Long-Range Input to Cortical Microcircuits Shapes EEG-BOLD Correlation

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Although generated by different mechanisms, electroencephalography (EEG) rhythms and blood-oxygen-level-dependent (BOLD) activity have been shown to be correlated. The level of correlation varies between EEG frequency bands, brain regions and experimental paradigms, but the underpinning mechanisms of this correlation remain poorly understood. Here we create a mathematical, data-informed model of a cortical microcircuit that encompasses all major neuron types across cortical layers, and use it to generate EEG and BOLD under various external input conditions. The model exhibits noise-driven fluctuations mimicking EEG rhythms, with external inputs modulating EEG spectral characteristics. Consistent with experimental results, we observe negative alpha-BOLD correlation and positive gamma-BOLD correlation across different input configurations. Temporal variability of the input is found to increase EEG-BOLD correlation and to improve the correspondence with experimental results. This study provides a mathematical framework to theoretically study the correlation of EEG and BOLD features in a comprehensive way.

EEG-BOLD Correlation | LFP | fMRI | Cortical Microcircuits | Interneurons
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Introduction

Electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) are widely used noninvasive methods for human brain imaging. EEG records the electric potentials on the scalp that reflect primarily the synaptic activity at the pyramidal cells (Buzsáki et al., 2012), whereas fMRI measures the blood-oxygen-level-dependent (BOLD) signal that reflects the metabolism of synaptic activity (Howarth et al., 2021). The two modalities provide complementary information for inferring the underlying cortical neural activity. Combining EEG and fMRI thus offers valuable insights into their neural origins.

The alpha rhythm is a prominent feature in human EEG over occipital areas first observed by Berger in 1929 (Berger, 1929). Functionally, alpha activity has been associated with task-negative states, exhibiting higher levels during rest compared to task performance (Clayton et al., 2018; Magosso et al., 2019). Simultaneous EEG-fMRI studies have found that alpha power is negatively correlated with BOLD signals in occipital regions and positively correlated with BOLD signals in areas such as the insula and thalamus (Goldman et al., 2002; Laufs, Kleinschmidt, et al., 2003; Laufs, Krakow, et al., 2003; Moosmann et al., 2003). At an individual level, the alpha-BOLD correlation exhibits intra-subject and inter-subject variability (Gonçalves et al., 2006). The gamma rhythm, usually anticorrelated with the alpha and beta rhythms, has been associated with sensory processing and tasks such as working memory (Shu et al., 2024). Local field potential (LFP) recordings, as opposed to spatially coarse-grained EEG recordings, can record this spatially localised, high-frequency neural activity at high signal-to-noise ratios. A simultaneous LFP-fMRI study demonstrated that gamma power correlates positively with BOLD responses and visual stimulus intensity (Niessing et al., 2005). This study also found a shift in oscillatory activity from theta and alpha bands to beta and lower gamma bands with increasing stimulus intensity. In short, simultaneous EEG-fMRI and LFP-fMRI recordings are helpful for investigating the location of brain rhythms and their relationship with the BOLD signal.

A few theoretical studies have sought to provide mechanistic explanations that integrate these experimental observations, but many questions remain unresolved. For instance, while alpha rhythms are generally attributed to network-level mechanisms (Halgren et al., 2019), their precise origin and relationship with BOLD activity are still debated. It was demonstrated that source-localised alpha power predicts BOLD activity and reproduces related phenomena in a whole-brain modeling framework (Schirner et al., 2018). However, it was assumed that a causal link exists between alpha power and BOLD without addressing the origin of alpha rhythms. By contrast, a thalamocortical model exhibited anticorrelations between the alpha power of the simulated EEG and a low-frequency BOLD proxy (Pang & Robinson, 2018), where the alpha rhythms were attributed to delays in the thalamocortical loop and explained alpha-BOLD anticorrelations by variations in corticothalamic and intrathalamic feedback strengths. However, this model did not address fast time-varying effects such as stimulus intensity on internal brain dynamics. Thus, a more comprehensive theoretical framework that integrates the generation of EEG rhythms and their relationships with BOLD signals is still lacking.

Given the fact that both EEG and BOLD signals predominantly originate from postsynaptic potentials (PSPs) (Biasiucci et al., 2019; Ekstrom, 2010), and considering that distinct inhibitory neuron types influence EEG rhythms differently (Whittington & Traub, 2003) and possess varied neurovascular coupling properties (Cauli et al., 2004), a cortical microcircuit model incorporating multiple inhibitory neuron types offers a promising framework for investigating local neural dynamics underlying EEG rhythms and their relationship with BOLD signals. Such a mesoscopic model has the advantage of providing insights into interactions between neural populations and potential factors contributing to heterogeneity in EEG-BOLD correlations, as observed in our experimental findings (Figure 1A-D). The data used here were simultaneous EEG and fMRI recordings at rest, and serve as a primer for the theoretical framework.

We developed a cortical microcircuit model that incorporates excitatory (E) and inhibitory (PV, SOM, and VIP) populations across cortical layers (L2/3, L4, L5, and L6) with realistic configurations, including connection probabilities, synaptic strengths, neuronal densities, and firing rate functions for each neuron type (Figure 1E). The model receives three types of external inputs: (1) lateral input from neighboring cortical microcircuits, targeting pyramidal cells and SOM interneurons in L2/3 (Adesnik et al., 2012; Yavorska & Wehr, 2016); (2) modulatory input from higher order cortical areas targeting VIP interneurons in L2/3 (Hertäg & Sprekeler, 2019); and (3) thalamic input targeting pyramidal cells and PV interneurons in L4 (Kloc & Maffei, 2014). In the simulations, Gaussian noise is independently applied to all synaptic connections, and EEG and BOLD signals are derived from the postsynaptic potentials (PSPs; Figure 1F). The analysis begins with the model behavior under constant external inputs (i.e., the constant input condition), where noise-driven fluctuations resem-

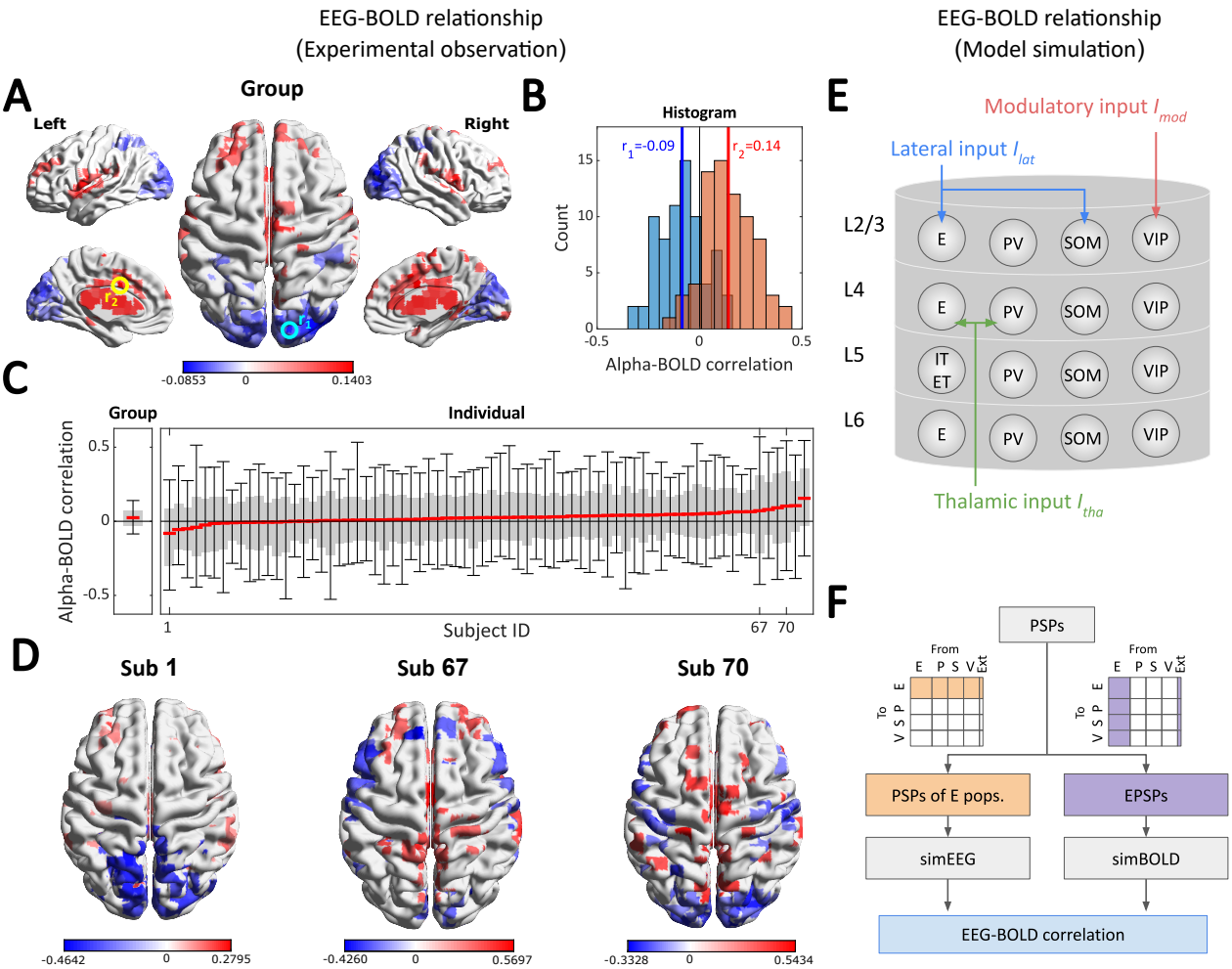

Figure 1. Heterogeneity of alpha-BOLD correlation and modeling approach. (**A**) Group-level alpha-BOLD correlation map across 72 subjects. Values from 5% to 95% are masked. (**B**) Histograms of alpha-BOLD correlations at two example voxels, highlighted by the yellow (middle cingulate gyrus) and cyan (middle occipital gyrus) circles in (**A**). (**C**) Box plot of group-level (averaged across subjects) and individual, voxel-wise alpha-BOLD correlations. Subjects are sorted by their median correlation values (red lines). Gray boxes represent the 5th to 95th percentiles, and whiskers indicate the minimum and maximum alpha-BOLD correlations. (**D**) Three individual examples: Subject 1 has the most negative median correlation, Subject 67 displays the widest range of correlations, and Subject 70 exhibits the highest spatial similarity with the group-level correlation map. (**E**) Model setup. The cortical microcircuit model consists of 17 neural populations, including excitatory (E, IT, and ET) and inhibitory (PV, SOM, and VIP) populations across cortical layers L2/3, L4, L5, and L6. The model receives three types of external inputs: lateral (I_{lat}), modulatory (I_{mod}), and thalamic (I_{tha}). Internal connections are not shown for clarity. (**F**) Model simulation. The simulated EEG signal (simEEG) is generated from the postsynaptic potentials (PSPs) at all excitatory populations (orange section), and the simulated BOLD signal (simBOLD) is generated from the PSPs by all excitatory inputs (purple section). EEG-BOLD correlation calculations follow experimental protocols (see Methods for details).

bling EEG rhythms are observed. EEG power, BOLD amplitude, and EEG-BOLD temporal correlations are characterised across a range of external input levels. The effect of input variability (i.e., the varying input condition) on EEG-BOLD temporal correlations is then explored, with a simulation example replicating the LFP-BOLD correlations reported in (Magri et al., 2012). To further investigate the sources of EEG rhythms and EEG-BOLD correlations, the contributions of individual neural populations (E, PV, SOM, and VIP across layers) to these phenomena are examined.

Results

Heterogeneity of alpha-BOLD correlation

In Figure 1A, we show a group-level alpha-BOLD correlation map across 72 healthy participants. Negative alpha-BOLD correlations are found in the parietal and occipital areas, with a minimum in a voxel in the middle occipital gyrus (r_1, highlighted by the cyan circle). Positive alpha-BOLD correlations are distributed in frontal and medial brain areas, with a maximum in a voxel in the middle cingulate gyrus (r_2, highlighted by the yellow circle). We select these two voxels and show the histograms across subjects in Figure 1B. The variability in alpha-BOLD correlation across individual subjects is substantial (r_1 = -0.09±0.11, and r_2 = 0.14±0.12), aligning with findings from a previous study (Gonçalves et al., 2006). In Figure 1C, we present the brain-wide distribution of individual and group-level alpha-BOLD correlations. The variability across brain voxels in individual alpha-BOLD correlations is also notably greater than that observed in the group-level correlations. Figure 1D shows the alpha-BOLD correlation maps of three representative participants to further illustrate the heterogeneity of alpha-BOLD correlation maps. In summary, the heterogeneity of alpha-BOLD correlations is evident at multiple levels (i.e., across brain voxels and between subjects). We attribute this heterogeneity to the noise in synaptic activity and the variability in long-range input to cortical microcircuits, as demonstrated later through simulations under constant and varying input conditions.

Noise-driven fluctuations

The external inputs to the cortical microcircuit model — lateral input I_{lat}, modulatory input I_{mod}, and thalamic input I_{tha} — determine whether it operates in an oscillatory or steady state. In this study, we focus on the range of external inputs where the model remains in a steady state without oscillatory behavior, and where it therefore exhibits noise-driven fluctuations when independent Gaussian noise is applied to internal connections (see Methods).

In Figure 2, we characterise the spectral properties of these noise-driven fluctuations under constant input conditions, with inputs set within the ranges I_{lat} = [2.5–4.5], I_{mod} = [0–25], and I_{tha} = [0–5]. The upper limits of these intervals ensure that the system remains in the steady state. The lower limit of I_{lat} = 2.5 is motivated by the fact that for smaller values, the system displays relatively uniform behavior with little variability in the EEG spectra. Furthermore, it is plausible that cortical microcircuits receive continuous input from nearby areas due to prevalent lateral connections (Grinvald et al., 1994), which would justify the non-zero lower limit of I_{lat}. Figure 2A illustrates the power change in decibel (dB) in frequency bands delta (0.5–4 Hz), theta (4–7 Hz), alpha (8–12 Hz), beta (13–30 Hz), and gamma (30–50 Hz) relative to baseline power at I_{lat}, I_{mod}, and I_{tha} = 0. Overall, the modulatory input I_{mod} induces a distinct switching behavior, altering the role of thalamic input between sharply contrasting regimes. At lower I_{mod}, the dominant frequency power of noise-driven fluctuations transitions from alpha to beta and gamma as thalamic input I_{tha} increases. In contrast, at higher I_{mod}, substantial delta and theta power emerge. This switching behavior becomes more pronounced with increasing lateral input I_{lat}, characterised by enhanced band power and a shifted dependence on thalamic input, such as the observed shift in theta power within the input space. These spectral features of the fluctuations align with experimental observations, such as EEG alpha in the eyes-closed resting state, corresponding to low I_{tha} (Barry et al., 2007), EEG gamma during sensory tasks, corresponding to high I_{tha} (Muthukumaraswamy & Singh, 2013), and EEG theta during attentional processes with concurrent reduction of alpha power, corresponding to high I_{mod} (Cona et al., 2020; Keller et al., 2017; Missonnier et al., 2006).

To facilitate visualization and conceptual understanding, we divide the input space into eight clusters based on the power spectra (0.5–50 Hz) of the modelled EEG using K-means clustering (Figure 2B). We then show the power spectra (z-scored in each frequency bin) sorted by cluster index in Figure 2C, as well as the mean power spectrum of each cluster in Figure 2D. The input space at low I_{lat} is dominated by Cluster 1 characterised by only small deviations of their spectra from the baseline spectra, which supports our choice of lower limit for I_{lat}. In Clusters 2 to 4, where the modulatory input I_{mod} is low, fluctuations predominantly occur in the alpha, beta, and gamma bands. In Clusters 5 to 8, where the modulatory input I_{mod} is high, fluctuations predominantly occur in the delta, theta, and gamma bands. It should be noted that the specific number of clusters is not critical, but has emerged as the optimal number of clusters based on centroid distance (Figure S1).

EEG alpha, gamma, and BOLD

First, we examine the BOLD amplitude and its relationship with EEG power in the alpha and gamma bands under constant input conditions. Figure 3A displays the eight input clusters and mean BOLD amplitudes in the input space. Generally, BOLD amplitude is higher at increased levels of external inputs and reaches its peak in Cluster 4, where strong beta and gamma activity are observed. Figure 3B illustrates the relationship between EEG alpha power, gamma power, and BOLD amplitude. Gamma power generally shows a positive correlation with BOLD amplitude (with some exceptions in Cluster 8), whereas alpha power typically exhibits a negative correlation with BOLD amplitude (with exceptions in Clusters 4 and 6). This result offers an intuitive explanation for experimental observations of positive gamma-BOLD correlations (Logothetis et al., 2001; Magri et al., 2012) and negative alpha-BOLD correlations (Goldman et al., 2002; Laufs, Kleinschmidt, et al., 2003; Laufs, Krakow, et al., 2003; Moosmann et al., 2003).

The BOLD amplitude and EEG power are time-averaged quantities here, which provide an indication about their interrelationship as input parameters are varied. However, to obtain results that are closer to experimental findings, it is necessary to investigate the EEG-BOLD correlation in a time-resolved manner.

EEG-BOLD temporal correlation: constant input condition

We proceed by examining the temporal correlation between simulated noise-driven electrophysiogical signal fluctuations (including EEG alpha and gamma power) and BOLD amplitude under constant input conditions. This analysis involved simulating 10 minutes of simultaneous EEG and BOLD data 100 times for each combination of input levels (which amounted to 100 $\times$ 5 $\times$ 11 $\times$ 51 = 280500 simulations). This allowed us to compute reliable mean values for the EEG-BOLD correlation, and to obtain informative distributions to illustrate its variability. Specifically, and in accordance with the analysis of the experimental data, the simulated BOLD signal was correlated with the envelope of the simulated EEG signal either in the alpha or the gamma band. Figure 4A and B present the mean alpha-BOLD and mean gamma-BOLD correlations throughout the input space, respectively. Notably, we observe both positive and negative alpha-BOLD correlations, whereas the gamma-BOLD correlations are predominantly positive. Interestingly, the region of negative alpha-BOLD correlations does not align with the high alpha region (Cluster 2) but with a region where both alpha and gamma coexist (Cluster 6).

Moreover, the region of positive alpha-BOLD correlations aligns with Cluster 7 where delta, theta, and gamma are strong (cf. Figure 2A). In the same region of input space, we observe large amplitude fluctuations of the BOLD signal, as quantified by the standard deviation of the time series (supplementary Figure S2C).

Figure 4C presents the distribution of EEG-BOLD correlations across 100 runs for two representative examples. The mean EEG-BOLD correlations under constant input conditions are relatively low, around $\pm$0.05. These low correlations are primarily attributable to neural populations resonating with synaptic noise, with resonance frequencies that depend on the model's external input levels. Importantly, the positive and negative correlations remain stable even when the EEG dipole orientation and amplitude are randomised (see supplementary Figure S3), indicating that the observed EEG-BOLD correlations are minimally influenced by the specifics of the EEG forward model. Interestingly, the mean and range of simulated alpha-BOLD correlations across 100 runs (Figure 4C) qualitatively correspond to distributions of empirical alpha-BOLD correlations of the most negatively/positively correlating voxels across subjects (Figure 1B) as well as whole brain alpha-BOLD correlations distributions for single subject maps (Figure 1C).

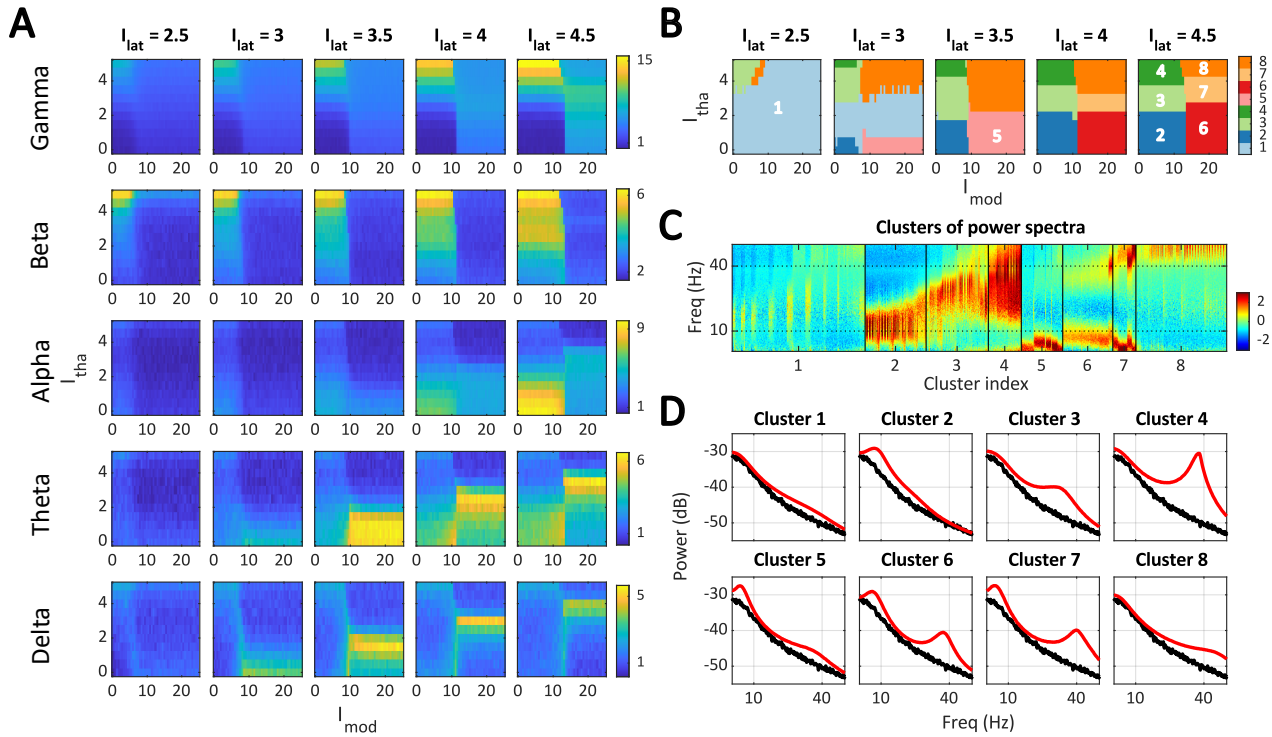

Figure 2. Spectral properties of noise-driven fluctuations. (**A**) Relative EEG power (in dB) compared to the baseline condition (I_{lat}, I_{mod}, I_{tha} = 0) across frequency bands: gamma (30–50 Hz), beta (13–30 Hz), alpha (8–12 Hz), theta (4–7 Hz), and delta (0.5–4 Hz), shown from top to bottom. (**B**) Eight K-means clusters by z-scored EEG spectral features (0.5–50Hz). For the choice of the number of clusters, check the supplementary Figure S1. (**C**) The z-scored power spectra sorted by cluster index to visually inspect spectral heterogeneity within each cluster. (**D**) The mean spectra (red) for each cluster, alongside the baseline spectrum (black).

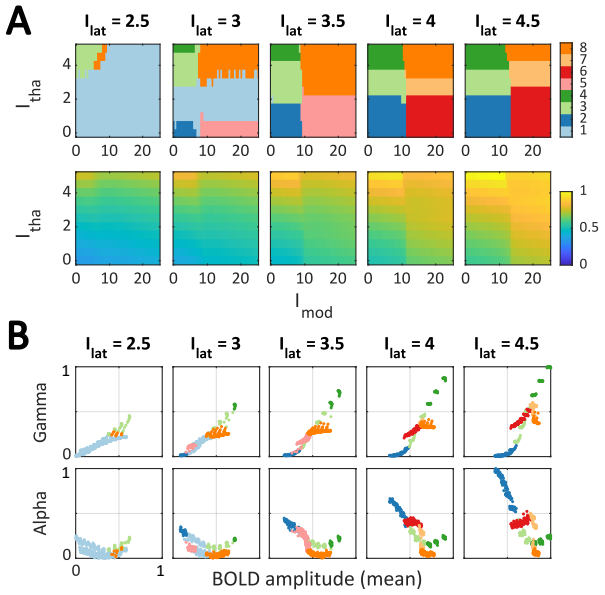

Figure 3. Mean BOLD amplitudes and corresponding EEG alpha and gamma powers. (**A**) K-means clusters (top row, same as in Figure 2**B**) and the mean BOLD amplitude (bottom row). (**B**) Scatter plots of gamma-BOLD (top) and alpha-BOLD (bottom) relationships. Mean BOLD amplitude (x-axis) and EEG band powers (y-axis) are normalised. The scatter plots and clusters share the same color scheme. For the full version covering other frequency bands, check the supplementary Figure S2.

EEG-BOLD temporal correlation: varying input condition

In the previous section, we constrain the external inputs to be constant and demonstrate that synaptic noise can contribute to weak EEG-BOLD correlations. Here, we consider time-varying external inputs, which more closely mimic realistic conditions, such as dynamic brain state transitions during rest (Khanna et al., 2015). To exemplify the effect of the variability of the input, two independent random-walk signals within predefined boundaries are used for I_{mod} and I_{tha}, while I_{lat} is kept constant. We then examine how the varying inputs affect the EEG-BOLD correlation.

In Figure 5A, we examine three example cases of varying input conditions, with the strength of I_{mod} set from low to high: Case 1 (I_{lat} = 4.5, I_{mod} = [0–2], and I_{tha} = [0–2]) lies in the region of Cluster 2 where there is strong alpha power, Case 2 (I_{lat} = 4.5, I_{mod} = [12.5–14.5], and I_{tha} = [0–2]) spans Clusters 2 and 6, and Case 3 (I_{lat} = 4.5, I_{mod} = [16–18], and I_{tha} = [0–2]) lies in the region of Cluster 6. In Figure 5B, we show a single run of the varying inputs, the EEG spectrogram, and the time series of alpha, gamma power, and BOLD amplitude for the three cases. In Cases 1 and 2, we observe negative alpha-BOLD correlations. Case 2 exhibits switches between two spectral patterns where alpha and gamma powers are anti-correlated. In Case 3, we observe a positive alpha-BOLD correlation, which would have been negative under constant input conditions. In Figure 5C, we run 100 simulations for each case and show the histogram of alpha-BOLD and gamma-BOLD correlations. The mean Gamma-BOLD correlations are positive in all three cases, while the mean alpha-BOLD correlations vary substantially (from -0.66 in Case 1 to 0.16 in Case 3). The result shows that the effect of external input variability on EEG-BOLD correlations is much greater than that of synaptic noise under constant input conditions. Compared to the heterogeneity in alpha-BOLD correlations observed in the experiment (Figure 1BC), the constant input condition (Figure 4C) qualitatively matches the mean and variance but appears less realistic. However, fluctuations in long-

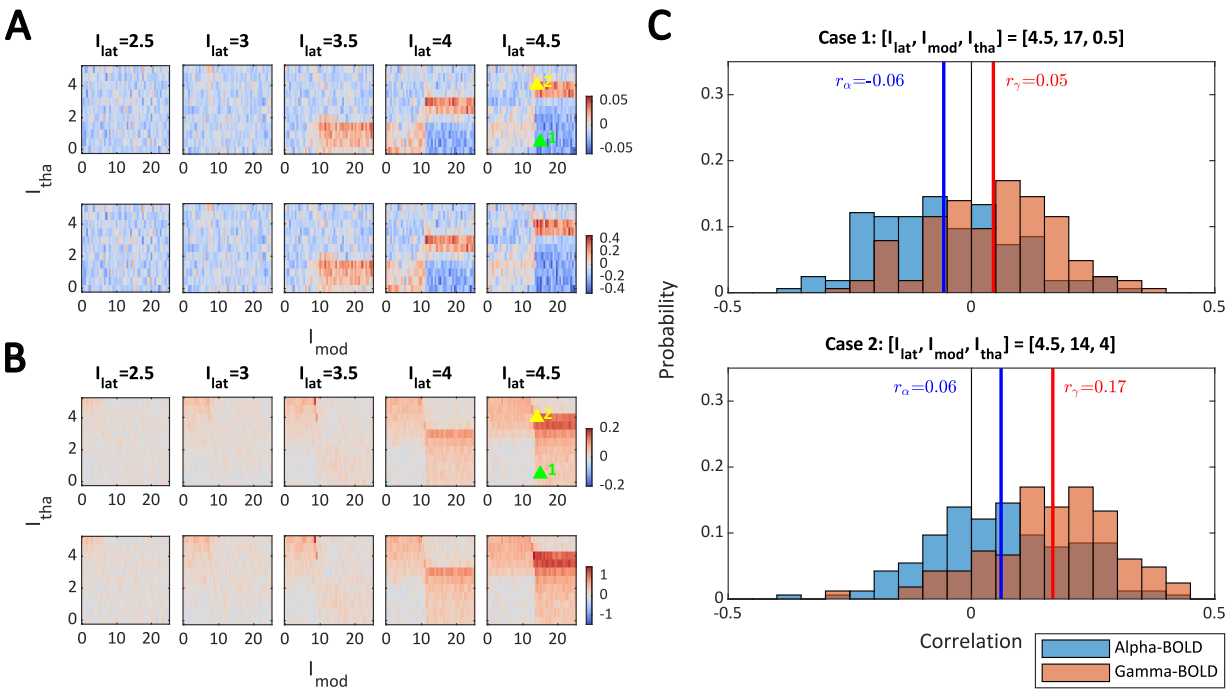

Figure 4. EEG-BOLD correlation under constant input conditions. (**A**) Mean alpha-BOLD correlation, and (**B**) mean gamma-BOLD correlation, across 100 runs (top row) and corresponding effect size (mean/std, bottom row). The correlations are calculated from t = [200–550] sec in each run. (**C**) Histogram for two example cases. In case 1 (I_{lat} = 4.5, I_{mod} = 17, and I_{tha} = 0.5), the mean alpha-BOLD correlation r_α is negative (blue line, blue probability distribution), and the mean gamma-BOLD correlation r_γ is positive (red line, orange probability distribution). In case 2 (I_{lat} = 4.5, I_{mod} = 14, and I_{tha} = 4), both r_α and r_γ are positive. The two example cases are indicated by green (case 1) and yellow (case 2) triangles in **A** and **B**.

range input are inevitable. Also, the strong alpha region (cluster 2 in Figure 2B) aligns with the cases of negative alpha-BOLD correlations under the varying input conditions, which makes the varying input conditions more plausible.

The effect of external input variability on EEG-BOLD correlations is substantial. The distinct alpha-BOLD correlations in the three example cases can be intuitively explained by viewing the distribution of mean alpha power and mean BOLD amplitude (second row in Figure 3B). In Case 1, the input ranges stay within Cluster 2 (blue dots), where the distribution of mean alpha power and mean BOLD amplitude forms a negative correlation. In Case 3, the input ranges stay within Cluster 6 (red dots), where the distribution of mean alpha power and mean BOLD amplitude forms a positive correlation. In Case 2, the input spans Clusters 2 and 6, resulting in an overall negative correlation.

In summary, resonance to internal synaptic noise produces weak EEG-BOLD correlations (Figure 4). However, introducing variability in external inputs can significantly and dynamically modify these correlations (Figure 5). Together, these two driving mechanisms shape the spectral properties of the cortical microcircuit model, resulting in diverse and dynamic EEG-BOLD relationships. Variations in input amplitude can drive larger fluctuations in EEG and BOLD signals than those caused by independent synaptic noise sources. Notably, the presence of time-varying inputs enhances EEG-BOLD correlations and increases synchrony between neural populations. Supplementary Figures S8 and S9 provide examples demonstrating how greater variability in external inputs strengthens the correlation of neural firing activity.

Replication of LFP-BOLD correlation

Alpha-BOLD anticorrelation and gamma-BOLD correlation have also been reported in localised brain regions in experimental studies. For instance, a simultaneous LFP-fMRI study reported alpha and gamma relationships with BOLD signals during spontaneous activity in the early visual cortices of anaesthetized monkeys (Magri et al., 2012). We validate our model by replicating their finding, where the *overall* alpha-BOLD correlation is positive, and the *fixed-power* alpha-BOLD correlation is negative (as shown in Figure 7 in Magri et al., 2012).

To reproduce this finding, we follow the methods described in (Magri et al., 2012). For overall correlation, we compute the Pearson correlation between LFP power at each frequency bin in the spectrogram (delayed by 3.5 seconds) and the BOLD signal. For fixed-power correlation, we divide the LFP power (the sum of the spectrogram from 0.5 to 100 Hz) into 10 percentile levels and compute the Pearson correlation at each level. Note that in this study, we use "LFP" and "EEG" interchangeably. (See model complexity and justification in the Discussion.)

We simulate 10 minutes of LFP and BOLD using random, time-varying inputs for 100 runs. Figure 6A shows a single simulation run, with inputs confined to I_{lat} = [2.5–3], I_{mod} = [0–25], and I_{tha} = [0–5]. The external inputs traverse Clusters 1, 2, 3, 4, 5, and 8 (indicated by colored stripes beneath the input subplot), and the spectrogram reflects corresponding spectral transitions. The LFP power and the BOLD signal are highly correlated. In Figure 6B, we present 2D histograms and correlations among LFP power, alpha power, gamma power, and BOLD amplitude in 100 runs. The overall gamma-BOLD, gamma-LFP, and LFP-BOLD correlations are positive, as in all other supplementary examples (Supplementary Figures S4, S5, and S6). The overall alpha-BOLD, alpha-LFP, and alpha-gamma correlations are slightly positive in this example (but mostly negative in the other supplementary examples). We highlight the overall alpha-BOLD distribution with a white ellipse on the 2D histogram in Figure 6B for a later comparison with the fixed-power alpha-BOLD distributions. Figure 6C shows the overall correlation (left) and the fixed-power correlation (middle) for each frequency bin. The overall correlations are positive across frequencies (red curve), whereas the mean

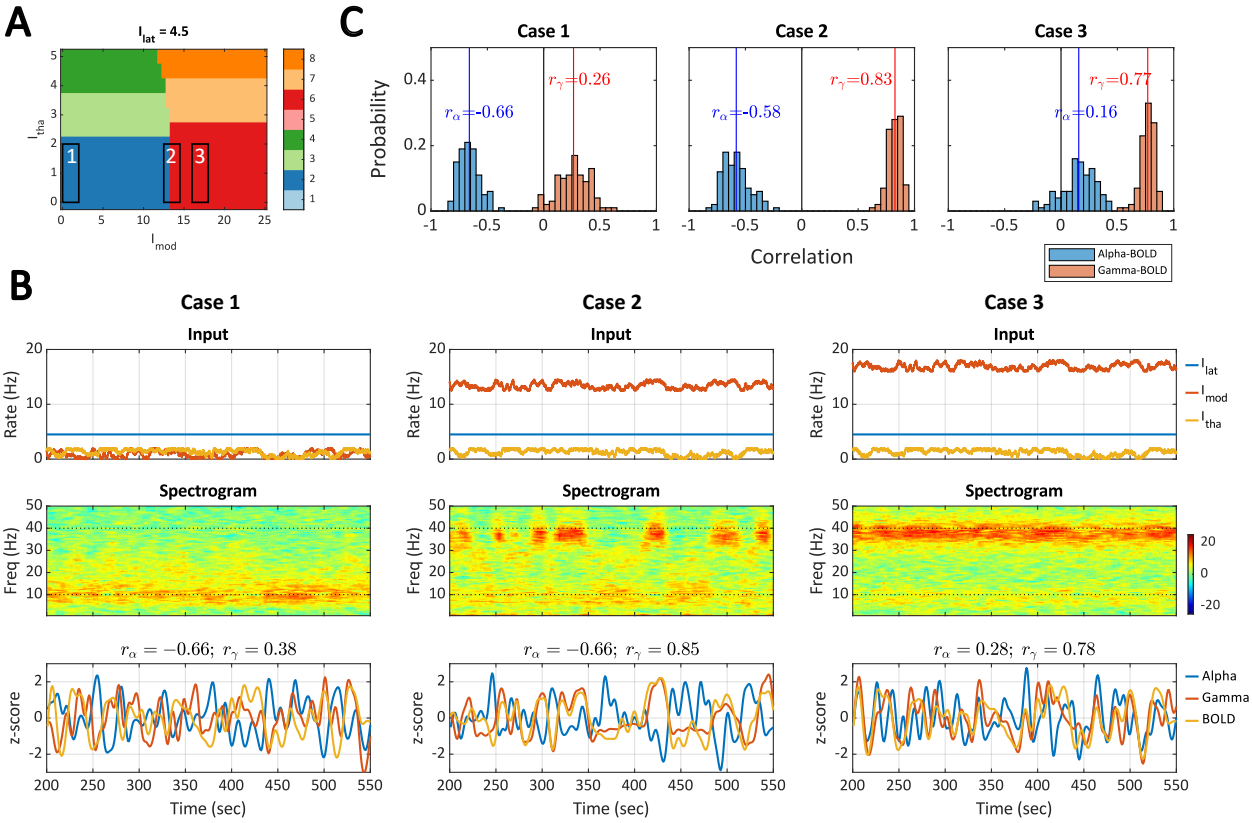

Figure 5. EEG-BOLD correlation under varying input conditions. (**A**) The K-means clusters (same as in Figure 2**B**) and three varying input cases where the input ranges are confined in the black rectangles: [I_{lat}, I_{mod}, I_{tha}] = [4.5, 0–2, 0–2] (Case 1), [4.5, 12.5–14.5, 0–2] (Case 2), and [4.5, 16–18, 0–2] (Case 3). The time-varying inputs are generated independently using a random walk process and then rescaled to the rectangular ranges. (**B**) A single run of 10 minutes under the three input cases. The top row shows the random walk inputs. The middle row shows the spectrogram of the simulated EEG signal. The bottom row shows the alpha power signal, the gamma power signal, and the simulated BOLD signal. The alpha-BOLD correlation r_α and gamma-BOLD correlation r_γ are calculated from t = [200–550] sec. (**C**) Histogram of alpha-BOLD (blue) and gamma-BOLD (orange) correlations of 100 runs under the three input cases.

fixed-power correlations can be negative at lower frequencies (black curve). Figure 6D shows that the fixed-power alpha-BOLD correlations for each percentile level are predominantly negative. These locally negative alpha-BOLD distributions (magenta ellipses) combine and produce a globally positive alpha-BOLD distribution (white ellipse), providing an intuitive interpretation of Figure 6C and the experimental findings in Figure 7 in (Magri et al., 2012). Finally, Figure 6E details the composition of spectral clusters at each percentile level for additional information. The external inputs traveling in Clusters 3, 4, and 8 (corresponding to a higher thalamic input I_{tha}) contribute to the higher LFP power percentiles, whereas the external inputs traveling in Clusters 1, 2, and 5 (corresponding to lower I_{tha}) contribute to the lower LFP power percentiles.

To further investigate the mechanism behind the locally (fixed power) negative but globally (overall) positive alpha-BOLD correlations observed by (Magri et al., 2012) and reproduced in Figure 6C, we present three example cases in which both global and local alpha-BOLD correlations are negative in the supplementary Figures S4, S5, and S6. A key factor in these cases is the alpha-gamma correlation. All three cases show a negative alpha-gamma correlation, contrasting with the positive alpha-gamma correlation in Figure 6B. A negative alpha-gamma correlation can arise when external inputs travel between clusters (e.g., between clusters 2 and 6), causing alpha-gamma switching (supplementary Figure S4); from reducing common noise in external inputs (Figure 5 vs. supplementary Figure S5); or increasing the alpha-gamma contrast in the spectrogram by increasing the lateral input I_{lat} (Figure 5 vs. supplementary Figure S6). These results suggest that the locally negative and globally positive alpha-BOLD correlations found in (Magri et al., 2012) may be associated with a positive alpha-gamma correlation, potentially due to the relatively low I_{lat} (reflecting the anaesthetized state of the monkey) or noisy external input.

Population activities and EEG spectra

Up to this point, we have only considered the model output in the form of EEG and BOLD. The model and its detailed structure, however, allow us to further investigate the factors that determine the phenomena that we have reported so far. In particular, we are interested in identifying specific neural populations whose activity drives the spectral features of the EEG, and the correlations observed between EEG and BOLD.

Since EEG spectra are an integral part in determining different dynamic regimes, we first focus on which neural populations drive the EEG spectra in different frequency bands. This is done by correlating the EEG activity, as obtained from the forward model, with the PSPs generated by individual neural populations in a frequency-resolved and baseline-corrected manner for each of the clusters identified previously. The input parameters in each cluster are scanned, and the range of EEG spectra (with baseline subtracted) are plotted in the top panels of Figure 7. The resulting correlation spectra elucidate the relationship between neural population activity and EEG power in different frequency bands (bottom panels of Figure 7). They show that some neural populations only have a marginal influence on the EEG spectra,

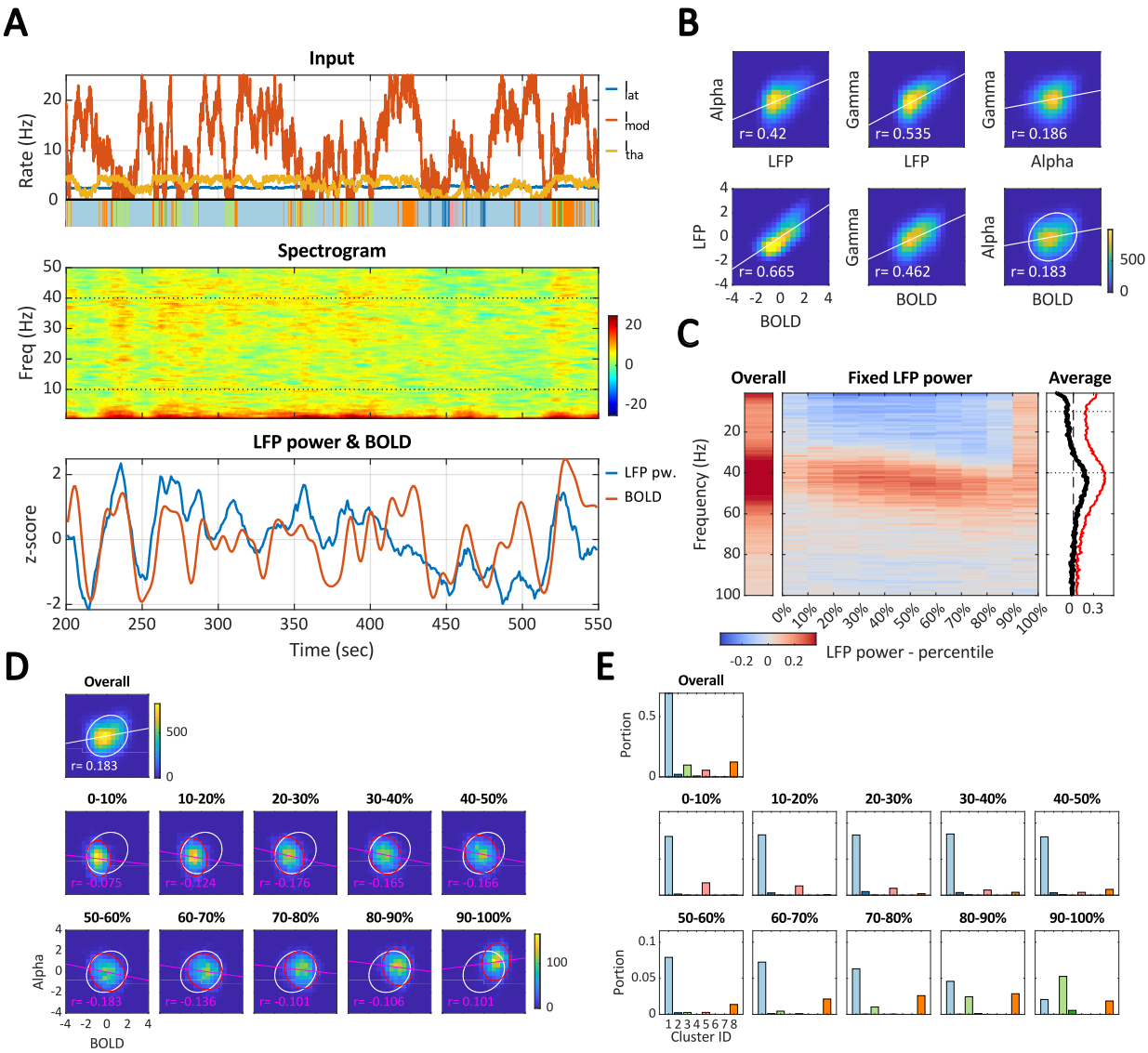

Figure 6. Reproducing the LFP-BOLD correlation from (Magri et al., 2012). (**A**) A single 10-minute simulation (start and end segments not shown). Top row: Varying inputs are constrained within I_{lat} = [2.5–3], I_{mod} = [0–25], and I_{tha} = [0–5]. Colored stripes beneath indicate the corresponding K-means cluster IDs. Middle row: LFP spectrogram (only showing 0.5–50 Hz for visual clarity). Bottom row: Time series of overall LFP power (sum of spectrogram from 0.5–100 Hz) and BOLD amplitude. (**B**) 2D histogram for overall LFP power, alpha power, gamma power, and BOLD amplitude across 100 runs. (**C**) Overall LFP-BOLD correlation at individual frequencies, averaged over 100 runs (left); fixed-power LFP-BOLD correlation, where the LFP power is divided into 10 percentile levels (middle); and average fixed-power correlation (black curve) compared with the overall correlation (red curve). (**D**) 2D histograms showing the alpha-BOLD distribution for overall correlation (with a white ellipse) and fixed-power correlations (with magenta ellipses) (**E**) Composition of spectral clusters for each power percentile level (cluster ID color code as in Figure 2B).

which include VIP interneurons across all layers, and the pyramidal cells and SOM interneurons in layer 6. This can be explained by the relatively weak connections that these cell populations have with pyramidal populations, and therefore the PSPs are dominated by synaptic noise (cf. Figure S7C). We note here that these results are obtained in the constant input condition, where the dynamics of the neural populations are driven by independent synaptic noise.

The correlation spectra show features that are relatively well delimited by the boundaries of the classical frequency bands. The strongest correlations in the delta and theta band can be observed in Clusters 5 to 7. The pyramidal cells in layers 2/3 and 5, PV interneurons across all layers, and SOM interneurons in layer 5 are the strongest drivers. In essence, neural populations across all layers appear to be involved in these slow rhythms.

Alpha band activity is most prominently represented by Cluster 2. Here, pyramidal cells in layers 2/3 and 5 (ET population), SOM interneurons in layers 2/3 and 5, and PV interneurons in layers 5 and 6 are the main drivers. This suggests that alpha activity is mostly, but not exclusively, driven by neural activity in the infragranular layers.

Clusters 1 to 4 and 8 show relatively strong correlations in the beta band, which are driven by layer 2/3 and 5 PV interneurons, and layer 4 pyramidal cells. This coincides with a strong overlap with the gamma band. Cluster 2 shows an overlap of beta-band activity with the theta and alpha band, and the correlations in the low beta band are driven by the same populations as in the alpha band.

Clusters that represent strong gamma activity (3, 4, and 6 to 8) show that it is driven by pyramidal cells in layers 2/3, 4 and 5 (but not the IT population), and PV interneurons across all layers. In Cluster 4, some of the strong correlation is limited to a narrow frequency band close to 40Hz, and also involves SOM interneurons from layer 2/3 and 4. In Clusters 3 and 4, where the gamma band

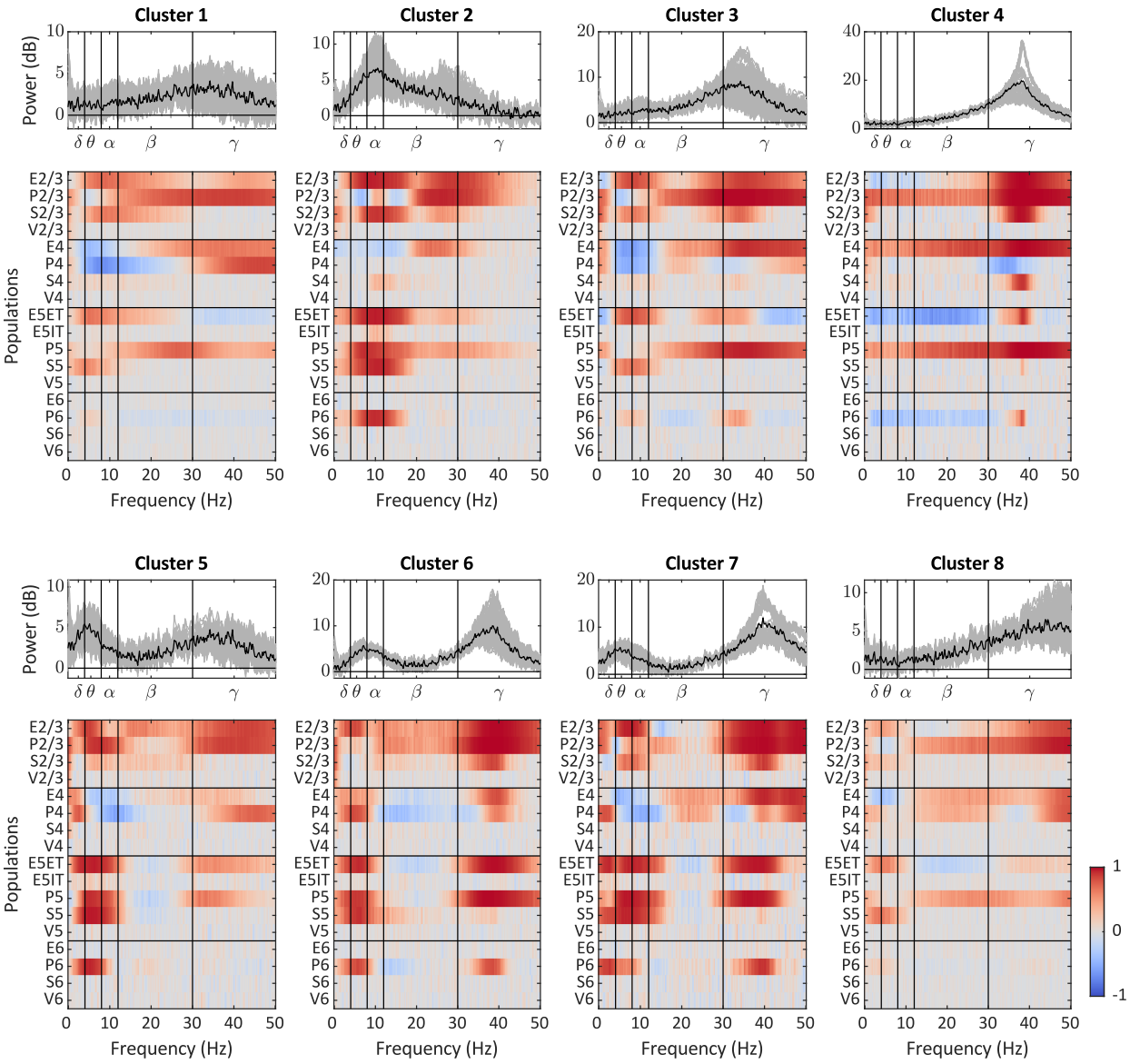

Figure 7. Relationship between the spectra of EEG and PSPs. The first and third rows display the baseline-corrected EEG power spectra (spectEEG) for k=8 clusters within the input space I_{lat} = [2.5–4.5], I_{mod} = [0–25], and I_{tha} = [0–5]. The second and fourth rows show the similarity (measured by correlation over input space) between spectEEG and spectPSP, where spectPSP (shown in supplementary Figure S7C) represents the baseline-corrected power spectra of the postsynaptic potentials (PSPs) from all populations to the excitatory populations.

activity overlaps with beta band activity (which is absent in Clusters 6 to 8), beta and gamma activity have similar drivers. This suggests that the classical division of the EEG spectrum can be too rigid to accommodate all scenarios.

Population activities and EEG-BOLD correlation

To elucidate the influence of population activity on the EEG-BOLD correlation, we computed the correlation between alpha-BOLD and gamma-BOLD correlations, and the mean and variance of the population firing rates in a broad-band as well as in a frequency-resolved manner. Since all of these measures yield only a single value for a specific set of parameters, we computed the correlation across the input space spanned by the parameters I_{lat}, I_{mod} and I_{tha}.

The alpha-BOLD correlation corresponds mainly with the variability of firing rates in a subset of neural populations, such as pyramidal cells in layer 5, SOM cells in layers 5 and 6, and PV cells in layer 6, while the mean firing rates show only little correspondence. A similar picture emerges when examining the correspondence of the frequency-resolved changes in power and the changes in alpha-BOLD coupling (Figure 8A). Here, the biggest correlation values are found in the delta and theta frequency bands in layer 2/3 pyramidal cells, in addition to the aforementioned populations. These results highlight a particularly strong correspondence with slow activity in infragranular populations. The stronger contribution of the delta and theta band (compared to the alpha band) seems counterintuitive. A potential explanation for this is that those input parameters where the alpha-BOLD correlation is relatively strong and positive (cf. Figure 4A), overlap well with those where the variability of the BOLD signal is the highest (cf. Figure S2C), which in turn strongly correlates with the power in the delta and (slightly less so) theta band (cf. Figure S2D).

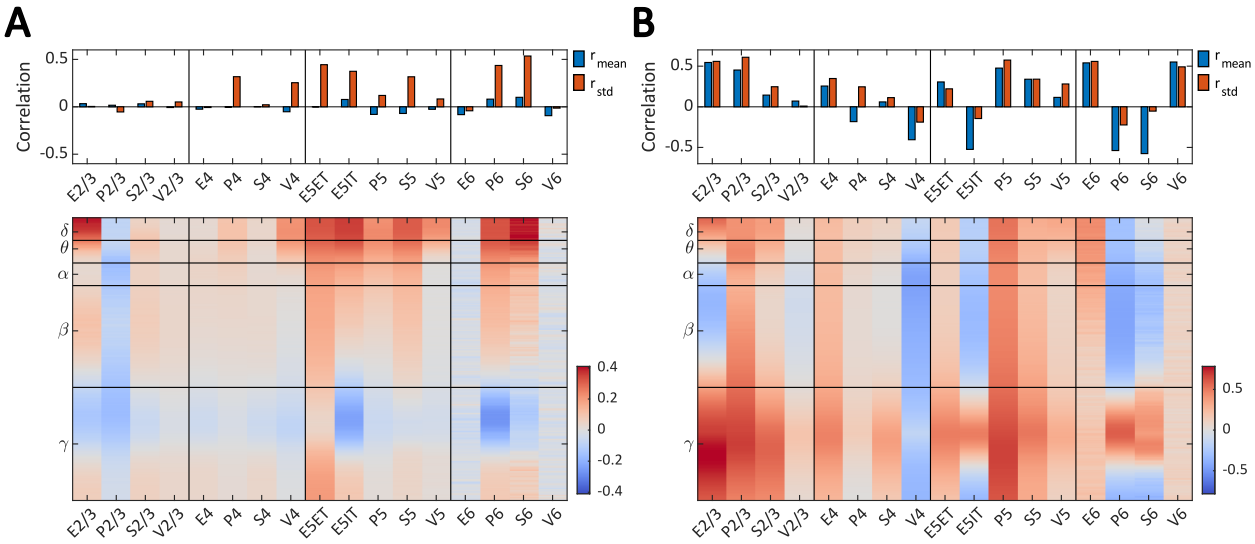

Figure 8. Populational relationship with alpha-BOLD and gamma-BOLD correlations. (**A**) Similarity (measured by correlation across the input space) between alpha-BOLD correlation and various metrics. Top panel: with mean firing rate in blue bars (cf. supplementary Figure S7A) and standard deviation of firing rate in red bars (cf. supplementary Figure S7B) (top row). Bottom panel: with relative power change in firing rate at each frequency bin (cf. supplementary Figure S7B). (**B**) Similarity between gamma-BOLD correlation and the same metrics as in (A).

The gamma-BOLD correlation corresponds to the mean firing rates, as well as their standard deviation, of neural populations across all layers (Figure 8B). We find a strong positive correlation with the mean firing rates of layer 2/3 and layer 6 pyramidal cells, layer 2/3 and layer 5 PV interneurons, and layer 6 VIP interneurons. Layer 2/3 pyramidal cells and PV interneurons, layer 5 PV interneurons, and layer 6 pyramidal cells and VIP interneurons also show a strong positive correlation in the standard deviation of their firing rates. A strong negative correlation with the gamma-BOLD correlation is found for the mean firing rates of layer 4 VIP interneurons, layer 5 pyramidal cells (IT population), and layer 6 PV and SOM interneurons. The majority of these populations also show strong correlations in the gamma band, except layer 4 VIP interneurons, which show a negative correlation across all frequency bands. The other populations that show a strong negative correlation in the mean firing rate also show the following peculiar behavior: the correlation is positive in a narrow frequency band around 40Hz (a subset of the gamma band), but negative in all other frequencies.

Discussion

In this study, we investigate how long-range inputs to cortical microcircuits contribute to the heterogeneity of EEG-BOLD correlations observed in experimental data (Figure 1A-D). We systematically examine the relationship between EEG rhythms and BOLD amplitudes by scanning the levels of external inputs in a detailed microcircuit model (Figures 2, 3, and S2). We further demonstrate that both constant and varying input conditions can produce positive or negative EEG-BOLD correlations. Under constant input conditions, the model produces weak EEG-BOLD correlations (Figure 4), which may correspond to the observed distribution of alpha-BOLD correlations (Figure 1B). However, time-varying inputs exert a more pronounced effect (Figures S8 and S9), resulting in stronger EEG-BOLD correlations (Figure 5) and better alignment with experimental data (e.g., LFP-BOLD correlation in Figure 6). For a typical case where strong alpha activity and negative alpha-BOLD correlations are observed in occipital regions during resting-state, a time-varying input condition (with moderate I_{lat}, low I_{tha}, and low I_{mod}) offers a more plausible explanation.

Sources of EEG rhythms and EEG-BOLD correlations

The detailed microcircuit model allows us to identify which neural populations drive the activity across EEG frequency bands, as well as the alpha-BOLD and gamma-BOLD correlations. While low- and high-frequency EEG bands are conventionally associated with SOM and PV neurons, respectively (Chen et al., 2017; Onorato et al., 2025; Vierling-Claassen et al., 2010), our findings reveal a more intricate involvement of neural populations in the correlation spectra, where SOM and PV neurons jointly contribute to shifts in the resonance frequency (Figure 7). We found that low-frequency EEG activity (from delta to low beta band) was driven more strongly by infragranular than supragranular populations. Conversely, high-frequency EEG activity (high beta and gamma band) is driven more strongly by supragranular populations. Nevertheless, drivers in both cases emerged from all layers, which doesn't justify to assign specific EEG frequency bands unequivocally to a specific layer. Furthermore, the same neural population can contribute to both low and high frequency EEG activity, which is particularly the case for pyramidal cells and PV interneurons in layers 2/3 and 5. As to the weak EEG-BOLD correlations under constant input condition (Figure 8), we found that alpha-BOLD correlation is almost exclusively driven by fluctuations (i.e. standard deviation of firing rates) in infragranular populations, with little contribution from the supragranular layer. Furthermore, average firing activity did not seem to influence alpha-BOLD correlation significantly, as determined by the correlation of mean firing rates with alpha-BOLD correlation. The gamma-BOLD correlation, on the other hand, has multiple drivers from across all layers, and here both fluctuations and average firing activity are strong contributors.

Comparing models of EEG rhythms

Our cortical microcircuit model produces EEG rhythms through a fundamental mechanism, where excitatory-inhibitory feedback loops, featuring nonlinear amplification and synaptic filtering, enable resonance to synaptic noise (Hahn et al., 2022; Vierling-Claassen et al., 2010). The nonlinear amplification is achieved

through a sigmoidal firing rate function, while the filtering is governed by the synaptic kernel in the form of an alpha function. Variations in the firing rate functions and the time constants of the synaptic kernels across different cell types enable the model to naturally exhibit diverse spectral properties of noise-driven fluctuations, depending on the configuration of external inputs. This mechanism does not require the model to enter oscillatory regimes to produce specific EEG rhythms. This noise-based mechanism is not in conflict with, but rather complements, other proposed mechanisms for EEG rhythm generation. For example, several studies have explored the roles of different inhibitory interneurons (e.g., PV, SOM, and VIP neurons) in the emergence of oscillations within local microcircuits (Domhof & Tiesinga, 2021; Hahn et al., 2022; Lee et al., 2018; Veit et al., 2017). Our model aligns with these works in many respects, such as the disinhibitory role of VIP neurons, the association of fast oscillations with PV-dominated states, and the emergence of slower oscillations in SOM-dominated states. However, these studies predominantly focused on EEG rhythms in higher frequency bands (e.g., beta and gamma, >20 Hz). Other studies, including cortical network models (Nakagawa et al., 2014) and thalamocortical models (Pang & Robinson, 2018), focus on structural connectivity and transmission delays at the brain scale to explain alpha and low-frequency oscillations. While these structural factors, such as connection strengths and delays, may account for inter-individual differences in alpha power, they are less relevant for capturing the dynamic changes in alpha power.

Comparing models of EEG-BOLD relationship

Studying the EEG-BOLD relationship has received relatively little attention by computational scientists thus far, even though modelling frameworks have been developed that allow for the simultaneous generation of EEG and BOLD signals (Bojak et al., 2010; Ritter et al., 2013; Sanz-Leon et al., 2015). We have identified two computational studies that have attempted to explain alpha-BOLD anti-correlation before. In one study, a network model was developed to study EEG-fMRI correlation at the whole-brain level (Schirner et al., 2018). In this study, the source-localised EEG signal is used as a driving input into cortical E-I circuits, and then compared with the model-generated fMRI signal. This study found consistently strong anti-correlations between the alpha power and the fMRI signal, which does not reflect the more nuanced findings of experimental studies. In another study, a thalamocortical model was proposed to address alpha generation and alpha-BOLD anticorrelation (Pang & Robinson, 2018). This thalamocortical model highlights the anticorrelation between alpha power (7.5–13 Hz) and low-frequency power (0–4 Hz), with the latter serving as a proxy for the BOLD signal. This study attributes changes in alpha power to structural factors, such as corticothalamic and intrathalamic feedback strengths. These structural factors are used to explain the alpha-BOLD anticorrelation observed in a group-level analysis. In contrast, our model captures this relationship in the temporal domain, explaining this phenomenon at the single-subject level. Moreover, our model directly simulates the BOLD signal by feeding the sum of excitatory postsynaptic potentials (PSPs) into the Balloon-Windkessel model, without assuming any low-frequency proxy for BOLD. We conclude that ours is the most realistic model to date that has been used to address the topic of EEG-BOLD correlation.

Model complexity and justification

The cortical microcircuit model, forward models for simulating EEG and BOLD signals, and the external inputs were configured in biologically realistic ways. However, several simplifications were made in order to focus on key factors, such as the role of different inhibitory neuron types, and the interactions among populations that influence the EEG-BOLD relationship.

We considered only AMPA channels (with fast time constants) in excitatory connections, assuming that NMDA channels (with slower time constants) are less active during resting states (Jiang et al., 2024). It has been shown that realistic LFP spectra can be obtained using only fast AMPA synapses in a reduced cortical microcircuit model (Sanchez-Todo et al., 2023). Including NMDA channels in scenarios involving evoked responses could introduce additional slow fluctuations. Likewise, short-term plasticity (STP) was not incorporated in this study. While ongoing activity remains similar with or without STP (Jiang et al., 2024), applying STP to synaptic connections may introduce slow fluctuations, particularly in evoked responses. The LFP/EEG forward model did not take into consideration the depth-dependence of the dipoles, or filtering effects of the cranium. The spatial distribution of synaptic locations, the depth-dependent location of the dipoles, and a realistic head model could be incorporated to improve the LFP/EEG forward model (Næss et al., 2021). Moreover, different neurovascular coupling mechanisms, such as the contributions of several cell types to the regulation of cerebral blood flow and metabolism (Howarth et al., 2021; Jolivet et al., 2015), could refine the currently used Balloon-Windkessel model. Lastly, the external inputs in this study were simplified into three distinct types with no overlap between them, and the ratios of input strengths to excitatory and inhibitory populations (e.g., PV and SOM) were not parameterised. Future studies could configure external inputs with realistic weights for specific applications.

Model predictions

Our microcircuit model makes tangible predictions, and its scalability makes it an ideal candidate for further extensions. A simple prediction is concerned with the variability of the EEG-BOLD correlation when it is computed from finite times series. Throughout the manuscript we use time series with a duration of 10 minutes, which is consistent with the data we analysed. We have provided examples where the standard deviation can actually be larger than the correlation averaged across trials (e.g. Figure 4C). The model provides evidence that this variability can be decreased by increasing the length of the time series (a four-fold increase halves the standard deviation). While longer recordings would be more costly in their acquisition, they would allow the detection of more subtle correlations that are otherwise missed. Longer recordings would also enable the test of another prediction the model makes: the power in the delta and theta band (Figure 2A) correlates with the standard deviation of the BOLD signal (Figure S2C). The challenge here is to obtain the time-resolved standard deviation (a proxy for the signal power) from time series with low sampling rate.

Our investigation focused on different forms of long-range external input (lateral, thalamic and modulatory), which targets distinct neural populations. The results could be tested experimentally in a mouse model using optogenetics to target specific neural populations, such as VIP interneurons to mimic modulatory input. The model in turn could also be used to help design optimal stimulation protocols for a variety of applications, including the effect of specific neural populations on LFP and BOLD.

Methods

Cortical microcircuit model

The cortical microcircuit model comprises 17 neural populations, including excitatory (E) neurons and three types of inhibitory

Table 1. Parameter setting for potential-to-rate operators.

	e_0 (Hz)	v_0 (mV)	r (1/mV)
E	31.40	32.11	0.13
PV	166.83	40.03	0.14
SOM	56.95	42.02	0.08
VIP	38.53	37.86	0.07

interneurons—parvalbumin-positive (PV), somatostatin-positive (SOM), and vasoactive intestinal peptide-positive (VIP) interneurons—distributed across cortical layers 2/3, 4, 5, and 6 (Figure 1E). The connectivity w_{ji} from population i to population j is derived from the connection probability p_{ji}, synaptic strength s_{ji}, and cell count c_i of source population i (Campagnola et al., 2022; Fang et al., 2022; Gonchar et al., 2008). The cell count c_i is normalised to total cell counts so that $\sum_{i=1}^{17} c_i = 1$. The final connectivity matrix W, consisting of these pairwise connectivity values w_{ji}, is rescaled by a global scaling factor G (corresponding to the number of neurons to be considered in the cortical microcircuit model) to ensure proper model behavior. In this study, we use $G = 20,000$, where the model fluctuates with the synaptic noise without entering oscillatory states in the defined input range (See External inputs).

$$w_{ji} = p_{ji} \cdot s_{ji} \cdot c_i \quad \textbf{(1)}$$

The dynamics of the cortical microcircuit model are described by two variables: firing rate $m(t)$ and postsynaptic potential $v(t)$. The evolution of the variables is governed by potential-to-rate and rate-to-potential operators.

The potential-to-rate operator translates the summed excitatory and inhibitory PSPs $v(t)$ of a population into its firing rate $m(t)$ using a sigmoid function:

$$m(t) = \frac{e_0}{1 + e^{r(v_0 - v(t))}}, \quad \textbf{(2)}$$

where e_0 is the maximum firing rate (Hz), v_0 is the potential threshold (mV), and r determines the steepness of the sigmoid curve. These parameters (listed in Table 1) are derived by fitting the sigmoid function to the mean F-I curve from the database of single cells from Mouse Brain of Allen Brain Atlas (https://celltypes.brain-map.org/) for each neuron type (E, PV, SOM, and VIP).

The rate-to-potential operator characterises the transmission of firing activity $m_i(t)$ from a source population i to the PSP $v_{ji}(t)$ of a target population j. This process accounts for dendritic and synaptic properties and is described by a second-order ordinary differential equation (ODE) (Jansen & Rit, 1995):

$$\left(\frac{\mathrm{d}^2}{\mathrm{d}t^2} + \frac{2}{\tau_i}\frac{\mathrm{d}}{\mathrm{d}t} + \frac{1}{\tau_i^2}\right) v_{ji}(t) = \frac{1}{\tau_i}\left(w_{ji} \cdot m_i(t) + \eta_{ji}(t)\right), \quad \textbf{(3)}$$

where τ_i is the time constant that depends on the source population i, w_{ji} is the connectivity, and η_{ji} is the synaptic noise. In this study, we use τ_{E} = 6 msec, τ_{PV} = 3 msec, τ_{SOM} = 20 msec, and τ_{VIP} = 15 msec for the connections from source populations E, PV, SOM, and VIP, respectively. Synaptic time constants vary widely even for the same type of connection (Campagnola et al., 2022). We set τ_{E} and τ_{PV} to reflect the finding that τ_{PV} is approximately twice as fast as τ_{E} (Kloc & Maffei, 2014). Although the decay times there were reported to be 6.4ms and 12.1ms, dividing those values by half accounts for the slower dynamics of the alpha synapses. Our choice is also close to the values used by Molaee-Ardekani et al., 2010 (5.5ms and 4.5ms, respectively), but smaller than those in the original Jansen-Rit model (10ms each) (Jansen & Rit, 1995). The slowest time scale is τ_{SOM} = 20 msec, which is chosen from Jansen and Rit, 1995, and slightly faster than the value chosen by Molaee-Ardekani et al., 2010 (30ms). Because synapses formed by VIP interneurons tend to be slightly faster than those of SOM interneurons (Campagnola et al., 2022), we set τ_{VIP} = 15 msec. The EPSP $v_{j,\mathrm{ext}}(t)$ introduced by an external input follows the same equation with τ_{ext} = 6 msec.

The synaptic noise $\eta(t)$ (zero-mean white Gaussian noise with standard deviation σ_η) is independently applied to all internal and external input connections. In this study, we use σ_η = 1 mV. Lower noise levels (e.g., $\sigma_\eta < 1$ mV) result in similar diverse spectral properties with a shift in the power spectrum, whereas higher noise levels (e.g., $\sigma_\eta \geq 10$ mV) lead to reduced signal-to-noise ratios (the signal being the PSPs from neural populations and external inputs) and diminish the diversity.

External inputs to the cortical microcircuit model

The cortical microcircuit model in this study is driven by three distinct types of external inputs: lateral input I_{lat}, modulatory input I_{mod}, and thalamic input I_{tha}, forming a three-dimensional input space for exploring model dynamics (Figure 1E). Each input targets specific neural populations within the cortical microcircuit, reflecting simplified interactions observed in real-world neural systems. The lateral input I_{lat} is directed to E2/3 and SOM2/3 populations, representing interactions with neighboring cortical microcircuits (Yavorska & Wehr, 2016). The modulatory input I_{mod} is delivered to VIP2/3 populations, simulating top-down signals originating from higher-order brain areas (Bastos et al., 2023). Meanwhile, the thalamic input I_{tha} targets E4 and PV4 populations, a reduced abstraction of thalamic projections, which in reality also reach L2/3, L5 and L6 populations in a more detailed manner (Ji et al., 2016). This specific input configuration balances simplicity and biological accuracy. While real-world cortical microcircuits receive spiking inputs targeting distinct neuron types in specific layers, examining such detailed interactions would necessitate a 17-dimensional input space, significantly complicating the analysis. By limiting the input space to three dimensions, the model maintains computational tractability while capturing key features of cortical microcircuit dynamics.

The model's behavior is then characterised under two distinct external input conditions. In the constant input condition, all external inputs remain fixed, providing a stable baseline for studying the model's dynamics. In the varying input condition, the external inputs are modeled as independent random-walk time series within predefined ranges, introducing temporal variability to investigate the system's response to dynamic inputs.

Forward models for simulating EEG and BOLD signals

The forward models in this study take a subset of postsynaptic potential (PSP) signals to simulate electroencephalography (EEG) and blood-oxygen-level-dependent (BOLD) signals (Figure 1F). These simulations are based on distinct biophysical principles that link neural activity to macroscopic brain signals.

The simulation of EEG signals relies on the understanding that EEG signals primarily originate from transmembrane currents at the aligned long dendrites of pyramidal cells (Biasiucci et al., 2019). This corresponds to the excitatory postsynaptic potentials (EPSPs) and inhibitory postsynaptic potentials (IPSPs) within the excitatory (E) populations, specifically E2/3, E4, E5IT, E5ET, and E6. Parameters such as dipole configuration d_{ji} and cell count

Table 2. Dipole configuration. Positive value means an upward direction, and negative value means a downward direction.

$d_{E\to E}$	$d_{PV\to E}$	$d_{SOM\to E}$	$d_{VIP\to E}$	$d_{ext\to E}$
-1	-0.1	1	1	0.1

Table 3. Cell count of populations (in %).

	E	PV	SOM	VIP
L2/3	31.76%	1.73%	1.32%	1.38%
L4	17.54%	0.97%	0.59%	0.32%
L5	16.64%	2.17%	1.27%	0.27%
L6	19.5%	1.19%	0.85%	0.29%

L5E: L5IT(8.32%) and L5ET(8.32%).

c_j of the target excitatory population j are incorporated to weigh the contribution of these currents to the EEG signal.

$$\text{simEEG} = \sum_{j}^{N_E} \sum_{i}^{N_{all}} c_j d_{ji} \left| v_{ji}(t) \right|, \quad (4)$$

where $|v_{ji}(t)|$ corresponds to the transmembrane current at the target E population j introduced by source population i, d_{ji} controls the length and direction of the current dipole, and c_j denotes the cell count of the target E population j. In this model, N_E includes 5 excitatory populations, and N_{all} includes 17 populations and the external input. The dipole configuration d (in Table 2) only roughly catches the distinct distribution of synapses on the pyramidal cells from different types of presynaptic populations. For example, PV targets the cell body of E, and SOM targets the dendrites of E. A more accurate estimation of d would rely on the simulation of a cortical microcircuit model consisting of neurons with detailed morphology, such as (Næss et al., 2021).

The simulation of the BOLD signal is based on the assumption that energy consumption is primarily driven by the synaptic activity of excitatory neurons (Howarth et al., 2012). The neural activity signal z is therefore calculated as the sum of EPSPs $v(t)$ to all populations (weighted by cell counts c in Table 3) introduced by the excitatory populations and external inputs. The signal z is then fed to the Balloon-Windkessel model (Friston et al., 2000, 2003), which captures the complex vascular and metabolic processes underlying the generation of the BOLD signal.

$$z(t) = \sum_{j}^{N_{all}} \sum_{i}^{N_{E,ext}} c_j v_{ji}(t) \quad (5)$$

$$\text{simBOLD} = Balloon(z) \quad (6)$$

Simulations under constant input condition

For simulations under the constant input condition, the average alpha-BOLD and gamma-BOLD correlations were calculated over 100 runs of 10-minute simulations for each combination of external inputs. The input space was explored with a step size of 1 within the ranges I_{lat}=[2.5–4.5], I_{mod}=[0–25], and I_{tha}=[0–5]. In this input range, the model maintained a fixed-point state in the absence of synaptic noise η applied to the connections.

A few preprocessing steps are applied to the simulated EEG (simEEG) and simulated BOLD (simBOLD) signals before calculating the correlation. First, simEEG is bandpass-filtered into the alpha band (8–12 Hz) and gamma band (30–45 Hz). The alpha envelope and gamma envelope are then extracted as the absolute values of the Hilbert transform of alpha and gamma signals, respectively. The alpha and gamma envelopes were subsequently fed into the Balloon-Windkessel model, using the same parameters as in BOLD signal simulation, to generate $\text{simEEG}_{\alpha\text{-en-hr}}$ and $\text{simEEG}_{\gamma\text{-en-hr}}$. To focus on low-frequency fluctuations, bandpass filtering (0.008–0.09 Hz) is applied to obtain $\text{simEEG}_{\alpha\text{-en-hr-bp}}$, $\text{simEEG}_{\gamma\text{-en-hr-bp}}$, and simBOLD_{bp}. Pearson correlations were then calculated for the stable simulation interval (from 200 to 550 seconds) for each simulation run.

Simulations under varying input condition

For simulations under the varying input conditions, correlations between BOLD signals and the power of each frequency bin (2–100 Hz) were calculated across 100 runs of 10-minute simulations. In this setup, the external inputs (I_{lat}, I_{mod}, and I_{tha}) followed random-walk time series independently generated for each simulation run. These pre-saved random-walk time series were rescaled to a defined range within the input space to maintain consistency.

Preprocessing of these simulations adhered to methods described by (Magri et al., 2012). The time series of overall LFP power was defined as the sum of the simEEG spectrogram over the 2–50 Hz frequency range. A fixed-LFP power time series was extracted at defined percentile intervals (0–100%, in steps of 10%) of the overall LFP power. When correlating these time series with simBOLD, a delay of 3.5 seconds was introduced to account for hemodynamic response lag.

Empirical EEG-fMRI data set

For the qualitative comparison of the proposed model behavior in terms of alpha-BOLD correlation, we analyzed a large 72 subjects (mean age: 31.4, range: 18.3 – 50.6, 36 males and 36 females) empirical EEG-fMRI data set acquired in the Central European Institute of Technology (CEITEC) in Brno, Czech Republic.

Data acquisition and preprocessing

Participants underwent a 20 minutes eyes-closed resting-state EEG-fMRI recording session. Specific details about the data acquisition and preprocessing can be found in our previous study (Jiricek et al., 2025). In short, the functional MRI was acquired via a multiband multi-echo EPI sequence (TR = 650 ms, TE = 14.60/33.56/52.52 ms, 48 slices, slice thickness 3 mm). EEG data were recorded at 1000 Hz sampling frequency using a 256-channel MR-compatible EGI Hydrocell electrode net, along with ECG and breathing signals. Functional MRI data were preprocessed using SPM12 (Penny et al., 2011) and in-house scripts, including spatial realignment, echo fusion via tSNR-weighted averaging, and artifact regression with RETROICOR (Glover et al., 2000) using ECG and breathing signals. Additional preprocessing included orthogonalizing the grey matter signal to potential artifacts (e.g., head motion, white matter/CSF PCA components) and applying a low-pass filter (cut-off 0.09 Hz). The voxel-wise grey matter BOLD time series, originally at a voxel size of 3×3×3 mm, were interpolated using nearest-neighbor interpolation to align with the 6mm regular grid of the EEG source model (described further in the text). This step was necessary to be able to compute local EEG alpha-BOLD coupling. Raw EEG data were preprocessed using a fully-automated pipeline (Liu et al., 2017, 2018; Marino et al., 2019) with MATLAB functions and toolboxes such as SPM (Penny et al., 2011), Fieldtrip (Oostenveld et al., 2011), and EEGLAB (Delorme & Makeig, 2004) toolboxes, starting with main artifacts removal (FASTR for gradient artifacts (Niazy et al., 2005) and adaptive optimal basis set (Marino et al., 2018) for ballistocardiogram artifacts). Bad

channels were identified based on low correlation and high variance in non-physiological frequency bands and interpolated using neighboring channels. EEG data were then filtered (1–80 Hz), and ICA (FastICA) was applied to remove artifacts like EOG and EMG based on correlation with reference signals, power spectrum similarity to 1/f, and kurtosis. Finally, we filtered the EEG data to alpha frequency band (8–12 Hz) and rereferenced to average reference.

Alpha-BOLD correlation

Since we model local microcircuit dynamics, we decided to compute alpha-BOLD correlation on the source-level EEG signals obtained by the very same analytical pipeline as in (Jiricek et al., 2025). Briefly, to estimate brain activity sources, we implemented a source localization pipeline using individual T1 images segmented into 12 compartments (Taberna et al., 2021), followed by head model creation. The source model was generated in the brain grey matter with a grid size of 6 mm. The leadfield matrix was computed using a finite element method (FEM) solver, and sources were estimated with the eLORETA inverse algorithm (Pascual-Marqui et al., 2011). To estimate a single EEG envelope time series, we combined dipole moment components in the three Cartesian axes by assuming freely rotating dipole directions as in (Jiricek et al., 2025). We further followed typical processing steps, including downsampling the EEG envelope to the BOLD TR, convolution with the canonical HRF, and bandpass filtering (0.008–0.09 Hz). For each subject and source model position, the BOLD time series was correlated with the alpha regressor using Pearson's correlation. All visualizations were performed using the BrainNet Viewer tool (Xia et al., 2013).

Code Availability

All code used in this study is openly available on GitHub at the following link: https://github.com/vscChien/EEGBOLDmodeling.

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Supplementary Figures

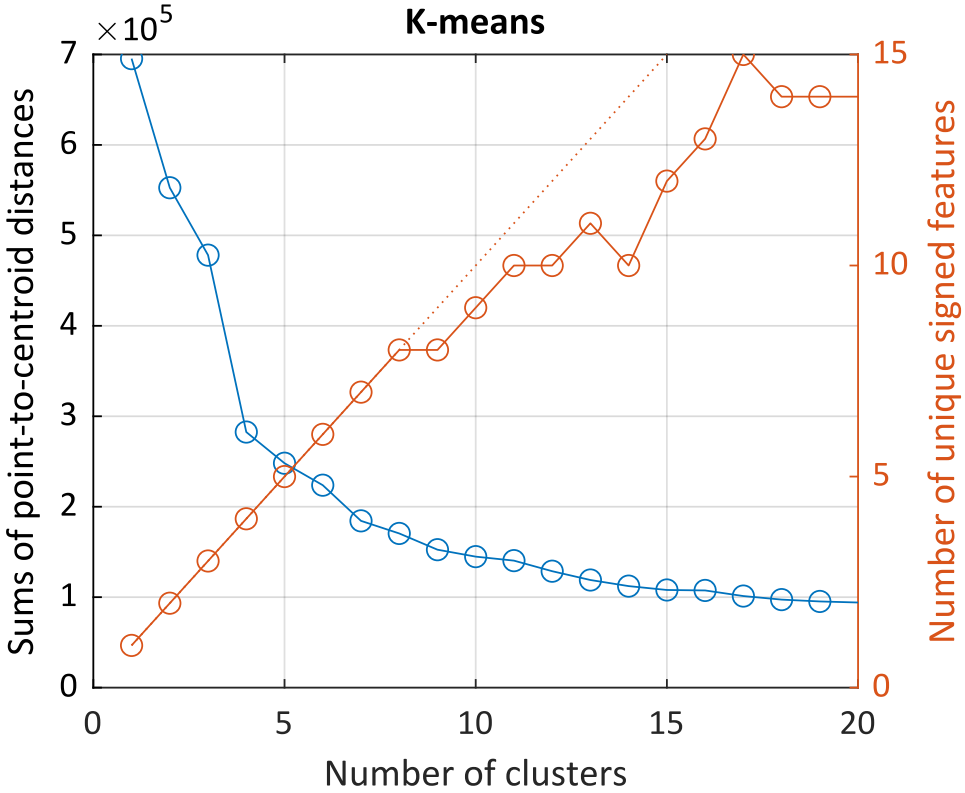

Figure S1. Determining the optimal number of K-means clusters. The K-means algorithm is applied to cluster z-scored power spectra (0.5–50 Hz) within the input space. The blue curve indicates the sum of point-to-centroid distances as a function of the number of clusters, k. The red curve represents the number of unique signed features across different values of k. A signed feature is defined as a [5×1] boolean vector that reflects the direction of mean power change (0: decrease, 1: increase) across delta, theta, alpha, beta, and gamma frequency bands, relative to the baseline. Choosing k = 8 maximizes the number of clusters without duplicating signed features while keeping the sum of point-to-centroid distances low.

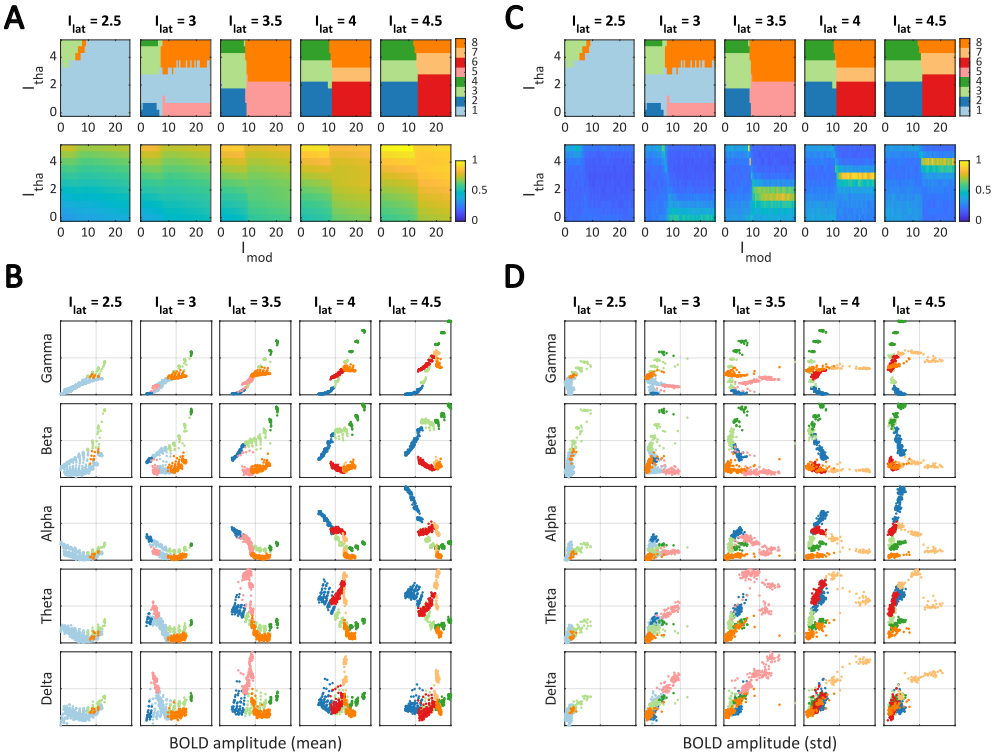

Figure S2. Relationship between EEG bands and BOLD (mean and standard deviation). (**A**) K-means clusters (top row, same as in Figure 2B) and the mean BOLD amplitude (bottom row). (**B**) Scatter plots showing the relationship between gamma, beta, alpha, theta, and delta EEG band powers (from top to bottom) and the mean BOLD amplitude. Both mean BOLD amplitude (x-axis) and EEG band powers (y-axis) are normalized to the range [0–1]. The scatter plots and clusters are represented using the same color scheme. (**C**, **D**) Same as (**A**) and (**B**), but for the standard deviation (std) of the BOLD amplitude instead of the mean.

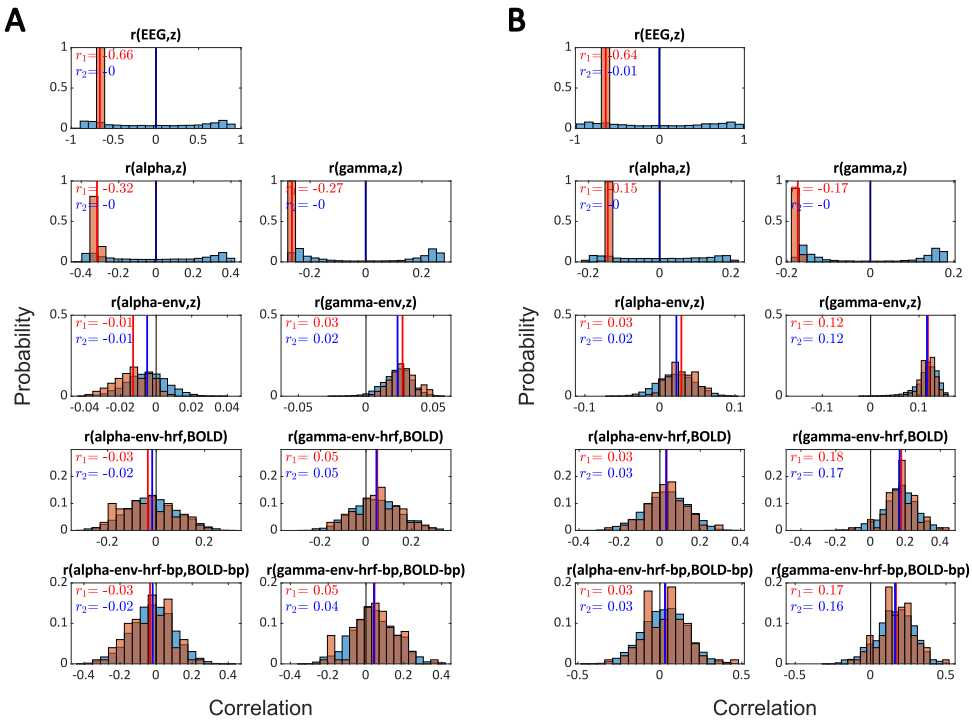

Figure S3. Analysis of dipole effect on EEG-BOLD correlation under constant input conditions. This analysis examines the two input conditions from Figure 4B: (**A**) input condition [I_{lat}, I_{mod}, I_{tha}] = [4.5, 17, 0.5], and (**B**) input condition [I_{lat}, I_{mod}, I_{tha}] = [4.5, 14, 4]. The correlation distribution r is calculated across 100 simulations of 10 minutes, each using the default dipole setting (orange histogram, with mean correlation r_1 shown by the red vertical line) and 100 randomized dipole settings per simulation (totaling 10,000 simulations, blue histogram, with mean correlation r_2 shown by the blue vertical line). Abbreviations: 'EEG' denotes the simulated EEG signal, 'z' refers to the neuronal input for the Balloon-Windkessel model, 'alpha' and 'gamma' represent the band-pass filtered signals at 8–12 Hz and 35–45 Hz, respectively, '-env' indicates the envelope (amplitude) of the filtered signal, '-hrf' is the hemodynamic response function output of the Balloon-Windkessel model, and '-bp' is the band-pass filtered signal at 0.008–0.09 Hz.

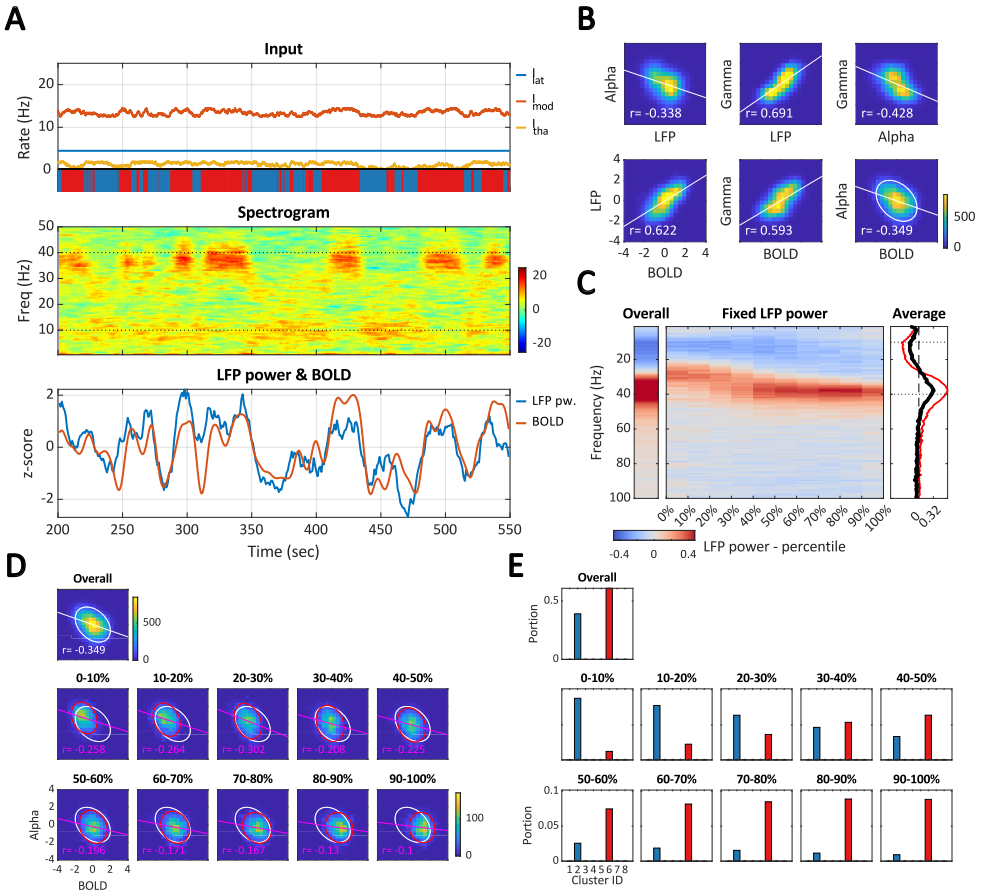

Figure S4. Example 1: alpha-gamma switching This example uses varying inputs confined to the same range as in Case 2 in Figure 5A: I_{lat} = 4.5, I_{mod} = [12.5–14.5], and I_{tha} = [0–2]. (**A**) The inputs primarily alternate between Clusters 2 (blue stripes) and 6 (red stripes), leading to alpha-gamma band switching in the spectrogram. (**B**) The alpha-LFP correlation, gamma-alpha correlation, and alpha-BOLD correlation are all negative (cf. Figure 6B). (**C**) The global (overall, red curve) and the average local (fixed-power, black curve) correlations are aligned. (**D**) Both global and local correlations are consistently negative. (**E**) Cluster 6 contributes more to higher LFP power than Cluster 2.

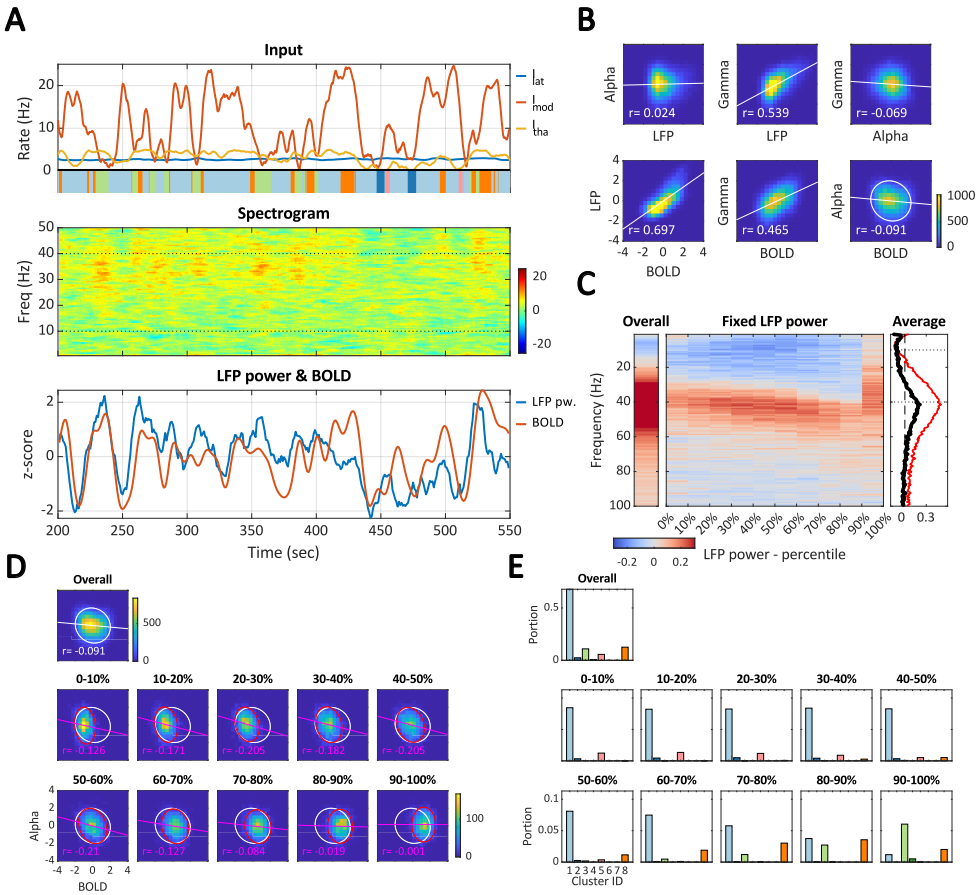

Figure S5. Example 2: smooth external input. This example uses smoothed, varying inputs within the same range I_{lat} = [2.5–3], I_{mod} = [0–25], and I_{tha} = [0–5] as in Figure 6. (**A**) and (**E**) visually resemble Figure 6A and E. (**B**) However, in this case, the gamma-alpha correlation and alpha-BOLD correlation are negative (cf. Figure 6B). (**C**) As a result, both the global (overall, red curve) and mean local (fixed-power, black curve) correlations in the alpha band are negative (cf. Figure 6C). (**D**) Both global and local correlations are consistently negative.

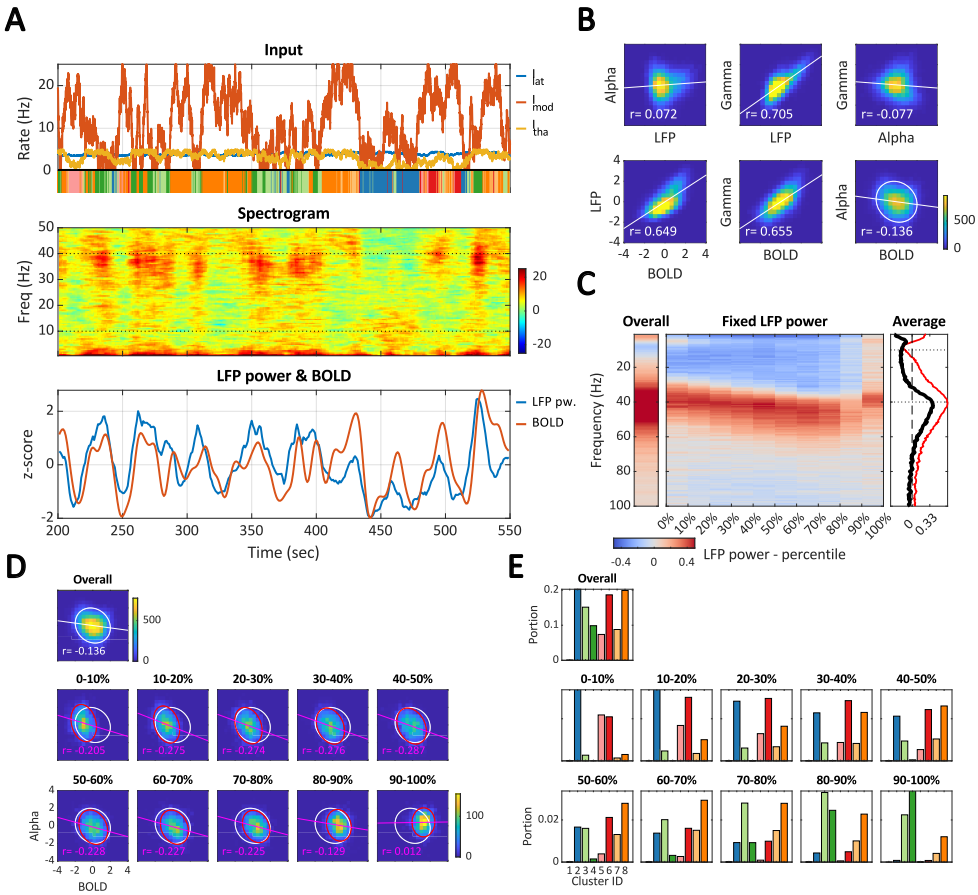

Figure S6. Example 3: increased lateral input. This example uses stronger I_{lat} compared to Figure 6: I_{lat} = [3.5–4.5], I_{mod} = [0–25], and I_{tha} = [0–5]. (**A**) and (**E**) The inputs cover a greater number of clusters compared to Figure 6A and E, and the spectrogram displays stronger contrast between spectral patterns due to the increased lateral input. (**B**) In this scenario, the gamma-alpha correlation and alpha-BOLD correlation are negative (cf. Figure 6B). (**C**) Consequently, both the global (overall, red curve) and mean local (fixed-power, black curve) correlations in the alpha band are negative (cf. Figure 6C). (**D**) Both global and local correlations are consistently negative.

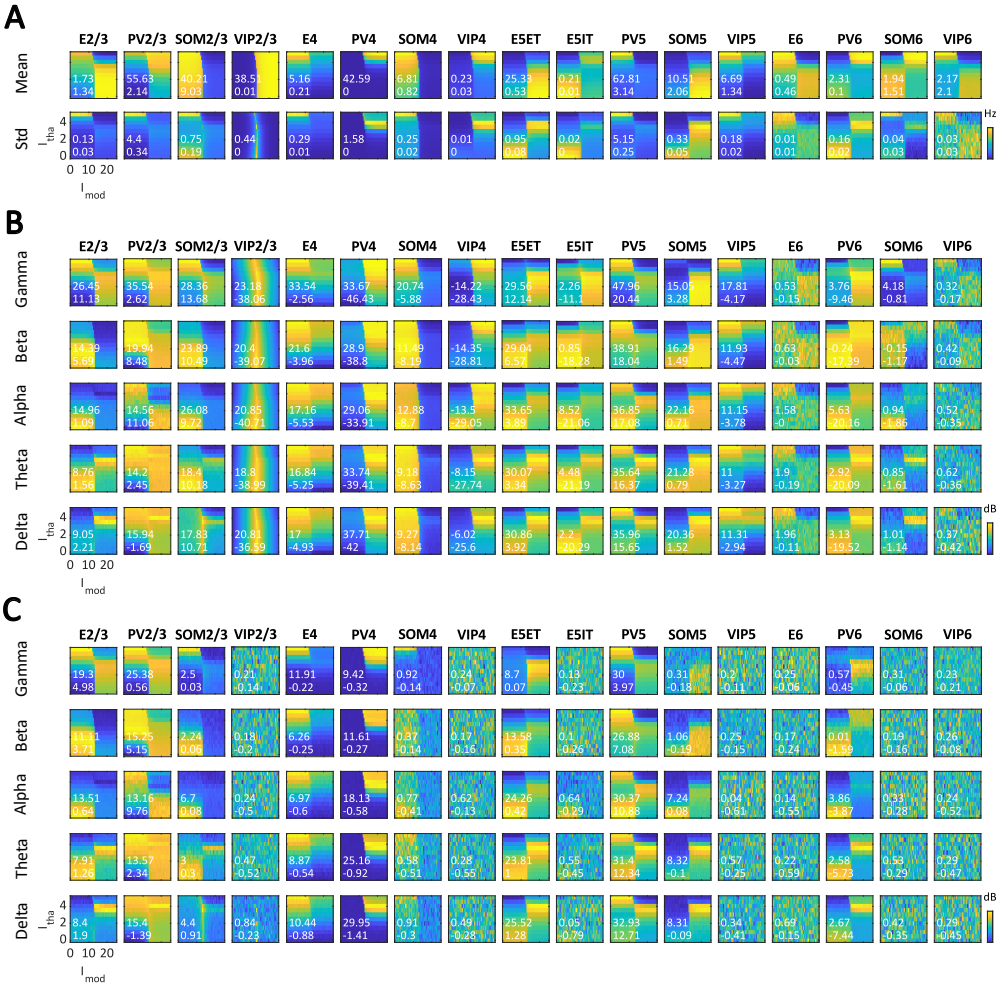

Figure S7. Population-level firing rates and power spectra. (**A**) Mean (top row) and standard deviation (bottom row) of firing rates at input range I_{lat} = 4.5, I_{mod} = [0–25], and I_{tha} = [0–5]. (**B**) Baseline-corrected power at five frequency bands (delta, theta, alpha, beta, and gamma, arranged from bottom to top rows) of the firing rates. (**B**) Baseline-corrected powers of the PSPs from all populations to the excitatory populations. The white text indicates max and min values.

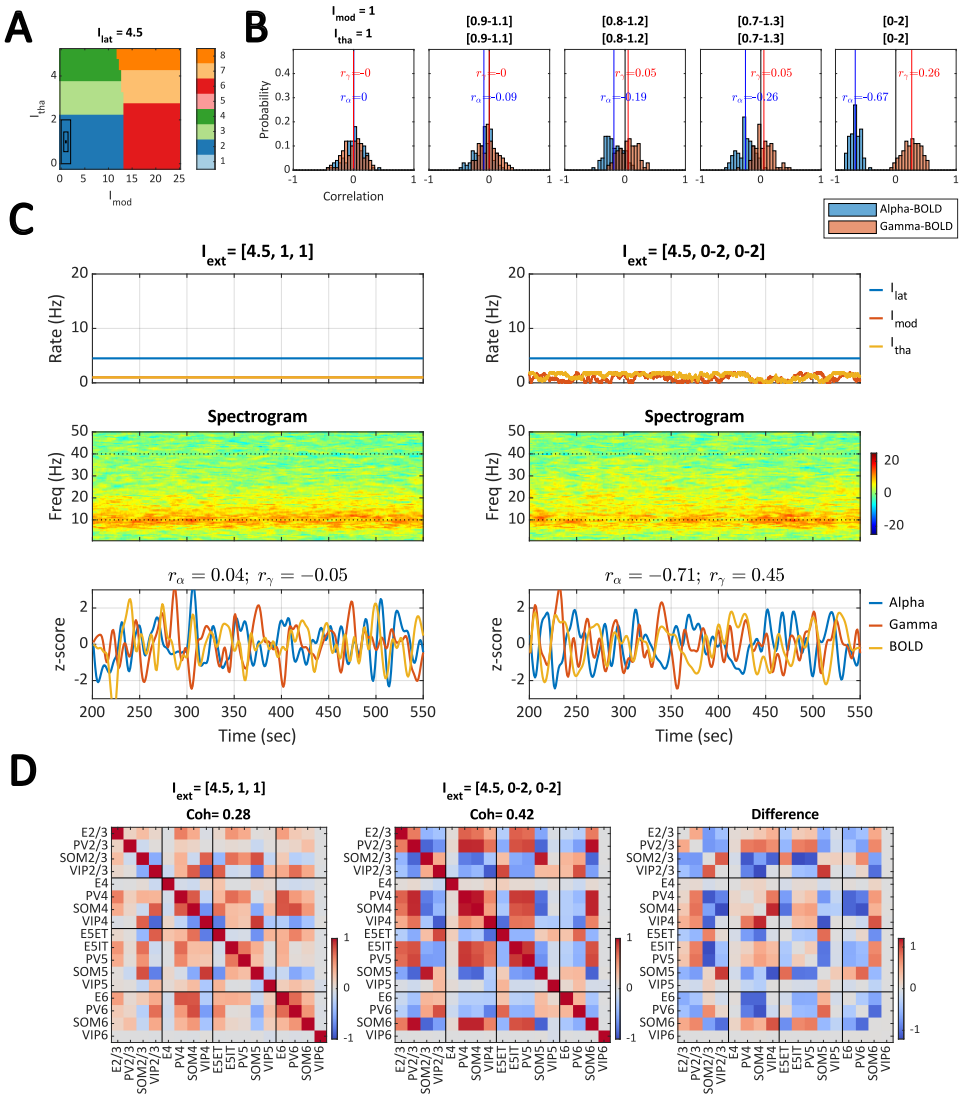

Figure S8. Effect of external input variability on EEG-BOLD correlation (cf. case 1 in Figure 5). (**A**) K-means clusters (same as in Figure 2**B**) within the input space I_{lat} = 4.5, I_{mod} = [0–25], and I_{tha} = [0–5]. The effect of external input variability (i.e., common driving inputs to specific populations) on alpha-BOLD and gamma-BOLD correlations is examined by incrementally increasing the input ranges (indicated by the black rectangles). The progression starts from the constant input condition (I_{mod} = 1 and I_{tha} = 1) to the varying input condition (I_{mod} = [0–2] and I_{tha} = [0–2]), as shown in Figure 5, case 1. (**B**) Histograms of alpha-BOLD (blue) and gamma-BOLD (orange) correlations across 100 runs for each step of the varying input range. The gradual increase in mean alpha-BOLD r_α correlation and mean gamma-BOLD correlation r_γ is evident, so only the first few steps and the final step are displayed. (**C**) Example time series from a single 10-minute run under the constant input condition (left) and the varying input condition (right). (**D**) Mean correlation of the firing rates of 17 populations under the constant input condition (left), the varying input condition (middle), and the difference between the two conditions (right). The populational coherence (Coh) is calculated as the mean absolute values of the correlation matrix (excluding the diagonal part).

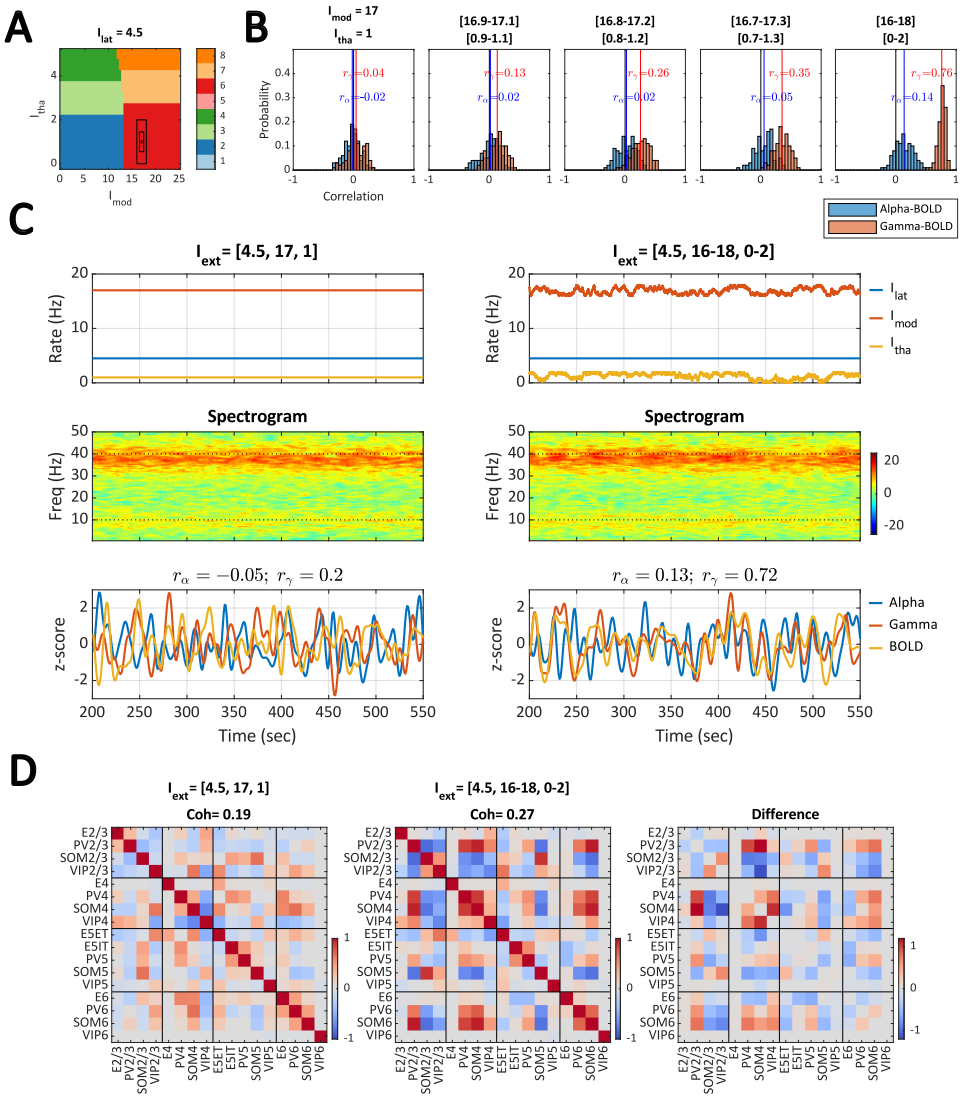

Figure S9. Effect of external input variability on EEG-BOLD correlation (cf. case 3 in Figure 5). (**A**) K-means clusters (same as in Figure 2**B**) within the input space I_{lat} = 4.5, I_{mod} = [0–25], and I_{tha} = [0–5]. The effect of external input variability (i.e., common driving inputs to specific populations) on alpha-BOLD and gamma-BOLD correlations is examined by incrementally increasing the input ranges (indicated by the black rectangles). The progression starts from the constant input condition (I_{mod} = 17 and I_{tha} = 1) to the varying input condition (I_{mod} = [16–18] and I_{tha} = [0–2]), as shown in Figure 5, case 3. (**B**) Histograms of alpha-BOLD (blue) and gamma-BOLD (orange) correlations across 100 runs for each step of the varying input range. The gradual increase in mean alpha-BOLD correlation r_α and mean gamma-BOLD correlation r_γ is evident, so only the first few steps and the final step are displayed. (**C**) Example time series from a single 10-minute run under the constant input condition (left) and the varying input condition (right). (**D**) Mean correlation of the firing rates of 17 populations under the constant input condition (left), the varying input condition (middle), and the difference between the two conditions (right). The populational coherence (Coh) is calculated as the mean absolute values of the correlation matrix (excluding the diagonal part).