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Talk Title:
Spatial-Selective Synaptic Homeostasis Accounts for a Graded Response Propagation Across Distance During Wakefulness

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Abstract

Auditory stimuli with subjective significance can arouse a sleeping subject, very much like a baby's cry awakens the parents, while innocuous sounds can go unnoticed without disrupting sleep. This perceptual switch occurring during the sleep–wake cycle is accompanied by physiological changes. For instance, the electrical activity of the cortex shifts from high-amplitude-low-frequency fluctuations during NREM sleep to low-amplitude-high-frequency components during wakefulness [1]. Thus, the ratio of high over low frequency content of the signals is larger during wakefulness than NREM sleep [2]. Also, the distribution of intra-/extracellular signals shifts from a bimodal to a unimodal distribution from NREM sleep to wakefulness [1]. Moreover, experimental evidence suggests that the conductance of excitatory synapses downscales during NREM sleep to compensate the net increase in strength taking place during wakefulness due to synaptic plasticity, a hypothesis known as synaptic homeostasis hypothesis [3, 4]. In spite of these changes, neurons in the primary auditory cortex show comparable responses during NREM sleep and wakefulness when pure tones are delivered to rats and primates [2, 5]. Nevertheless, auditory responses in higher-order cortical areas in rats and humans are attenuated during NREM sleep as opposed to what happens in primary auditory cortex [6, 7].

We have used a computational neural-mass model (see Figure 1 for the schematic) to investigate what mechanisms can explain differences in neural responses across cortical distance and brain state. The model describes two cortical columns, each consisting of one pyramidal and one inhibitory population, to model the population firing rate signals [8]. We modeled the psychometric function describing the relationship between the input strength to the pyramidal population in one of the cortical columns (perturbed population) and the input response by the pyramidal population in the other cortical column (unperturbed population) as follows. First, the perturbed population was subject to an external input modeled as a brief square pulse. Next, we computed an independent t-test comparing the poststimulus versus prestimulus firing rate signals of the unperturbed population at every time point and formed clusters of consecutive time points above a critical t-value, called t-cluster statistic. Then, a Monte Carlo method was carried out to obtain the significance of the t-cluster statistics. Exhibiting a significant t-cluster statistic indicated an input response in the unperturbed column. After, the procedures were

repeated 20 times for various input strengths to model the psychometric function of the unperturbed population. Finally, the psychometric functions were fitted by a cumulative distribution function for the two-parameter Weibull distribution.

Following the synaptic homeostasis hypothesis, upscalying of the excitatory conductances allows us to switch the model's dynamics from NREM sleep to wakefulness. Simulated spontaneous population firing rate signals exhibit the idiosyncratic dynamics of the cortex mentioned before (see Figure 2). Interestingly, we have found that the ratio of the inter- to intra-conductance of cortical excitatory synapses, called β, should raise to facilitate the propagation of the input to the unperturbed column during wakefulness as opposed to blockage during NREM sleep (see Figure 3). The psychometric functions of the unperturbed population during wakefulness indicate that propagation of response to lower input strengths is not graded for $\beta = 1$ compared to NREM sleep, even when potentiating the excitatory conductances from 2 to 5. Importantly, increasing β induces a significant response in the unperturbed population that leads to a shift of the psychometric function towards lower input strengths.

Our results suggests the existence of a spatial-selective synaptic homeostasis policy [9], whereby potentiation of excitatory conductances during wakefulness occurs preferentially between distant neural networks over local and recurrent connections.

keyword: synaptic homeostasis hypothesis; psychometric function; neural-mass model; wakefulness; NREM sleep

Figures

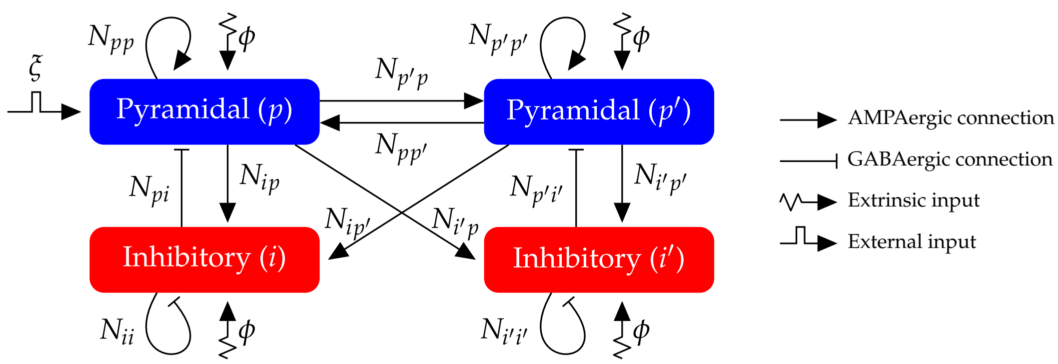

Figure 1: Diagram of the neural mass model. Neural mass model describing two mutually coupled cortical columns. N_{mn} is the mean number of synaptic connections from a presynaptic population n to a postsynaptic populations m. The solid arrow and bar line correspond to excitation and inhibition connectivity, respectively. Coupling between pyramidal and inhibitory populations are mediated through AMPAergic and GABAergic connections, respectively. The noise ϕ is simulated independently for each cortical population as a Gaussian process with zero autocorrelation time constant and zero mean. ξ represents the transient external input impinging only in one cortical column for 100 ms.

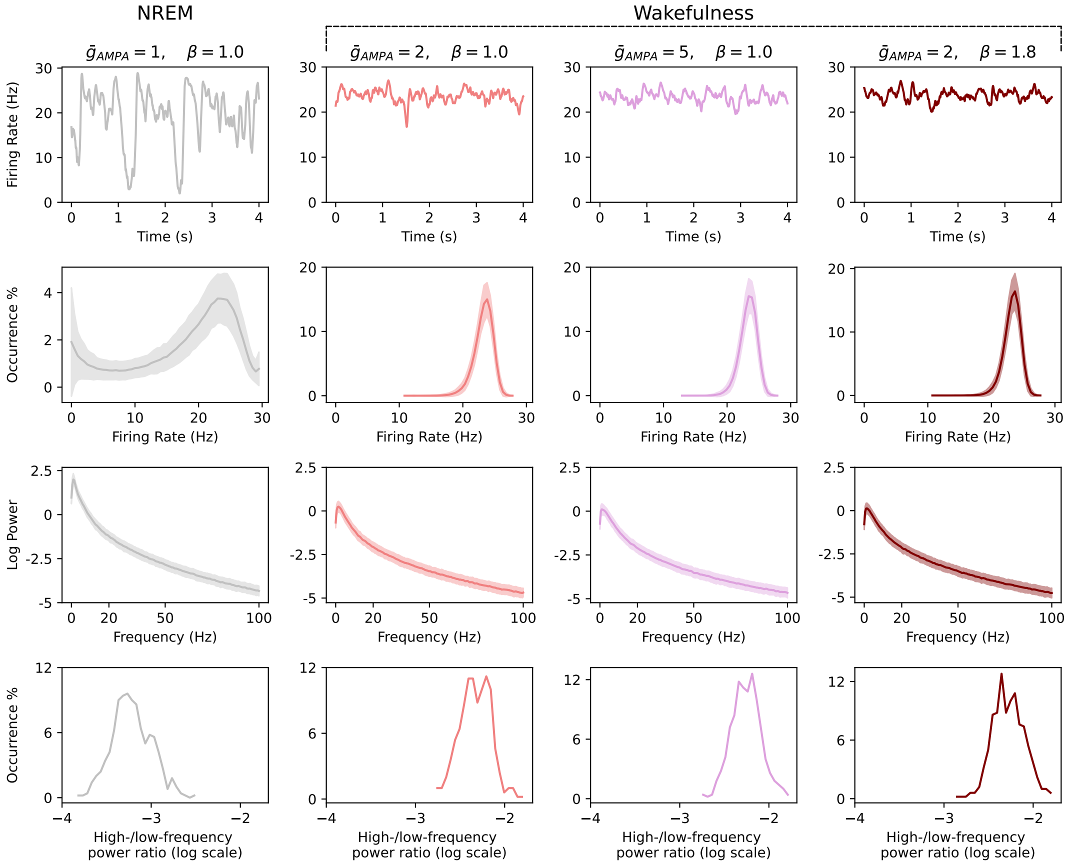

Figure 2: Spontaneous activity ($\xi = 0$) during NREM sleep and wakefulness. Simulated population firing rate signals from one random simulation (first row) showing large amplitude fluctuations during NREM sleep (first column). Lower amplitude fluctuations appear during wakefulness (second to fourth columns). The distribution of the population firing rate signals (second row) is bimodal during NREM sleep and unimodal during wakefulness. The third row represents the average power spectrum density (PSD) of signals during NREM sleep and wakefulness. The fourth row represents the distribution of high-/low-frequency (where high is above 30 Hz and low is below 4 Hz) power ratio in the signals during NREM sleep and wakefulness. The shaded area corresponds to the standard deviation of the mean of PSD over 500 simulations during the corresponding brain state.

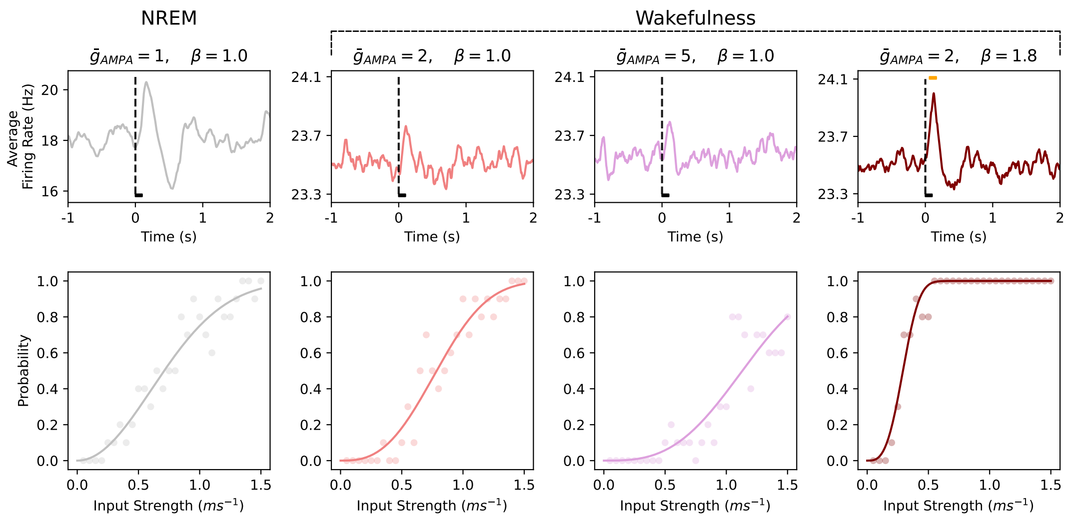

Figure 3: Psychometric functions of the unperturbed population in response to various input strengths. The first row represents the average population firing rate signal of unperturbed population across 500 simulations for NREM sleep (first column) and wakefulness (second to fourth columns) for one of 20 repetitions when the external input strength to the perturbed population is $\xi = 0.6\ \text{ms}^{-1}$. Orange horizontal bars show the location and length of significant evoked responses ($p < 0.0005$). Stimulus onset and duration are represented by a dashed vertical and black horizontal line, respectively. The second row shows the probability (out of 20 repetition) of observing a significant response in the unperturbed population when the perturbed population is subjected to various input strengths during NREM sleep and wakefulness. Increasing β induces a significant response in the unperturbed population that leads to a shift of the psychometric function towards lower input strengths (fourth column).

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