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Stimulus detection rate and latency, firing rates and 1–40 Hz oscillatory power are modulated by infra-slow fluctuations in a bistable attractor network model

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ABSTRACT

Recordings of membrane and field potentials, firing rates, and oscillation amplitude dynamics show that neuronal activity levels in cortical and subcortical structures exhibit infra-slow fluctuations (ISFs) on time scales from seconds to hundreds of seconds. Similar ISFs are salient also in blood-oxygenation-level dependent (BOLD) signals as well as in psychophysical time series. Functional consequences of ISFs are not fully understood. Here, they were investigated along with dynamical implications of ISFs in large-scale simulations of cortical network activity. For this purpose, a biophysically detailed hierarchical attractor network model displaying bistability and operating in an oscillatory regime was used. ISFs were imposed as slow fluctuations in either the amplitude or frequency of fast synaptic noise. We found that both mechanisms produced an ISF component in the synthetic local field potentials (LFPs) and modulated the power of 1–40 Hz oscillations. Crucially, in a simulated threshold-stimulus detection task (TSDT), these ISFs were strongly correlated with stimulus detection probabilities and latencies. The results thus show that several phenomena observed in many empirical studies emerge concurrently in the model dynamics, which yields mechanistic insight into how infra-slow excitability fluctuations in large-scale neuronal networks may modulate fast oscillations and perceptual processing. The model also makes several novel predictions that can be experimentally tested in future studies.

Introduction

Infra-slow (~0.01−0.1 Hz) fluctuations (ISFs) are a pervasive feature of spontaneous mammalian brain activity (Palva and Palva, 2012). At the single-neuron level, ISFs characterize the firing rates of neurons in, for instance, thalamus (Albrecht and Gabriel, 1994; Werner and Mountcastle, 1963) and basal ganglia (Allers et al., 2002). These firing rate fluctuations are correlated with infra-slow amplitude modulations of fast theta- (4–8 Hz) (Allers et al., 2002) and alpha-band (8–14 Hz) (Hughes et al., 2011) oscillations in field potential recordings. Generally, ISFs are prominent in direct recordings of spontaneous cortical activity (Leopold et al., 2003; Nir et al., 2008) and in non-invasive magnetoencephalography (MEG) recordings of ongoing human brain activity (Linkenkaer-Hansen et al., 2001). ISFs are salient also in the blood-oxygenation-level dependent (BOLD) signals (Biswal et al., 1995) and are correlated between anatomically distributed brain regions that form functionally distinct brain systems (Fransson, 2005; Greicius et al., 2003; Power et al., 2011). The BOLD ISFs are directly correlated with ISFs in 1–100 Hz EEG and oscillatory power of local field potentials (LFPs) (Goldman et al., 2002; Leopold et al., 2003; Mantini et al., 2007) and, in addition, MEG-recorded amplitude dynamics and BOLD-ISFs have similar anatomical patterns of temporal correlations (Brookes et al., 2011). Furthermore, ISFs are observable directly in neuronal membrane potentials (Lörincz et al., 2009), cortical potentials (Aladjalova, 1957; Norton and Jewett, 1965) and in human EEG (Monto et al., 2008; Vanhatalo et al., 2004). Importantly, they are correlated both with >1-Hz oscillation amplitudes and psychophysical performance fluctuations (Monto et al., 2008). Also, bistable switching between low and high amplitude modes of EEG alpha oscillations on a comparably slow time scale has recently been reported (Freyer et al., 2009).

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ISFs are thus a widespread phenomenon but surprisingly little is known about the mechanisms underlying their generation and, in particular, mediating their functional consequences. Modeling studies have typically been focused on their genesis (Deco and Jirsa, 2012; Deco et al., 2009; Ghosh et al., 2008; Honey et al., 2007). Common for these models is that they operate close to a critical point at the edge of stability, a regime that has been linked to cortical dynamics in earlier models (Robinson et al., 1997, 2001). Self-organized criticality has accordingly been proposed to underlie experimentally observed long-range temporal correlations of fast oscillations and to be crucial for the generation of ISFs (Linkenkaer-Hansen et al., 2001). In vitro recordings, on the other hand, have demonstrated that astrocytic Ca^{2+} oscillations are associated with periodic ATP release and hyperpolarizing potentials in neurons, and thereby directly underlie the generation of ISFs both in the neuronal firing rates and oscillation amplitudes (Lörincz et al., 2009).

Here, we rather address the functional implications of imposed ISFs in synaptic background noise that could conceivably arise through any of the aforementioned mechanisms. We employ a hierarchical modular cortical attractor network structure (Djurfeldt et al., 2008; Lundqvist et al., 2006, 2010) comprising more than 30,000 Hodgkin–Huxley type cells distributed in two patches. The attractor dynamics of this network with a stable ground state and stimulus-triggered retrieval of memory patterns stored in the recurrent connections is used as a model for stimulus detection. This approach allows us to explicitly address the effects of ISFs both on the amplitude dynamics of 1–40 Hz oscillations and also on stimulus detection probabilities and latencies. Consistently with experimental data (Albrecht and Gabriel, 1994; Allers et al., 2002; Lörincz et al., 2009; Monto et al., 2008; Nir et al., 2008; Ruskin et al., 2003; Vanhatalo et al., 2004; Werner and Mountcastle, 1963), the simulated ISFs modulate the firing rates, amplitudes of fast neuronal oscillations and the probability of detecting sensory stimuli. In addition, the model predicts that detection latency as well as the peak frequency of alpha oscillations should be modulated by ISFs, and that simultaneous bursts in delta/theta and upper beta/gamma bands should accompany detected stimuli.

Methods

Network model

We used a biophysically detailed network model of cortical layer 2/3 developed earlier (Djurfeldt et al., 2008; Lundqvist et al., 2006, 2010) and now translated (Silverstein and Lansner, 2011) to the parallel NEURON simulator (Carnevale and Hines, 2006). Simulations were performed on a supercomputer with a 128-node partition in virtual node mode, providing 256 processors, each of which ran one message passing interface (MPI) process simulating a single minicolumn. Each cortical simulation was typically run for 100 s of cortical activity with a fixed simulation time step of 50 μs.

The model had both hypercolumnar and minicolumnar organizations (Fig. 1A). Each layer 2/3 portion of a minicolumn contained 30 pyramidal cells (Peters and Yilmaz, 1993) and one basket cell. Each minicolumn also included a rudimentary layer 4, with 5 pyramidal cells transmitting simulated sensory input in a feedforward fashion to layer 2/3. The connectivity was defined as the probability, P, that a cell in the pre-synaptic population was connected to a cell in the post-synaptic population. In consequence, it served as the estimate of the percentage of cells in the pre-synaptic population that are connected to the post-synaptic population. Each layer 4 cell randomly connected to the layer 2/3 pyramidal cells with $P = 0.5$ in the same minicolumn, while the layer 2/3 cells formed recurrent connections ($P = 0.25$) within each minicolumn.

Every hypercolumn contained 49 such minicolumns and a pool of 49 basket cells. These basket cells provided feedback inhibition to all the minicolumns within each hypercolumn, consistent with the finding that parvalbumin-positive interneurons in layer 2/3 provide non-specific inhibition within a few hundred microns while pyramidal cells form smaller, interconnected clusters in this volume (Kampa et al., 2006; Yoshimura et al., 2005). The hypercolumns were assumed to have strict borders in the sense that all basket cells were connected to minicolumns within their hypercolumn and to none outside (Fig. 1A). We did however perform simulations removing this constraint using a setup where the extent of feedback inhibition was determined by the geometrical position rather than predefined hypercolumn identity (see section Continuous hypercolumns).

A cortical patch was represented by 9 hypercolumns. In total, 49 non-overlapping attractor memory patterns were stored by means of selective sparse long-range connectivity between minicolumns from separate hypercolumns (c.f. Figs. 1A and B). This connectivity was set manually prior to a simulation by selecting a single unique minicolumn in each hypercolumn to constitute a specific distributed pattern and by adding reciprocal connections between the selected minicolumns. Each pattern was thus composed of 9 unique minicolumns. On a single cell level these long-range pyramidal–pyramidal connections had a fixed probability ($P = 0.3$) for cells sharing a pattern and zero probability otherwise. Further, the synaptic strengths were identical for all long-range connections (Fig. 1A).

The minicolumns had a diameter of 30 μm and were closely packed on a two-dimensional square grid with 1.5 mm side. All pyramidal cells in a minicolumn shared the same x and y coordinates but were uniquely spread out on the z-axis along 500 μm. Interneurons were placed near the center of each minicolumn with respect to the z-axis. Synaptic conductances and connectivity were compatible with biological data (Thomson et al., 2002; c.f. Lundqvist et al., 2006). In simulations of the two-patch model, there was a hierarchical organization of two identical, connected networks where the first patch (receiving external input, see below) acted as a "lower-order" network and the other acted as an "associative" network later in the input stream (Fig. 1B), receiving sensory input indirectly via feedforward connections from the first network. These feedforward projections were local in the sense that a specific minicolumn in the associative network only received input from its twin minicolumn in the lower-order network. Each pyramidal cell in the sending minicolumn connected with $P = 0.1$ to the cells selected randomly in the receiving minicolumn, and the conductance for each connection was half of the conductance used in the local connections within the minicolumn (except when otherwise stated). Each cell in the associative network therefore received on average only 3 connections from the lower-order network compared to ~90 recurrent connections from other cells in the associative network. Taking connection strengths and their number into account the ratio between inter- and intra-patch excitation was roughly 0.1. Single minicolumns in the lower-order network could be selectively stimulated by pyramidal cells mimicking layer 4 input cells. These were activated by spike trains generated by Poisson processes such that they produced 2–3 spikes during 30 ms of stimulation. Typically, 4 out of 9 minicolumns in a distributed attractor pattern were stimulated in such a manner.

All conduction delays within a patch were calculated assuming a conduction speed of 0.5 m/s, while projections between patches had velocities of 2.5 m/s (Girard et al., 2001).

Continuous hypercolumns

In the version of the model referred to as a continuous hypercolumn model, we laid out all 441 minicolumns of each cortical patch on a row with one basket cell close to each minicolumn (Fig. 1C). Pyramidal cells in a given minicolumn were connected ($P = 0.7$) to the 25 closest basket cells (12 in each direction plus the basket cell directly adjacent to the minicolumn). Basket cells