Balanced Gamma Oscillations Support Ultra-Slow Dynamics in the Cortex at Rest

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Abstract

While it has been suggested that gamma (∼40Hz) oscillations are an important driver of the spontaneous dynamics of the large-scale cortical networks, whole-brain models often neglect fast excitatory AMPA synapses, responsible for the generation of gamma rhythms through reciprocal excitatory-inhibitory (E-I) interactions. Importantly, these interactions are balanced through homeostatic plasticity mechanisms, ensuring stable activity. However, the joint role of gamma oscillations and E-I balance in supporting large-scale cortical dynamics has not been tested systematically. Therefore, we built a large-scale model of the human cortex with E-I homeostasis and fast and slow excitation through AMPA and NMDA receptors, respectively. By selectively knocking out fast excitation and E-I homeostasis, we demonstrate that models with both features better reproduce the resting-state dynamics of the human cortex, measured through ultra-slow blood- oxygenation-level–dependent (BOLD) signals. While E- I homeostasis ensures the emergence of empirical connectivity networks, their dynamic aspect is best captured in models with gamma oscillations generated by AMPA-mediated excitation. Therefore, our results help elucidate the emergence of collective dynamics in the cortex, advancing balanced gamma oscillations as a fundamental generative mechanism behind ultra-slow fluctuations of cortical activity

Keywords: excitatory-inhibitory balance; gamma oscillations; network dynamics; cortical networks; resting-state fMRI

Background

The rich fluctuations of resting-state BOLD signals in the cortex are an example of the emergence of complex collective dynamics in networks of relatively simple units. While the key principles underlying their emergence are not yet understood, BOLD fluctuations have also been associated with gamma rhythms (∼40 Hz) (Logothetis et al., 2001; Niessing et al., 2005; Schölvinck et al., 2010). Furthermore, computational studies have demonstrated that models with gamma oscillations generated by balanced E-I interactions can reproduce resting-state cortical dynamics (Páscoa dos Santos et al., 2023; Castaldo et al., 2023; Páscoa dos Santos & Verschure, 2025b). However, while this process of gamma generation requires fast excitation through AMPA receptors (Wang, 2010; Buzsáki & Wang, 2012), these are not commonly accounted for in large-scale models of BOLD signals in the cortex (Deco et al., 2014, 2021; Naskar et al., 2021). For this reason, no study has systematically explored how fast and slow excitation shape the collective dynamics of the cortex. With that in mind, and given the role of E-I homeostasis in regulating edge-of-bifurcation gamma oscillations (Freeman, 2005; Páscoa dos Santos & Verschure, 2025a, 2025b), we hypothesize that the interaction between gamma oscillations and E-I balance underpins the spontaneous collective dynamics of the cortex.

Results

To test our hypothesis, we developed a large-scale model based on empirical structural connectivity data (Fig. 1A) and the reduced Wong-Wang model (Wong & Wang, 2006) with fast (τ=4ms) AMPA and slow (τ=100ms) NMDA synapses (Fig. 1A). Local parameters were adjusted to reproduce the micrcocircuitry of layer 2/3 circuits (Jiang et al., 2024), the relative strength of AMPA and NMDA currents (Myme et al., 2003), and the spontaneous firing rates of pyramidal (PY) (∼5Hz) and fast-spiking cells (∼17Hz) (Wilson et al., 1994). E-I homeostasis was implemented through the regulation of excitatory and inhibitory synapses and pyramidal cell excitability (Turrigiano, 2011; Wen & Turrigiano, 2024; Páscoa dos Santos & Verschure, 2025a), maintaining PY firing close to 5 Hz while displaying noise-driven oscillations (Fig. 1B)

We then analyze the performance of models with selectively removed AMPA receptors, E-I homeostasis, or both. In each case, we apply a Bayesian optimization algorithm (Hadida et al., 2018) to find the combination of hyper-parameters (global and local coupling) optimizing the fit to empirical functional connectivity (FC) and FC (dynamics), evaluated by a cross-feature score, detailed in Páscoa dos Santos and Verschure (2025b). Our results show that the network with AMPA and E-I homeostasis achieves the best cross-feature fitting score, demonstrating the importance of balanced gamma oscillations (Fig. 2A). More specifically, balancing excitation and inhibition substantially improves the fit to FC (Fig. 2A and B). Conversely, while including AMPA of synapses does not contribute to the emergence of empirical FC networks (Fig. 2A), it significantly improves the fit to FC dynamics in models both with and without homeostasis. Nonetheless, E-I homeostasis is necessary to replicate the large-scale co-activation events observed in empirical data (Fig. 2B), suggesting a contribution of E-I homeostasis for collective behaviors beyond FC dynamics.

Main Conclusions

Our results demonstrate the fundamental role of gamma oscillations generated by balanced E-I interactions in the ultra-slow fluctuations of BOLD signals. Therefore, we advance edge-of-bifurcation gamma oscillations as one of the fundamental generative mechanisms of resting-state cortical dynamics.

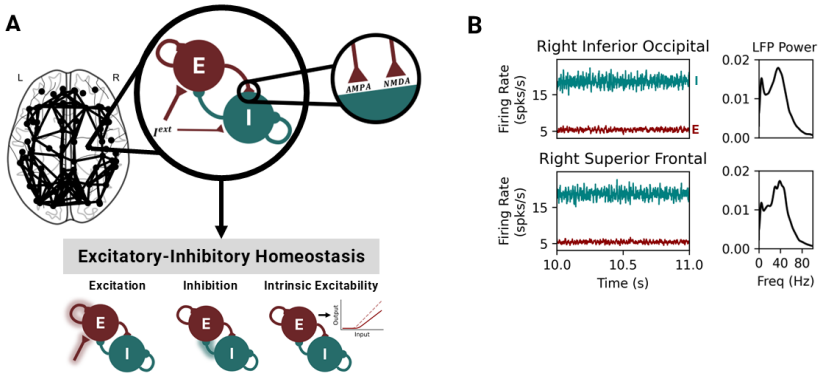

Figure 1: **Model Architecture** A) E-I circuits constrained by empirical structural connectivity data. Excitation operates through fast (AMPA) and slow (NMDA) synapses. E-I balance is maintained by three distinct homeostatic mechanisms (Páscoa dos Santos & Verschure, 2025a). B) Firing rate of excitatory (red) and inhibitory (blue) populations in the occipital (top) and frontal (bottom) lobes. On the right, we show the power spectrum of an LFP proxy computed from post-synaptic currents.

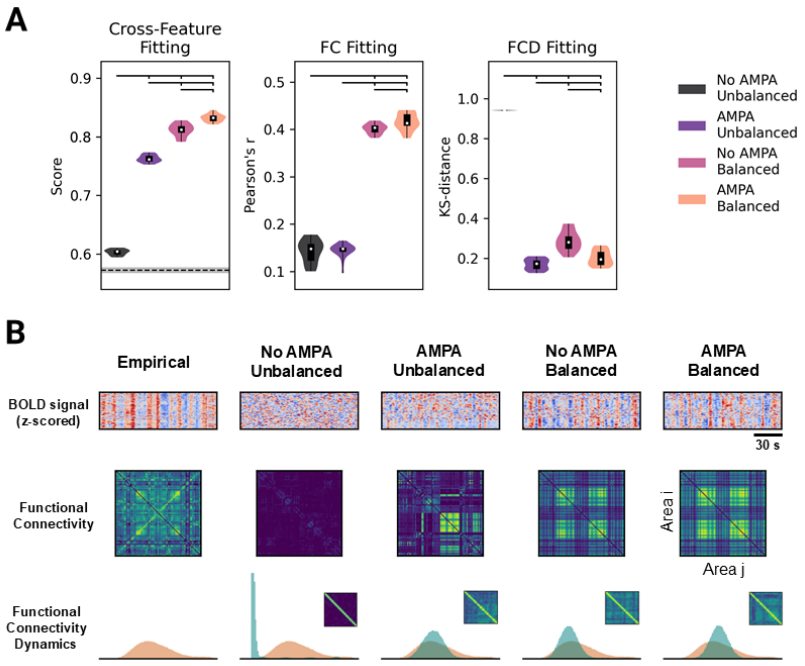

Figure 2: **Model Performance** A) Fitting scores of models with or without AMPA receptors and E-I homeostasis. (Left) Cross-feature fitting score, aggregating the correlation coefficient and mean-squared error between FC matrices and the KS-difference between correlations in the FC dynamics matrices. The black dashed line and shaded area represent the mean and standard deviation of scores obtained from 20 random BOLD time series (Middle) Pearson's correlation coefficient between FC matrices (Right) KS-distance between FCD distributions. Distributions correspond to 20 simulations. Brackets represent a significant difference ($p<0.05$) between samples from a Mann-Whitney U-test. All p-values were corrected for multiple comparisons with FDR correction. B) Features of empirical and simulated data (Top) 2 minutes of z-scored and band-pass filtered BOLD signals (Middle) Average FC matrices (Bottom) FCD distributions. Simulated distributions (blue) are plotted with the empirical distribution (orange) for comparison. Insets show the matrix of correlations between FC matrices computed from sliding windows of $\sim$60 s, from which the distributions are then drawn (see Páscoa dos Santos and Verschure (2025b))

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