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How Synchronization Protects from Noise

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Abstract

The functional role of synchronization has attracted much interest and debate: in particular, synchronization may allow distant sites in the brain to communicate and cooperate with each other, and therefore may play a role in temporal binding, in attention or in sensory-motor integration mechanisms. In this article, we study another role for synchronization: the so-called “collective enhancement of precision”. We argue, in a full nonlinear dynamical context, that synchronization may help protect interconnected neurons from the influence of random perturbations—intrinsic neuronal noise—which affect all neurons in the nervous system. More precisely, our main contribution is a mathematical proof that, under specific, quantified conditions, the impact of noise on individual interconnected systems and on their spatial mean can essentially be cancelled through synchronization. This property then allows reliable computations to be carried out even in the presence of significant noise (as experimentally found e.g., in retinal ganglion cells in primates). This in turn is key to obtaining meaningful downstream signals, whether in terms of precisely-timed interaction (temporal coding), population coding, or frequency coding. Similar concepts may be applicable to questions of noise and variability in systems biology.

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Introduction

Synchronization phenomena are pervasive in biology. In neuronal networks [1–3], a large number of studies have sought to unveil the mechanisms of synchronization, from both physiological [4,5] and computational viewpoints (see for instance [6] and references therein). In addition, the *functional* role of synchronization has also attracted considerable interest and debates. In particular, synchronization may allow distant sites in the brain to communicate and cooperate with each other [7–9] and therefore may play a role in temporal binding [10,11] and in attention and sensory-motor integration mechanisms [12–14].

In this article, we study another role for synchronization: the so-called *collective enhancement of precision* (see e.g. [15–17]), an intuitive and often quoted phenomenon with comparatively little formal analysis [18]. We explain mathematically why synchronization may help *protect* interconnected nonlinear dynamic systems from the influence of random perturbations. In the case of neurons, these perturbations would correspond to so-called “intrinsic neuronal noise” [19], which affect all of the neurons in the nervous system. In the presence of significant noise intensities (as experimentally found in e.g. retinal ganglion cells in primates [20]), this property would be required for meaningful and reliable computations to be carried out.

It should be noted that “protection of systems from noise” and “robustness of synchronization to noise” are two different concepts. The latter concept means that the synchronized systems remain so in presence of noise, whereas the former concept means that, thanks to synchronization, the behaviors of the coupled systems are close to the noise-free behaviors. This difference is further addressed in the Discussion.

The influence of noise on the behaviors of nonlinear systems is very diverse. In chaotic systems, a small amount of noise can yield dramatic effects. At the other end of the spectrum, the effect of noise on nonlinear *contracting* systems is bounded by σ^2/λ where σ is the noise intensity – which can be arbitrarily large – and λ is the contraction rate of the system [21]. Between these two extremes, it has been shown analytically that some limit-cycle oscillators commonly used as simplified neuron models, such as FitzHugh-Nagumo (FN) oscillators, are basically unperturbed when they are subject to a small amount of white noise [22]. Yet, a larger amount of noise breaks this “resistance”, both in the state space and in the frequency space [Figures 1(A)–(D)]. This suggests that both temporal coding and frequency coding may be unusable in the context of large neuronal noise.

One might argue that it could be possible to recover some information from the noisy FN oscillators by considering the activities of a large number of oscillators *simultaneously* [19,23]. Figure 2(A) shows that the spatial mean of the noisy oscillators still carries very little information when the noise intensities are large, making the population coding hypothesis also unlikely in this context. In other words, if the underlying dynamics are fundamentally *nonlinear*, as in the case of our FN oscillators, the spatial mean of the signals is “clean,” but contains very little information: the nonlinear nature of the systems dynamics prevents the familiar “averaging out” of noise through multiple measurements, and getting rid of the noise also gets rid of the signal.

By contrast, one can observe that when oscillators are *synchronized* through mutual couplings, then they become “protected” from noise, whether in temporal [Figure 1(E)], frequential

Author Summary

Synchronization phenomena are pervasive in biology, creating collective behavior out of local interactions between neurons, cells, or animals. On the other hand, many of these systems function in the presence of large amounts of noise or disturbances, making one wonder how meaningful behavior can arise in these highly perturbed conditions. In this paper we show mathematically, in a general context, that synchronization is actually a means to *protect* interconnected systems from effects of noise and disturbances. One possible mechanism for synchronization is that the systems jointly create and then share a common signal, such as a mean electrical field or a global chemical concentration, which in turn makes each system directly connected to all others. Conversely, extracting meaningful information from average measurements over populations of cells (as commonly used for instance in electro-encephalography, or more recently in brain-machine interfaces) may require the presence of synchronization mechanisms similar to those we describe.

[Figure 1(F)] or “populational” aspects [Figure 2(B)]. Thus, in some sense, the linear effect of averaging noise while preserving signal [24] can be achieved for these highly nonlinear dynamic components *through the process of synchronization*. Our aim in this article is to give mathematical elements of explanation for this phenomenon, in a full nonlinear setting. It is also to suggest elements of response to a more general question, namely: what is the precise *meaning* of ensemble measurements or population codes, and what information do they convey about the underlying dynamics and signals?

Results

General analytical result

Consider a diffusive network of d -dimensional noisy non-linear dynamical systems

$$d\mathbf{x}_i = \left(\mathbf{f}(\mathbf{x}_i, t) + \sum_{j \neq i} \mathbf{K}_{ji}(\mathbf{x}_j - \mathbf{x}_i) \right) dt + \sigma dW_i, \quad i = 1 \dots n \quad (1)$$

where $\mathbf{f} = (f_1, \dots, f_d)^T$ is a $\mathbb{R}^d \rightarrow \mathbb{R}^d$ function. Note that the noise intensity σ is intrinsic to the dynamical system (i.e. independent of the inputs), which is consistent with experimental findings [20]. For simplicity, we set σ to be a constant in this article, although the case of time- and state-dependent noise intensities can be easily adapted from [21].

We consider four mathematical assumptions that will enable us to relate the trajectory of any noisy element of the network \mathbf{x}_i to the trajectory of the noise-free system $\mathbf{x}_{\text{noise-free}}$ driven by equation

$$d\mathbf{x}_{\text{noise-free}} = \mathbf{f}(\mathbf{x}_{\text{noise-free}}, t) dt.$$

(A1) is an assumption on the form of the network. (A2) gives a bound on the nonlinearity of the dynamics \mathbf{f} . (A3) states that the system trajectories are resistant to small perturbations. Finally, (A4) requires that the dynamical systems in the network are synchronized.

(A1). The network is balanced, that is, for any element of the network, the sum of the incoming connection weights equals the

sum of the outgoing connection weights

$$\forall i \quad \sum_j \mathbf{K}_{ji} = \sum_j \mathbf{K}_{ij}.$$

Remark that any symmetric network is balanced.

A particular kind of balanced network consists of an all-to-all network with identical couplings, i.e. $\mathbf{K}_{ij} = k/n$ for all i and j . In general, assuming all-to-all coupling needs not be unduly restrictive, since such coupling can be implemented through mechanisms such as *quorum sensing* [25–27]. Indeed, assuming that the mean value of the \mathbf{x}_i 's can be provided by the environment as $\mathbf{x}^* = \frac{1}{n} \sum_i \mathbf{x}_i$, then the all-to-all network (1) can be written as a star network where damping is added locally and each cell \mathbf{x}_i is only connected to the common signal

$$d\mathbf{x}_i = (\mathbf{f}(\mathbf{x}_i, t) + k(\mathbf{x}^* - \mathbf{x}_i)) dt + \sigma dW_i.$$

Quorum sensing, and more generally the measurement of a common mean signal, can thus be seen as a practical (and biologically plausible) way to implement all-to-all coupling with $2n$ connections instead of n^2 .

(A2). Let \mathbf{H}_j denote the Hessian matrix of the function f_j and let $\lambda_{\max}(\mathbf{H}_j)$ denote its largest eigenvalue. For all j , we assume that $\lambda_{\max}(\mathbf{H}_j)$ is uniformly upper-bounded by a constant $\frac{1}{\sqrt{d}} \mathbf{H}_{\text{bd}}$. This implies in particular that

$$\forall \mathbf{x}, j, t \quad \mathbf{x}^T \mathbf{H}_j \mathbf{x} \leq \frac{\mathbf{H}_{\text{bd}}}{\sqrt{d}} \|\mathbf{x}\|^2.$$

This assumption gives us a bound on the nonlinearity of \mathbf{f} , the extreme case being $\mathbf{H}_{\text{bd}} = 0$ for a linear system.

(A3). The dynamics \mathbf{f} is resistant to small perturbations. More precisely, consider two systems starting from the same initial conditions but driven by slightly different dynamics

$$\dot{\mathbf{x}}_{\text{noise-free}} = \mathbf{f}(\mathbf{x}_{\text{noise-free}}, t)$$

and

$$\dot{\mathbf{x}}_{\text{perturbed}} = \mathbf{f}(\mathbf{x}_{\text{perturbed}}, t) + P,$$

(where P is a real time stochastic process) then $\mathbb{E}(\|P\|) \rightarrow 0$ implies $\|\mathbf{x}_{\text{noise-free}} - \mathbf{x}_{\text{perturbed}}\| \rightarrow 0$.

In particular, such a property has been demonstrated in the case of FN oscillators, with P representing a white noise process [22].

(A4). After exponential transients, the expected sum of the squared distances between the states of the elements of the network is bounded by a constant ρ

$$\mathbb{E} \left(\sum_{i < j} \|\mathbf{x}_i - \mathbf{x}_j\|^2 \right) \leq \rho.$$

This is where synchronization will come into play, because synchronization is an effective way to reduce the bound ρ . Some precise conditions for this will be given later.

We show in **Methods** that under these assumptions and when $n \rightarrow \infty$ and $\rho/n^2 \rightarrow 0$, the distance between the trajectory of any noisy element \mathbf{x}_i of the network and that of the noise-free system $\mathbf{x}_{\text{noise-free}}$ tends to zero, with the impact of noise on the mean

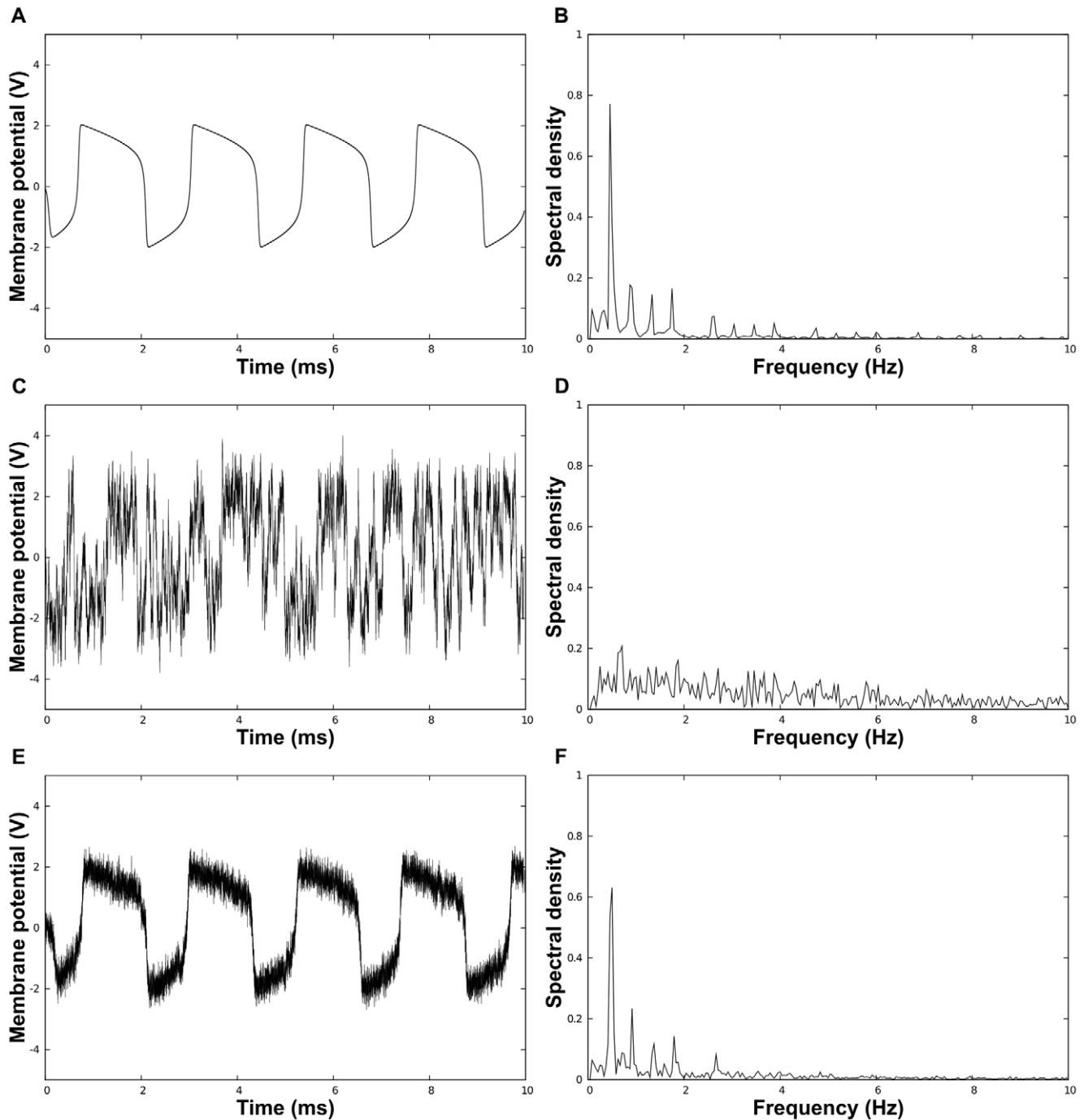


Figure 1. Simulations of a network of FN oscillators using the Euler-Maruyama algorithm [47]. The dynamics of coupled FN oscillators are given by equation (2). The parameters used in all simulations are $a=0.3$, $b=0.2$, $c=30$. (A) shows the trajectory of the “membrane potential” of a noise-free oscillator and (B) depicts the frequency spectrum of this trajectory computed by Fast Fourier Transformation. (C) and (D) present the trajectory (respectively the frequency spectrum) of a *noisy uncoupled* oscillator ($\sigma=10$). (E) and (F) show the trajectory (respectively the frequency spectrum) of a *noisy synchronized* oscillator within an all-to-all network ($\sigma=10$, $k_{ij}=5$, $n=200$). Note the temporal and frequential similarities between a noise-free oscillator and a noisy synchronized one. For instance, the main frequency and the first harmonics are very similar in the two frequency spectra. In contrast, the frequency spectrum of a noisy uncoupled oscillator shows no clear harmonics. doi:10.1371/journal.pcbi.1000637.g001

trajectory evolving as

$$\frac{\rho \mathbf{H}_{bd}}{2n^2} + \frac{\sigma}{\sqrt{n}}.$$

In particular, when \mathbf{f} is a time-varying linear system of the form

$\mathbf{f}(\mathbf{x}, t) = \mathbf{A}(t)\mathbf{x} + \mathbf{b}(t)$, we recover the known result [28] that the impact of noise evolves as the inverse square root of n . More generally, linear components of the system dynamics (including, in particular, the input signals) do not contribute to the first term of the above upper bound.

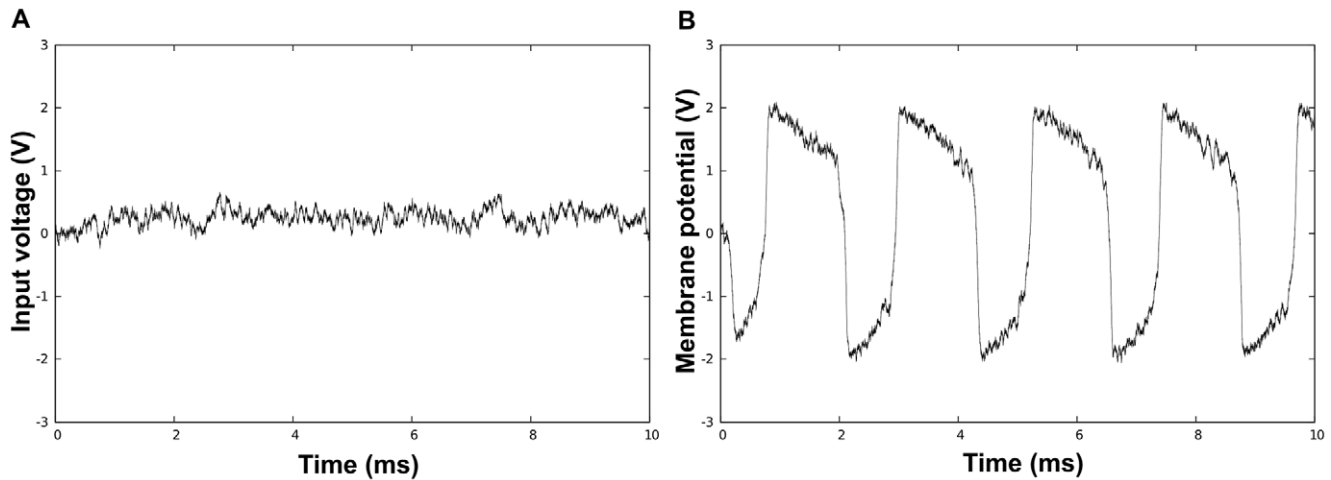


Figure 2. “Spatial mean” of FN oscillators. Note that the same set of random initial conditions was used in the two plots. (A) shows the average “membrane potential” computed over $n=200$ noisy uncoupled oscillators ($\sigma=10$). (B) shows the average “membrane potential” computed over $n=200$ noisy synchronized oscillators within an all-to-all network ($\sigma=10$, $k_{ij}=5$). Observe that, in the first plot, the average trajectory of uncoupled oscillators carries essentially no information, while in the second plot, the average trajectory of synchronized oscillators is very similar to a noise-free one. doi:10.1371/journal.pcbi.1000637.g002

Synchronization in networks of noisy FN oscillators

We now give conditions to guarantee assumption (A4) for all-to-all networks of FN oscillators with identical couplings. The dynamics of n noisy FN oscillators coupled by (gap-junction-like) diffusive connections is given by

$$\begin{cases} dv_i &= \left(cf(v_i, w_i, I) + \sum_j \frac{k}{n} (v_j - v_i) \right) dt + \sigma dW_i \\ dw_i &= -\frac{1}{c} (v_i - a + bw_i) dt \end{cases} \quad (2)$$

where $f(v, w, I) = v - \frac{1}{3}v^3 + w + I$. We show in **Methods** that, after exponential transients of rate k ,

$$\mathbb{E} \left(\sum_{i < j} (v_i - v_j)^2 \right) \leq \frac{n(n-1)\sigma^2}{k}. \quad (3)$$

Thus, (A4) is verified with

$$\rho = \frac{n(n-1)\sigma^2}{k}. \quad (4)$$

For large n , we have $\rho/n^2 \sim \sigma^2/k$, which converges to 0 when $k \rightarrow \infty$. Figure 3(A) provides a comparison of this theoretical bound with simulations.

Assumption (A1) is also verified because an all-to-all network with identical couplings is symmetric, therefore balanced. Since the $(v_i, w_i)^T$ are oscillators with stable limit cycles, it can be shown that the trajectories of the v_i are bounded by a common constant M . Thus (A2) is verified with $\mathbf{H}_{bd} = 2cM$. Finally, (A3) may be adapted from [22]. Indeed, we believe that the arguments of [22] can be extended to the case of non-white noise. Making this point precise is the subject of ongoing work.

Using now the “general analytical result”, we obtain that, given any (non necessarily small) noise intensity σ , in the limits for $k \rightarrow \infty$ and $n \rightarrow \infty$ and after exponential transients, the behavior of any oscillator will be arbitrary close to that of a noise-free oscillator (Figure 1).

This statement can be further tested by constructing a model-based nonlinear state estimator (observer) [29]. Let $(v_i, w_i)^T$ be a noisy synchronized oscillator and consider the observer

$$\begin{cases} v_{\text{obs}} &= cf(v_{\text{obs}}, w_{\text{obs}}, I) + k_{\text{obs}}(v_i - v_{\text{obs}}) \\ w_{\text{obs}} &= -\frac{1}{c}(v_{\text{obs}} - a + bw_{\text{obs}}). \end{cases} \quad (5)$$

If v_i has the same trajectory as a noise-free FN oscillator, then it can be shown that $(v_{\text{obs}}, w_{\text{obs}})^T$ tends exponentially to $(v_i, w_i)^T$, independently of the observer’s initial conditions [29]. Thus the squared distance $(v_{\text{obs}} - v_i)^2$ indicates how close v_i is from a noise-free oscillator [see Figure 3(B) for a comparison this theoretical result with simulations].

Simulations of more generic networks

We provide in this section simulation results which show that similar observations can be made even for more general network classes that are not yet covered by the theory. We believe that this simulations show the genericity of the concepts presented above.

Probabilistic networks. In practice, all-to-all neuronal networks of large size are rare. Rather, the mechanisms of neuronal connections in the brain are believed to be probabilistic in nature (see [30] for a review). Here, we consider a probabilistic symmetric network of n oscillators, where any pair of oscillators has probability p to be symmetrically connected and probability $1-p$ to be unconnected. Figure 4 shows simulation results for randomly chosen network with $p=0.1$. Concretely, we have built a network by randomly deciding for any pair of connections if the connection exists or not.

Hindmarsh-Rose oscillators. Hindmarsh-Rose oscillators are three-dimensional dynamical systems that are also often used as neuron models

$$\begin{cases} dV &= (I - n - m - V^3 + g_V V + E_V V^2) dt + \sigma dW \\ dn &= (G_{Na} + E_{Na} V^2 - n) dt \\ dm &= (g_{Ca}(E_{Ca}(V + V_{const}) - m)) dt \end{cases}$$

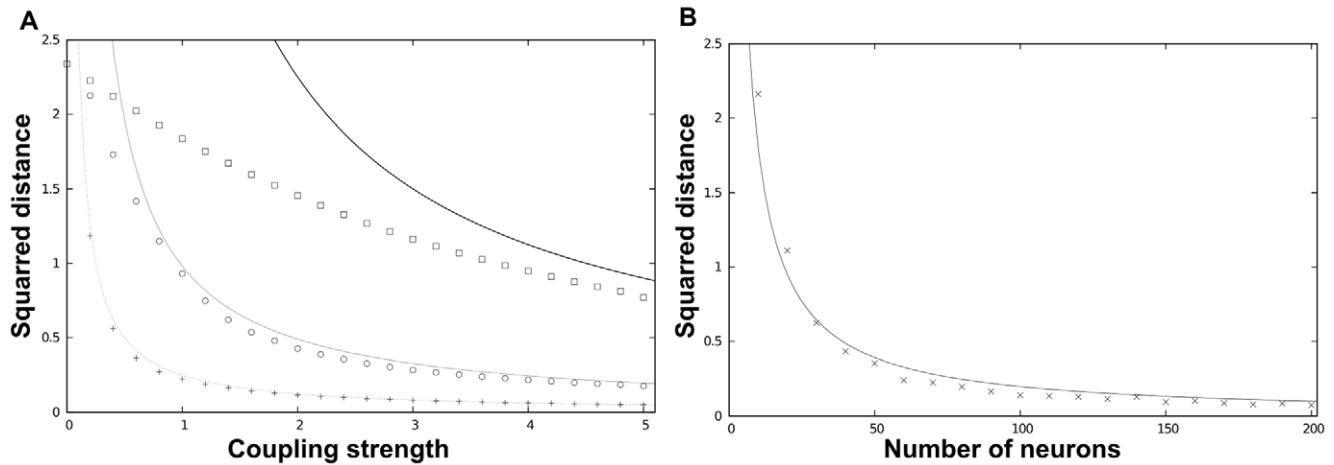


Figure 3. Asymptotic appraisal of the theoretical bounds. Note that the experimental expectations were computed assuming the ergodic hypothesis. (A) Expectation of the average squared distance between the v_i 's and v^* (given by $\frac{1}{n} \mathbb{E} \sum_i (v_i - v^*)^2$) as a function of the coupling strength k_{ij} ($\sigma=10$). Theoretical bound $\frac{(n-1)\sigma^2}{n^2 k_{ij}}$ (cf equations (7) and (4)) for $n=10$ (bold line), for $n=50$ (plain line), for $n=200$ (dashed line); simulation results for $n=10$ (squares), for $n=50$ (triangles), for $n=200$ (crosses). (B) Expected squared distance between a noisy synchronized oscillator and its observer (given by $(v_{\text{obs}} - v_i)^2$) as a function of n ($\sigma=10$, $k_{ij}=5$). The bound $\frac{(n-1)\sigma^2}{n^2 k_{ij}}$ was plotted in plain line and the simulation results were represented by crosses. doi:10.1371/journal.pcbi.1000637.g003

with $g_V=0.5$; $E_V=2.8$; $G_{Na}=0$; $E_{Na}=4.4$; $g_{Ca}=0.001$; $E_{Ca}=9$; $V_{\text{const}}=7/E_{Ca}$. These oscillators can exhibit more complex behaviors (including spiking and bursting regimes [31]) than FitzHugh-Nagumo oscillators. The proofs of (A3) and (A4) for Hindmarsh-Rose oscillators are the object of ongoing research.

We made the inputs time-varying in this simulation. In fact, all the previous calculations can be straightforwardly extended to the case of time-varying inputs, as long as those inputs are the same for all the oscillators [6].

One can observe from the simulations (see Figure 5) that the synchronized oscillators preserve the input signal, while the uncoupled oscillators completely blur it out.

Discussion

We have argued that synchronization may represent a fundamental mechanism to protect neuronal assemblies from noise, and have quantified this hypothesis using a simple nonlinear neuron model. This may further strengthen our understanding of synchronization in the brain as playing a key functional role, rather than as being mostly an epiphenomenon.

It should be noted that the causal relationship studied here – effect of synchronization on noise – is converse to one usually investigated formally in the literature – effect of noise on synchronization: under certain conditions, adding noise can desynchronize already synchronized oscillators (destructive effect)

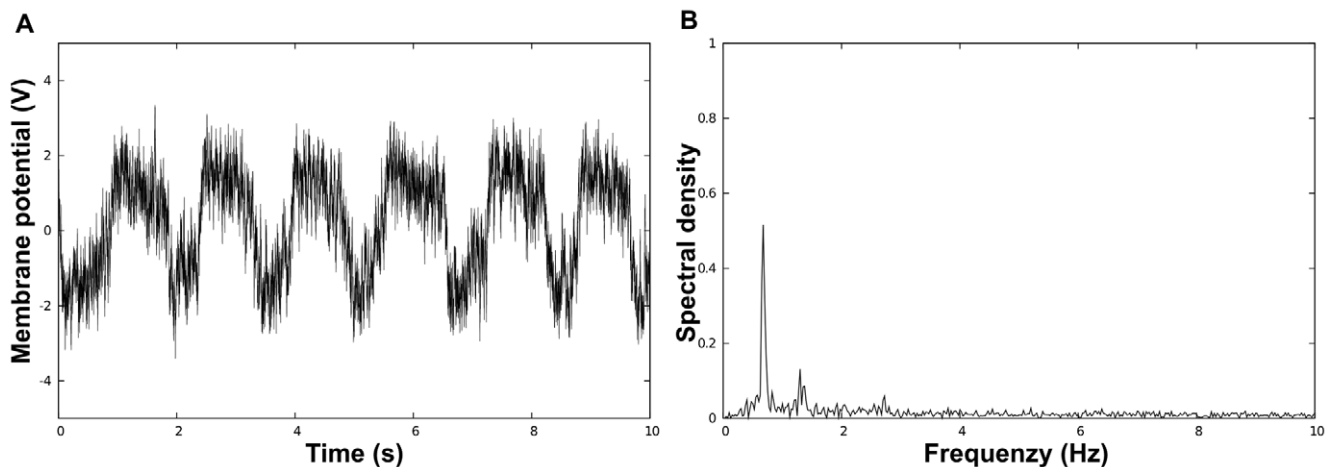


Figure 4. Simulation for a probabilistic symmetric network ($n=200$, $p=0.1$, $\sigma=10$, $k_{ij}=5$). (A) shows the trajectory of the “membrane potential” of an oscillator in the network. (B) shows its frequency spectrum. Compare these two plots with those in Figure 1. doi:10.1371/journal.pcbi.1000637.g004

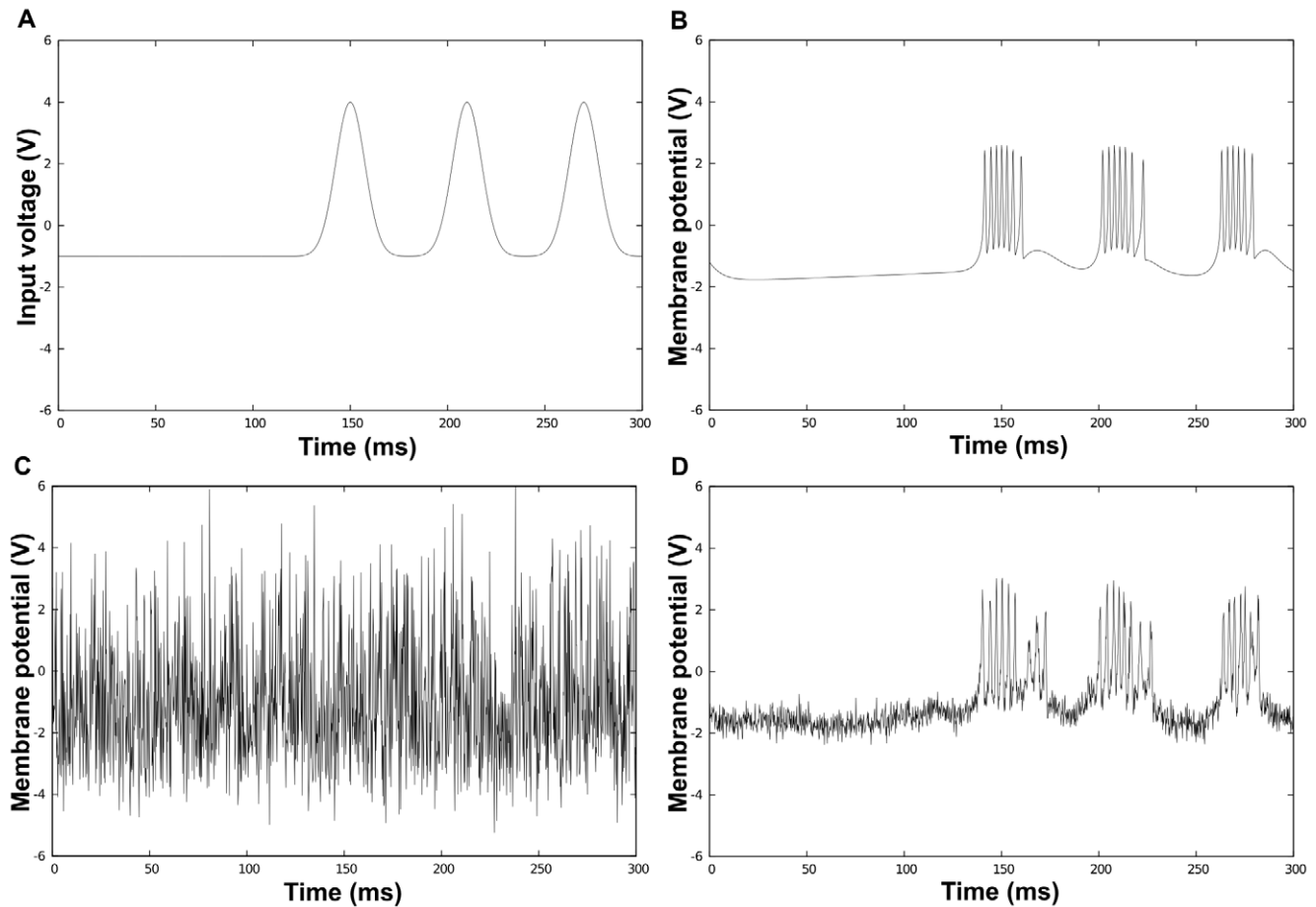


Figure 5. Simulation of Hindmarsh-Rose oscillators with time varying inputs. (A) The time-varying input voltage. (B) Trajectory of the “membrane potential” of a noise-free oscillator. (C) Trajectory of a *noisy uncoupled* oscillator. (D) Trajectory of a *noisy synchronized* oscillator ($n=200$, $\sigma=10$, $k_{ij}=5$).

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[32]; under other conditions, adding noise can, on the contrary, synchronize oscillators that were not synchronized (constructive effect) [33,34]; for a review, see [35]. Also, previous papers have studied a similar phenomenon of improvement in precision by synchronization. Enright [28] shows \sqrt{n} improvement in a model of coupled relaxation oscillators, all interacting through a common accumulator variable (possibly being the pineal gland). This \sqrt{n} improvement has been experimentally shown in real heart cells [36]. More recently, [37] shows a way to get better than \sqrt{n} improvement. However, their studies primarily focused on the case of phase oscillators, which are linear dynamical systems. In contrast, we concentrate here on the more general case of nonlinear oscillators, and quantify in particular the effect of the oscillators’ nonlinearities. The assumptions we consider are also different: while most existing approaches (including [37]) assume weak couplings and small noise intensities, we consider here strong couplings and arbitrary noise intensities.

The mechanisms highlighted in the paper may also underly other types of “redundant” calculations in the presence of noise and variability. In otoliths for instance, ten of thousands of hair cells jointly compute the three components of acceleration [38,39]. In muscles, thousands of individual fibers participate in the control of one single degree of freedom. Similar questions may also arise in systems biology, e.g., in cell mechanisms of quorum sensing where individual cells measure global chemical concentrations in their environment in a fashion functionally similar to all-to-all coupling

[25–27], in mechanical coupling of motor proteins [40], in the context of transcription-regulation networks [41,42], and in differentiation dynamics [43].

Finally, the results point to the general question: what is the precise meaning of ensemble measurements or population codes, what information do they convey about the underlying signals, and is the presence of synchronization mechanisms (gap-junction mediated or other) implicit in this interpretation? As such, they may also shed light on a somewhat “dual” and highly controversial current issue. Ensemble measurements from the brain can correlate to behavior, and they have been suggested e.g. as inputs to brain-machine interfaces. Are these ensemble signals actually available to the brain [44], perhaps through some process akin to quorum sensing, and therefore functionally similar to (local) all-to-all coupling? Are local field potentials [45] plausible candidates for a role in this picture?

Methods

Proof of the general analytical result

In the noise-free case ($\sigma=0$), it can be shown that, for strong enough coupling strengths, the elements of the network synchronize completely, that is, after exponential transients, we have $\rho=0$ in (A4) [6]. Thus, all the \mathbf{x}_i tend to a common trajectory, which is in fact a nominal trajectory of the noise-free system $\dot{\mathbf{x}}_{\text{noise-free}} = \mathbf{f}(\mathbf{x}_{\text{noise-free}}, t)$, because all the couplings vanish on the synchronization subspace.

In the presence of noise, it is not clear how to relate the trajectory of each \mathbf{x}_i to a nominal trajectory of the noise-free system. Nevertheless, we still know that the \mathbf{x}_i live “in a small neighborhood” of each other, as quantified by (A4). Thus, if the center of this small neighborhood follows a trajectory similar to a nominal trajectory of the noise-free system, then one may gain some information on the trajectories of the \mathbf{x}_i .

To be more precise, let \mathbf{x}^\bullet be the center of mass of the \mathbf{x}_i , that is

$$\mathbf{x}^\bullet = \frac{1}{n} \sum_i \mathbf{x}_i. \tag{6}$$

Observe that, after expansion and rearrangement, the sum $\sum_{i < j} \|\mathbf{x}_i - \mathbf{x}_j\|^2$ can be rewritten in terms of the distances of the \mathbf{x}_i from \mathbf{x}^\bullet

$$\sum_{i < j} \|\mathbf{x}_i - \mathbf{x}_j\|^2 = n \sum_i \|\mathbf{x}_i - \mathbf{x}^\bullet\|^2.$$

Using (A4) then leads to

$$\mathbb{E} \left(\sum_i \|\mathbf{x}_i - \mathbf{x}^\bullet\|^2 \right) \leq \frac{\rho}{n}. \tag{7}$$

Summing over i the equations followed by the \mathbf{x}_i and using assumption (A1), we have

$$d\mathbf{x}^\bullet = \frac{1}{n} \left(\sum_i \mathbf{f}(\mathbf{x}_i, t) \right) dt + \frac{1}{n} \sum_i \sigma dW_i. \tag{8}$$

We now make the dynamics explicit with respect to \mathbf{x}^\bullet by letting

$$\varepsilon = \frac{1}{n} \left(\sum_{i=1}^n \mathbf{f}(\mathbf{x}_i, t) \right) - \mathbf{f}(\mathbf{x}^\bullet, t) \tag{9}$$

so that Equation (8) can be rewritten as

$$d\mathbf{x}^\bullet = (\mathbf{f}(\mathbf{x}^\bullet, t) - \varepsilon) dt + \frac{1}{n} \sum_i \sigma dW_i. \tag{10}$$

Using the Taylor formula with integral remainder, we have

$$\begin{aligned} & f_j(\mathbf{x}_i, t) - f_j(\mathbf{x}^\bullet, t) - \mathbf{F}_j(\mathbf{x}^\bullet, t)^T (\mathbf{x}_i - \mathbf{x}^\bullet) \\ &= \int_0^1 (1-s) (\mathbf{x}_i - \mathbf{x}^\bullet)^T \mathbf{H}_j((1-s)\mathbf{x}_i + s\mathbf{x}^\bullet) (\mathbf{x}_i - \mathbf{x}^\bullet) ds \end{aligned} \tag{11}$$

where \mathbf{F}_j is the gradient of f_j or, equivalently, the j^{th} vector of the Jacobian matrix of \mathbf{f} . Summing Equation (11) over i and using assumption (A2), we get

$$\left| \sum_i (f_j(\mathbf{x}_i, t) - f_j(\mathbf{x}^\bullet, t)) \right| \leq \frac{\mathbf{H}_{bd}}{2\sqrt{d}} \sum_i \|\mathbf{x}_i - \mathbf{x}^\bullet\|^2. \tag{12}$$

Summing now inequality (12) over j and using inequality (7), we get

$$\mathbb{E}(\|\varepsilon\|) \leq \frac{\rho \mathbf{H}_{bd}}{2n^2} \tag{13}$$

which implies that $\mathbb{E}(\|\varepsilon\|) \rightarrow 0$ when $\rho/n^2 \rightarrow 0$.

Turning now to the noise term $\frac{1}{n} \sum_i \sigma dW_i$ in Equation (10), we have

$$\frac{1}{n} \sum_i \sigma dW_i \cong \frac{\sigma}{\sqrt{n}} dW \tag{14}$$

since the intrinsic noises of the elements of the network are mutually independent.

Thus, for a given (even large) noise intensity σ , the difference between the *dynamics* followed by \mathbf{x}^\bullet and the noise-free dynamics \mathbf{f} tends to zero when $n \rightarrow \infty$ and $\rho/n^2 \rightarrow 0$. Assumption (A3) then implies that $\|\mathbf{x}^\bullet - \mathbf{x}_{\text{noise-free}}\| \rightarrow 0$. More precisely, the impact of noise on the mean trajectory (quantified by $\mathbb{E}(\|\mathbf{x}^\bullet - \mathbf{x}_{\text{noise-free}}\|)$) evolves as

$$\frac{\rho \mathbf{H}_{bd}}{2n^2} + \frac{\sigma}{\sqrt{n}}. \tag{15}$$

Finally, Equation (7) and the triangle inequality

$$\|\mathbf{x}_{\text{noise-free}} - \mathbf{x}_i\| \leq \|\mathbf{x}_{\text{noise-free}} - \mathbf{x}^\bullet\| + \|\mathbf{x}^\bullet - \mathbf{x}_i\| \tag{16}$$

imply that the *trajectory* of any synchronized element of the network \mathbf{x}_i and that of the noise-free system $\mathbf{x}_{\text{noise-free}}$ are also similar [compare Figure 1(A) and Figure 1(E)].

FN oscillators in an all-to-all network

Two FN oscillators. Consider first the case of two coupled FN oscillators driven by Equation (2). Construct the following auxiliary system (or virtual system, in the sense of [46]), where v_1 and v_2 are considered as *external inputs*

$$\begin{cases} dx_1 &= ((c - (v_1^2 + v_1 v_2 + v_2^2) - k)x_1 + cx_2) dt + \sqrt{2} \sigma dW \\ dx_2 &= \left(-\frac{1}{c} x_1 - \frac{b}{c} x_2 \right) dt. \end{cases} \tag{17}$$

Remark that $(x_1, x_2)^T = (v_1 - v_2, w_1 - w_2)^T$ is a particular trajectory of this system.

Let $\lambda_1 = k + (v_1^2 + v_1 v_2 + v_2^2) - c$ and $\lambda_2 = b/c$. Assume that the coupling strength is significantly larger than the system’s parameters, i.e. $k \gg c$, $k \gg 1/c$ and $k \gg b/c$. Since $v_1^2 + v_1 v_2 + v_2^2$ is nonnegative for any v_1 and v_2 , we have either $\lambda_1 \geq k$ or $\lambda_1 \simeq k$, depending on the actual value of $v_1^2 + v_1 v_2 + v_2^2$. This implies in particular that $\lambda_1 \gg c$, $\lambda_1 \gg 1/c$ and $\lambda_1 \gg \lambda_2 = b/c$.

Given these asymptotes, the evolution matrix of system (17) is diagonalizable with eigenvalues $-\lambda_1$ and $-\lambda_2$ and eigenvectors respectively $(\lambda_1, 1/c)^T$ and $(c, \lambda_1)^T$. Furthermore, it is not difficult to see that all those λ ’s are asymptotically close to each other, that is $\lambda_i \simeq \lambda'_i \simeq \lambda''_i \simeq \lambda'''_i$ ($i=1,2$). We now define

$$\begin{cases} y_1 = \lambda''_1 x_1 + \frac{1}{c} x_2 \\ y_2 = c x_1 + \lambda'''_1 x_2 \end{cases} \tag{18}$$

leading to

$$\begin{cases} dy_1 = -\lambda'_1 y_1 dt + \sqrt{2} \sigma \lambda''_1 dW \\ dy_2 = -\lambda'_2 y_2 dt + \sqrt{2} \sigma c dW. \end{cases}$$

Since these equations are in fact uncoupled, they can be solved independently. Using the stochastic contraction results

(corollary 1 of [21]) and the approximations $\lambda_i \simeq \lambda'_i \simeq \lambda''_i$, this yields

$$\begin{cases} \mathbb{E}(y_1^2) \leq \sigma^2 \lambda_1, & \text{after transients of rate } \lambda_1 \\ \mathbb{E}(y_2^2) \leq \frac{c^2 \sigma^2}{\lambda_2}, & \text{after transients of rate } \lambda_2. \end{cases}$$

These bounds can be translated back in terms of the x_i by inverting (18)

$$\begin{cases} x_1 \simeq \frac{1}{\lambda_1} y_1 - \frac{c}{\lambda_1^2} y_2 \\ x_2 \simeq -\frac{1}{c \lambda_1^2} y_1 + \frac{1}{\lambda_1} y_2. \end{cases}$$

Thus, after transients of rate λ_1 ,

$$\mathbb{E}(x_1^2) \leq \frac{\sigma^2}{\lambda_1} \quad \mathbb{E}(x_2^2) \leq \frac{\sigma^2 c^2}{\lambda_1^2 \lambda_2}.$$

Since $(v_1 - v_2, w_1 - w_2)^T$ is a particular trajectory of system (17) as we remarked earlier, one finally obtains that, after transients of rate k ,

$$\mathbb{E}((v_1 - v_2)^2) \leq \frac{\sigma^2}{k} \quad \mathbb{E}((w_1 - w_2)^2) \leq \frac{\sigma^2 c^3}{bk^2}. \quad (19)$$

General case. Consider now an all-to-all network with identical couplings as in Equation (2). Construct as above the following $n(n-1)$ auxiliary systems indexed by $(i, j) \in [1 \dots n]^2$, where the v_i are considered as external inputs

$$\begin{cases} dv_{ij} &= \left((c - (v_i^2 + v_i v_j + v_j^2) - k)v_{ij} + cw_{ij} \right) dt \\ &+ \sqrt{2} \sigma dW \\ dw_{ij} &= \left(-\frac{1}{c} v_{ij} - \frac{b}{c} w_{ij} \right) dt. \end{cases}$$

Remark that, similarly to the case of two oscillators, $((v_{ij}, w_{ij})^T)_{i,j} = ((v_i - v_j, w_i - w_j)^T)_{i,j}$ is a particular solution of

References

- Singer W (1993) Synchronization of cortical activity and its putative role in information processing and learning. *Annu Rev Physiol* 55: 349–74.
- Buzsaki G (2006) *Rhythms of the Brain* Oxford University Press.
- Tiesinga P, Fellous J, Sejnowski T (2008) Regulation of spike timing in visual cortical circuits. *Nature Reviews Neuroscience* 9: 97.
- Hestrin S, Galarreta M (2005) Electrical synapses define networks of neocortical gabaergic neurons. *Trends Neurosci* 28: 304–9.
- Fukuda T, Kosaka T, Singer W, Galuske RAW (2006) Gap junctions among dendrites of cortical gabaergic neurons establish a dense and widespread intercolumnar network. *J Neurosci* 26: 3434–43.
- Pham QC, Slotine JJ (2007) Stable concurrent synchronization in dynamic system networks. *Neural Netw* 20: 62–77.
- Crick FC, Koch C (2005) What is the function of the claustrum? *Philos Trans R Soc Lond B Biol Sci* 360: 1271–9.
- Canolty RT, Edwards E, Dalal SS, Soltani M, Nagarajan SS, et al. (2006) High gamma power is phase-locked to theta oscillations in human neocortex. *Science* 313: 1626–8.
- Womelsdorf T, Schoffelen JM, Oostenveld R, Singer W, Desimone R, et al. (2007) Modulation of neuronal interactions through neuronal synchronization. *Science* 316: 1609–12.
- Grossberg S (2000) The complementary brain: unifying brain dynamics and modularity. *Trends Cogn Sci* 4: 233–246.

these equations. Remark also that each pair (v_{ij}, w_{ij}) is in fact uncoupled with respect to other pairs. This allows us to use (19) to obtain that, after transients of rate k ,

$$\forall i, j, i \neq j, \quad \mathbb{E}((v_i - v_j)^2) \leq \frac{\sigma^2}{k}.$$

Summing over the i, j yields

$$\mathbb{E} \left(\sum_{i < j} (v_i - v_j)^2 \right) \leq \frac{n(n-1)\sigma^2}{k}.$$

Thus, (A4) is verified with

$$\rho = \frac{n(n-1)\sigma^2}{k}.$$

For large n , we have $\rho/n^2 \sim \sigma^2/k$, which converges to 0 when $k \rightarrow \infty$ [see Figure 3(A)].

Assumption (A1) is also verified because an all-to-all network with identical couplings is symmetric, therefore balanced. As for (A2), observe that $\mathbf{H}_w = \mathbf{0}$ and

$$\mathbf{H}_v = \begin{pmatrix} 2cv & 0 \\ 0 & 0 \end{pmatrix}.$$

Since the $(v_i, w_i)^T$ are oscillators with stable limit cycles, it can be shown that the trajectories of the v_i are bounded by a common constant M . Thus (A2) is verified with $\mathbf{H}_{bd} = 2cM$.

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Author Contributions

Performed the experiments: NT. Contributed reagents/materials/analysis tools: NT JJS QCP. Wrote the paper: NT JJS QCP.

21. Pham QC, Tabareau N, Slotine JJ (2009) A contraction theory approach to stochastic incremental stability. *IEEE Trans Automatic Control* 54: 816–820.
22. Tuckwell HC, Rodriguez R (1998) Analytical and simulation results for stochastic fitzhugh-nagumo neurons and neural networks. *J Comput Neurosci* 5: 91–113.
23. Dayan P, Abbott L (2001) *Theoretical neuroscience: computational and mathematical modeling of neural systems* MIT Press.
24. Gelb A (1974) *Applied Optimal Estimation* MIT Press.
25. Garcia-Ojalvo J, Elowitz MB, Strogatz SH (2004) Modeling a synthetic multicellular clock: repressilators coupled by quorum sensing. *Proc Natl Acad Sci U S A* 101: 10955–60.
26. Waters C, Bassler B (2005) Quorum Sensing: Cell-to-Cell Communication in Bacteria. *Annu Rev Cell Dev Biol* 21: 319–346.
27. Taylor A, Tinsley M, Wang F, Huang Z, Showalter K (2009) Dynamical Quorum Sensing and Synchronization in Large Populations of Chemical Oscillators. *Science* 323: 614.
28. Enright J (1980) Temporal precision in circadian systems: a reliable neuronal clock from unreliable components? *Science* 209: 1542–1545.
29. Lohmiller W, Slotine J (1998) On Contraction Analysis for Non-linear Systems. *Automatica* 34: 683–696.
30. Strogatz SH (2001) Exploring complex networks. *Nature* 410: 268–76.
31. Izhikevich EM (2004) Which model to use for cortical spiking neurons? *IEEE Trans Neural Netw* 15: 1063–70.
32. Teramae J, Kuramoto Y (2001) Strong desynchronizing effects of weak noise in globally coupled systems. *Physical Review E* 63: 36210.
33. Mainen Z, Sejnowski T (1995) Reliability of spike timing in neocortical neurons. *Science* 268: 1503–1506.
34. Teramae J, Tanaka D (2004) Robustness of the Noise-Induced Phase Synchronization in a General Class of Limit Cycle Oscillators. *Physical Review Letters* 93: 204103.
35. Ermentrout GB, Galán RF, Urban NN (2008) Reliability, synchrony and noise. *Trends Neurosci*.
36. Clay J, DeHaan R (1979) Fluctuations in interbeat interval in rhythmic heart-cell clusters. Role of membrane voltage noise. *Biophysical Journal* 28: 377–389.
37. Needleman D, Tiesinga P, Sejnowski T (2001) Collective enhancement of precision in networks of coupled oscillators. *Physica D: Nonlinear Phenomena* 155: 324–336.
38. Kandel E, Schwartz J, Jessell T (2000) *Principles of Neural Science* McGraw-Hill.
39. Eliasmith C, Anderson C (2004) *Neural Engineering: Computation, Representation, and Dynamics in Neurobiological Systems* MIT Press.
40. Hendricks A, Epureanu B, Meyhöfer E (2009) Collective dynamics of kinesin. *Phys Rev E* 79: 031929.
41. Alon U (2007) *An Introduction to Systems Biology: Design Principles of Biological Circuits* Chapman & Hall/CRC.
42. Barkai N, Shilo B (2007) Variability and robustness in biomolecular systems. *Molecular Cell* 28: 755–760.
43. Suel G, Kulkarni R, Dworkin J, Garcia-Ojalvo J, Elowitz M (2007) Tunability and noise dependence in differentiation dynamics. *Science* 315: 1716.
44. El Boustani S, Marre O, Béhuret S, Baudot P, Yger P, et al. (2009) Network-state modulation of power-law frequency-scaling in visual cortical neurons. *PLoS Computational Biology* 5: e1000519.
45. Pesaran B, Pezaris J, Sahani M, Mitra P, Andersen R (2002) Temporal structure in neuronal activity during working memory in macaque parietal cortex. *Nature Neuroscience* 5: 805–811.
46. Wang W, Slotine JJE (2005) On partial contraction analysis for coupled nonlinear oscillators. *Biol Cybern* 92: 38–53.
47. Higham D (2001) An algorithmic introduction to numerical simulation of stochastic differential equations. *SIAM Review* 43: 525–546.