Taming desynchronized bursting with delays in the Macaque cortical network*

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Inhibitory coupled bursting Hindmarsh–Rose neurons are considered as constitutive units of the Macaque cortical network. In the absence of information transmission delay the bursting activity is desynchronized, giving rise to spatiotemporally disordered dynamics. This paper shows that the introduction of finite delays can lead to the synchronization of bursting and thus to the emergence of coherent propagating fronts of excitation in the space-time domain. Moreover, it shows that the type of synchronous bursting is uniquely determined by the delay length, with the transitions from one type to the other occurring in a step-like manner depending on the delay. Interestingly, as the delay is tuned close to the transition points, the synchronization deteriorates, which implies the coexistence of different bursting attractors. These phenomena can be observed by different but fixed coupling strengths, thus indicating a new role for information transmission delays in realistic neuronal networks.

Keywords: synchronization, bursting, information transmission delay, Macaque cortical network, inhibitory coupling

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1. Introduction

The brain is a complex network of neurons exhibiting a fascinating richness of behaviour, which allow it to perform the most intricate tasks with cognition and reliability. Synchronization[1] of the dynamics in the cortical network has been suggested as particularly relevant for the efficient processing and transmission of neuronal signals (see e.g. Refs. [2] and [3]). To this date, synchronized states have been demonstrated to occur in many special areas of the brain, such as the olfactory system or the hippocampal region.[4−6] Based on mainly theoretical analysis, neuronal synchronization on complex networks has been explored in detail,[7−16] leading to several insights which have the potential of applicability on realistic problems in the neurosciences. For example, synchronization of gap–junction-coupled neurons has been investigated, where the dependence of neuronal synchronization on the coupling strength was explored.[12] Moreover, the synaptically coupled Hodgkin–Huxley neurons with time-dependent conductance of the synapse were demonstrated to exhibit rich dynamics including in-phase, anti-phase and chaotic oscillations.[13] Synchronization and coherence of chaotic Morris–Lecar neural networks have been investigated and it has been found that there is an optimal number of shortcuts at which the collective behaviour of neurons is most ordered.[14] The influence of the coupling strength and network topology on synchronization was investigated also for networks of bursting Hindmarsh–Rose neurons with chemical synapses.[15] Interestingly, it was reported that chemical and electrical synapses perform complementary roles in the synchronization of interneuronal networks.[16]

Bursts of spikes, as opposed to single spikes, are considered to enhance the reliability of communications between neurons by facilitating transmitter release. Bursting synchronization likely plays many subtle information processing roles in healthy neuronal tissue.[17] Experimentally, burst synchronization has been considered within cell cultures, where the interaction of spontaneous bursts, stimulation-induced bursts and propagation of activity could be studied conveniently.[18] Theoretical studies considering the

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synchronization of bursting oscillations have also attracted considerable attention in recent years.[19−21] In particular, the dependence of the chaotic phase synchronization on the coupling properties and an externally applied time-periodic signal were demonstrated on scale-free networks of bursting neurons.[19] Moreover, bursting synchronization was investigated also for a ring neuronal network, in which each neuron exhibited chaotic bursting behaviour.[21]

Because of finite (non-zero) and varying signal transmission speeds between different pairs of coupled neurons, delays in information processing and signal transmission in spatially distributed neuronal systems are unavoidable. As such, they should not be neglected and dismissed as being irrelevant. Some experiments have actually shown that the delays can reach up to 80 ms in cortical networks. Delays have thus far been found responsible for several interesting phenomena in coupled dynamical systems.[22−28] For example, Ernst *et al.*[25] have identified mechanisms of synchronization between pulse-coupled oscillators in the presence of time delays. Very recently, it has been found that synchronization transitions between clustering anti-phase synchronization and in-phase synchronization can be induced by information transmission delays in map-based neuronal networks.[26,27] Also recently, Liang *et al.* studied the effects of distributed time delays on phase synchronization of bursting neurons.[28]

Here we aim at extending previous studies on this topic by considering a real-life Macaque cortical network,[29,30] hosting inhibitory coupled Hindmarsh–Rose neurons[31] individually set to bursting mode. We thus combine experimental findings with mathematical modeling to investigate the impact of information transmission delays on the spatiotemporal dynamics and function of neuronal networks. If information transmission delays are neglected, individual neurons exhibit bursting oscillations which are virtually completely uncorrelated across the whole network, thus giving rise to an essentially disordered spatiotemporal dynamics. Quite remarkably, if information transmission delays are introduced as an integral part of the setup, we find that the disorder can be tamed effectively by appropriately tuned delay lengths. A further interesting fact is that increasing delays not only lead to synchronized bursting, but can also evoke period-adding bifurcations such that the bursting pattern becomes increasingly complex, i.e. which are characterized by an increasing number of intra-burst spikes. Near these bifurcation points the synchrony of excitatory bursts deteriorates slightly, which suggests the coexistence of bursting attractors in coupled neurons. We interpret these findings in terms of eigen-frequencies which are routed in each individual Hindmarsh–Rose bursting neuron, both in the damped oscillations around the quasi-stable focus as well as the so-called global-resonant frequencies that can be linked to intra-burst spikes.[32] We also examine the robustness of our findings to different coupling and external stimulus strengths and briefly discuss their relevance for the field of neuroscience.

2. Mathematical model and setup

For the network hosting individual Hindmarsh–Rose neurons,[31] we employ the cortical network of one hemisphere of the Macaque monkey, as described in Refs. [29] and [30] (data were obtained from http://www.biological-networks.org). The connections among different cortical areas were obtained so that the average spatial positions of cortical areas were estimated on the basis of surface colouring using the CARET software (van Essen Lab, http://brainmap.wustl.edu/caret). The resulting network consists of 95 cortical regions and 2402 links among them, as shown in Fig. 1. A detailed analysis of this network was performed in Refs. [29] and [30], where it was shown, for example, that the distribution of distances between nodes, i.e. the length of connections, contains also long-range links. For more details we refer the reader to the original papers.[29,30]

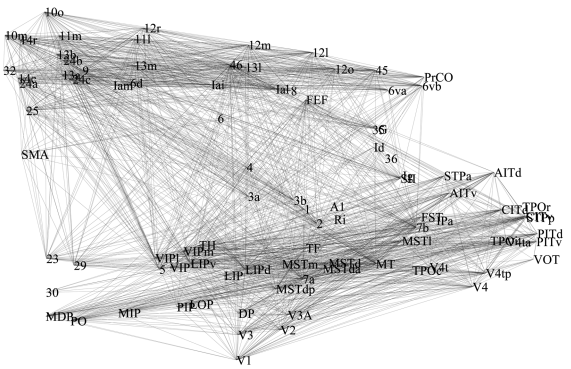


Fig. 1. Schematic presentation of the employed Macaque cortical network, consisting of 95 nodes and 2402 links, thus having average degree ≈ 25.3.

The mathematical model of the studied Macaque cortical network is thus described by the following set of equations:

$$\dot{x_i} = y_i - ax_i^3 + bx_i^2 - z_i + I_{\text{ext}}^i$$

$$+ D(V_{\rm syn} - x_i) \sum_{j=1}^{N} a_{ij} \Gamma(x_j), \quad (1)$$

$$\dot{y_i} = c - dx_i^2 - y_i, \quad (2)$$

$$\dot{z_i} = r[s(x_i - X_0) - z_i], \quad (3)$$

where x_i is the membrane potential of the i-th neuron, y_i is associated with the fast current, Na^+, or K^+ and z_i is associated with the slow current, for example, Ca^{2+}. The parameters are taken as $a = 1.0, b = 3.0, c = 1.0, d = 5.0, s = 4.0, X_0 = -1.60$ and $r = 0.006$. The $I^i_{\rm ext}$ is the external current of the i-th neuron. With the change of parameter $I^i_{\rm ext}$, the Hindmarsh–Rose neuron exhibits rich firing behaviour such as periodic spiking and bursting as well as chaotic spiking and bursting. The D is the synaptic coupling strength. The $V_{\rm syn}$ is the synaptic reversal potential, which is dependent on the type of synaptic transmitter released from a presynaptic neuron and its receptors. It determines whether the synapse is excitatory or inhibitory. In this paper, we consider the inhibitory network, thus setting $V_{\rm syn} = -1.8$. The delayed synaptic coupling function is modeled by the sigmoidal function $\Gamma(x_j) = 1/(1 + \exp\{-\lambda[x_j(t-\tau) - \Theta_s]\})$, where $\Theta_{\rm s}$ is the threshold, above which the postsynaptic neuron is affected by the presynaptic one. We here take $\Theta_{\rm s} = 0$. The $\lambda = 30$ represents a constant rate for the onset of excitation or inhibition. The τ is the information transmission delay among neurons, which is the main parameter to be varied in this paper. Finally, regarding the network links, we consider the non-weighted case, that is, if the i-th neuron is connected to the j-th neuron, $a_{ij} = a_{ji} = 1$. Otherwise, $a_{ij} = a_{ji} = 0$ and $a_{ii} = 0$.

3. Results

For the studied Macaque cortical network with inhibitory synapses, we first investigate the effects of different information transmission delays on the spatiotemporal behaviour of neurons via space-time plots presented in Fig. 2. We set the external stimulus $I^i_{\rm ext} = 3.2$ so that every neuron in the network is initially chaotically bursting. Results depicted in Fig. 2 illustrate the spatiotemporal dynamics of neurons for characteristic values of the delay τ. It can be observed that in the absence of information transmission delay, neurons are chaotic and unsynchronized (see Fig. 2(a)). However, when the delay is set to $\tau = 7.0$, neurons can exhibit regular period one bursting synchronization (see Fig. 2(b)). Subsequently, by increasing the delay further, the synchronized bursting pattern transits from a simple period-one to more complex period-two, then to period-three and finally period-four bursting, as evidenced in Figs. 2(c)–2(e). Hence, it is demonstrated that the spatiotemporal chaos of the network can be tamed effectively by means of finite (non-zero) information transmission delays. Moreover, it can be observed that the complexity of the synchronized pattern increases with longer delays. This shows that the firings of individual neurons go through a series of period-adding bifurcations. It can thus be concluded that finite information transmission delays can play a central role in the generation of bursting patterns of neuronal activity on the Macaque cortical network.

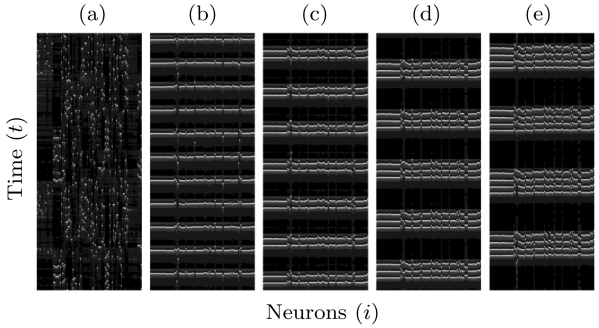


Fig. 2. Space-time plots of $x_i(t)$ obtained for $D = 2.0$ and $I^i_{\rm ext} = 3.2$ with different information transmission delays τ: (a) 0, (b) 7, (c) 14, (d) 22, (e) 30. Notice how the bursting synchronization and the number of spikes in one burst increase as τ increases. In all panels the system size is $i = 1, 2, \ldots, 95$ and the colour profile is linear, white depicting -2.0 and black depicting 2.5 values of $x_i(t)$ (the scale is partitioned into ten different shades of gray to enable the colour coding of small-amplitude deviations from the quasi-stable foci).

In order to supplement the visual assessment of space-time plots presented in Fig. 2, it is instructive to introduce and examine the average membrane potential of the network. Accordingly, we introduce the average membrane potential of all neurons $X(t)$ as follows:

$$X(t) = \frac{1}{N} \sum_{n=1}^{N} x_i(t). \quad (4)$$

It is evident from Eq. (4) that if the dynamics of individual neurons is weakly correlated, i.e. desynchronized, $X(t)$ should fluctuate irregularly with small amplitudes as the time is evolving. Conversely, $X(t)$ should exhibit regular bursting dynamics if all neurons burst coherently. Hence, $X(t)$ is a simple alternative indictor, which can help us to identify the evolutionary

behaviour of neurons constituting the Macaque cortical network. Temporal courses depicted in Figs. 3(a)–3(e) represent $X(t)$ corresponding to the space-time plots presented in Figs. 2(a)–2(e). Evidently, it can be concluded that the desynchronized out-of-phase bursting of individual neurons and the corresponding spatiotemporally chaotic dynamics at $\tau = 0$ gives way to synchronized in-phase neuronal activity as τ increases, thus supporting the conclusion that delays can be considered as important mediators of coherent neuronal activity on realistic networks. The increment of the complexity of the synchronous bursting pattern can also be appreciated via $X(t)$, as the simple bursting oscillations at $\tau = 7$ (see Fig. 3(b)) are replaced by increasingly complex bursting oscillations with an ever increasing number of intra-burst spikes as τ increases [see Figs. 3(c)–3(e)].

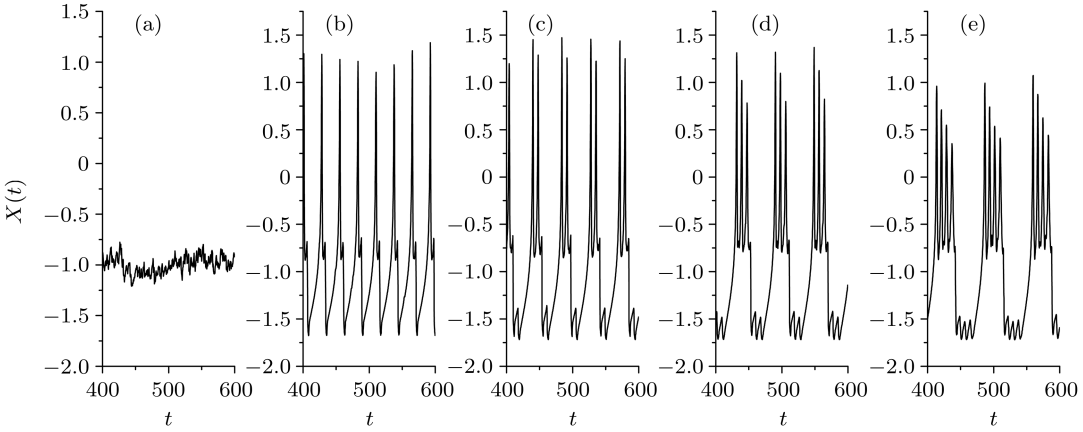


Fig. 3. Temporal courses of the average membrane potential $X(t)$, corresponding to the space-time plots presented in Figs. 2(a)–2(e). Notice the increment in the number of intra-burst spikes as the delay increases. It is also worth while noting that the synchronization seems to deteriorate minutely, if at all, as the complexity of the bursting pattern increases [note that $X(t)$ would deteriorate in amplitude drastically in case of desynchronization or even phase slips].

It remains interesting to analyse the observed patterns of neuronal activity also quantitatively by means of measures which can characterize spatiotemporal system dynamics as well as synchronization. For this purpose, we define two quantities. First is the membrane potential covariance, defined as

$$m = \langle x_i x_j - \langle x_i \rangle_{t,N}^2 \rangle_{t,N}, \tag{5}$$

with $\langle \cdots \rangle_{t,N}$ denoting time and network averages. The membrane potential covariance m is a measure of the average global network synchronization. The more synchronous the neuronal network is, the larger the parameter m is. In addition, it can also identify transitions between different patterns of bursting, as we will show below. Thus, m can be dubbed as the bursting synchronization transition parameter. The second quantity is the characteristic correlation time q, which measures the ordered behaviour of neuronal firings. Based on the normalized autocorrelation function $c_i(\tau_d)$, it is defined as

$$c_i(\tau_d) = \frac{\langle (x_i(t) - \langle x_i(t) \rangle)(x_i(t+\tau_d) - \langle x_i(t) \rangle) \rangle}{\langle (x_i(t) - \langle x_i(t) \rangle)^2 \rangle}, \tag{6}$$

where $x_i(t)$ is the membrane potential of the i-th neuron at time t, τ_d is the time delay and $\langle \cdot \rangle$ denotes the average over the time. The characteristic correlation time for the i-th neuron is then evaluated by $\tau_{i,c} = (1/T) \int_T c_i^2(t) \mathrm{d}t$ (see Ref. [33]). In the present case of the limited and discrete sampling with N_0 data points for each neuron, the characteristic correlation time is given as follows:

$$\tau_{i,c} = \frac{1}{N_0 \Delta t} \sum_{k=1}^{N} c_i^2(\tau_k) \Delta t, \tag{7}$$

where $\tau_k = k\Delta t$ with Δt being the sampling time, and $N_0 \Delta t$ the length of time series. Then, q is defined as

$$q = \langle \tau_{i,c} \rangle, \tag{8}$$

where $\langle \cdot \rangle$ is the average value over all neurons. It is known that the more ordered a neuron is, the longer its characteristic correlation time is. Therefore, q is called the order parameter and can be used to measure the degree of spatiotemporal order in the considered neuronal network.

The bursting synchronization transition parameter m is plotted in Fig. 4(a) for different values of D in dependence on τ. It can be observed that m increases steadily with τ almost independently of D (as expected, higher values of D altogether elevate m slightly, but the characteristic features remain preserved). This thus agrees with the above visual observations, indicating that finite information transmission delays promote synchronous bursting activity and tame the disordered behaviour observed for $\tau = 0$. Moreover, the step-like increase in the parameter m indicates that the number of spikes in each burst increases from one to four through the whole network as the delay increases, as indicated by the added labels in Fig. 4(a). Interestingly, in-between two different bursting patterns the finite slope in m suggests that there exists a narrow region, where the two attractors coexist. These observations can be further supplemented by examining the order parameter (characteristic correlation time) q, which is depicted in dependence on τ in Fig. 4(b). The descends in q following nearby the period-adding bifurcations agree nicely with the behaviour of m, thus affirming the coexistence of different bursting attractors in a narrow region of τ near the transition points. However, the order is quickly regained as one of the two bursting attractors competing for supremacy in the system's spatiotemporal dynamics fully gives way to the other.

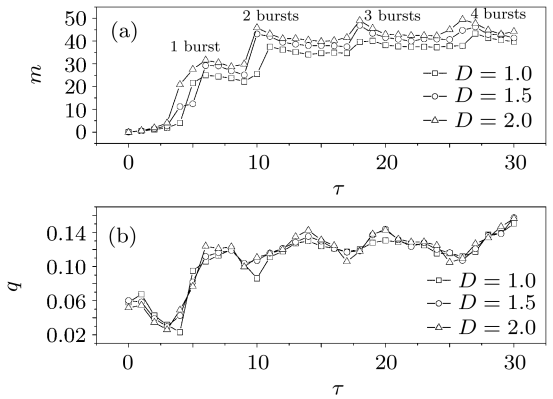


Fig. 4. (a) Dependence of the bursting synchronization parameter m on τ for different values of the coupling strength D. (b) Dependence of the order parameter (characteristic correlation time) q on τ for different values of the coupling strength D. See also main text for details.

An interpretation of the observed impact of finite (non-zero) values of τ on the spatiotemporal neuronal dynamics can be obtained by studying the robustness of the results upon varying the external stimulus I. The latter parameter determines the inherent dynamics of each neuron and it is instructive to examine how the delay lengths, responsible for the onset of synchrony of different bursting patterns, vary dependently on I. In Fig. 5, we plot m in dependence on τ for different values of I. It can be observed that the bursting synchronization transitions still occur (denoted by integer values indicating the number of intra-burst spikes), yet at lower values of I, an increase of larger τ is required for the same effect. We argue that the transitions to synchrony are due to a resonant match between the delay length and the eigen-frequency of each Hindmarsh–Rose neuron which is routed in the damped oscillations around the quasi-stable foci.[32] Since the latter decreases as I decreases (the distance between consecutive burst becomes larger; note that for low I a Hopf bifurcation to steady state dynamics occurs[31]), the information transmission delay required for inducing synchronized bursting increases. Accordingly, more frequent transitions can be observed when I is large. For example, for $I = 2.0$ the neurons transit from period-one bursting to period-two bursting in the considered delay interval; whereas for $I = 3.2$ they transit from period-one up to period-four bursting inclusive in the same delay interval. We speculate that the synchronous bursting patterns following the period-one bursting are probably related to the global resonant frequency which manifests through the intra-burst inter-spike intervals and cannot be detected by the traditional local stability analysis,[32] although we were unable to show this conclusively with our resources. Nevertheless, the presented results clearly attest to the fact that appropriately tuned delay lengths can tame the desynchronized bursting in the Macaque cortical network, with further increments of the delay enabling the selection of complexity of the bursting patterns in terms of the number of intra-burst spikes.

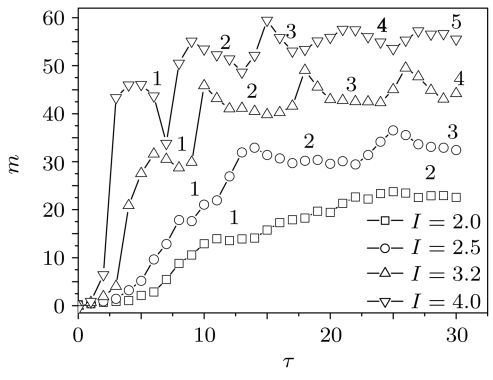


Fig. 5. Dependence of the bursting synchronization parameter m on τ for different values of the external stimulus I. See also main text for details.

4. Summary and discussion

In summary, we have demonstrated the possibility of taming desynchronized bursting activity with finite information transmission delays. We have shown that finite, i.e. non-zero, delays induce synchronized bursts of activity, with the bursting type depending intricately on the delay length. In general, longer delays have been found to induce synchronized bursting with a larger number of intra-burst spikes. The transitions between different bursting types are accompanied by a decrease in the synchronization, which implies the coexistence of two different bursting attractors competing for supremacy in the system's spatiotemporal dynamics. These observations are, however, typically limited to a rather narrow interval of delay lengths. We have also tested the robustness of these findings on variations of the coupling strength and the external stimulus, concluding that they are robust to the alterations and may provide insights explaining the observed behaviour. Importantly, the observed transitions to bursting synchronization are the sole consequence of finite information transmission delays, which are in this form not attainable by increasing the coupling strength or other system parameters. In this sense, the results suggest that delays could play a crucial role in both synchronization as well as pattern formation in networked neuronal systems.

Bursting synchronization likely plays many subtle information-processing roles in neuronal tissue,[34,35] though these roles are far from being completely understood at the present time.[36] Clinically, the connection between bursting and synchronization is extremely important, since synchronization in large neuronal populations is widely viewed as a hallmark of seizures. Hopefully, the results of this paper will be instructive for understanding the properties of collective behaviour in realistic neuronal networks.

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