transitions* (Springer, Berlin, 1984).
- [21] P. Hänggi, P. Talkner, and M. Borkovec, *Rev. Mod. Phys.* **62**, 251 (1990).
- [22] P. Tass *et al.*, *Phys. Rev. Lett.* **81**, 3291 (1998).
- [23] C. Soto-Trevino, N. Kopell, and D. Watson, *J. Math. Biol.* **35**, 114 (1996).
- [24] For the sake of simplicity and generality we did not include additional canal oscillations [15] in the model. The inclusion of the canal oscillator does not change the qualitative results of noise-induced bursting and synchronization.
- [25] W. Wojtenek, M. H. Hofmann, and L. A. Wilkens, *Neurocomputing* **38**, 451 (2001).
- [26] J. A. Freund *et al.*, *Phys. Rev. E* **63**, 031910 (2001).