INCREASING SPECIFIC CELL TYPE SYNAPTIC STRENGTHS DRIVES DECORRELATION OF NEURAL ACTIVITY IN A CORTICAL NETWORK MODEL

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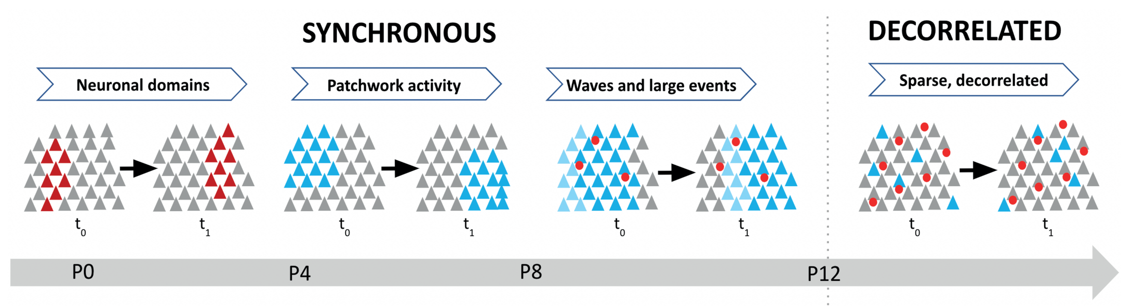
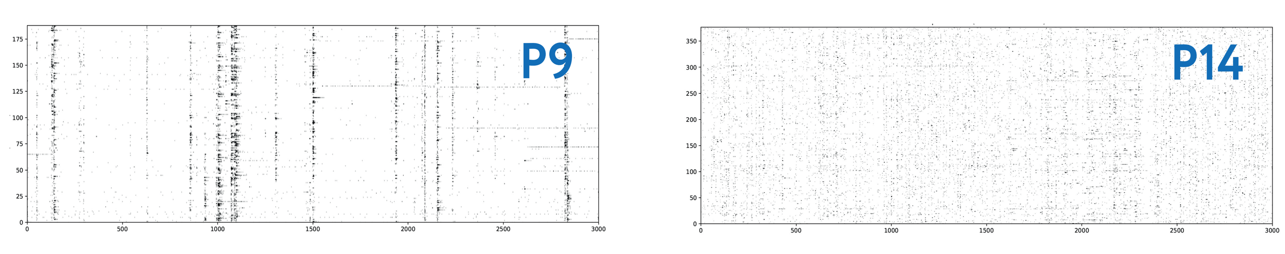
INTRODUCTION

During cortical development, neural activity transitions from highly synchronized to sparse, decorrelated firing. Sparse activity is more efficient and characteristic of the mature cortex. This developmental progression is seen in both humans and rodents, but the driving mechanisms are not understood.[1]



This transition is marked by a decrease in spike train correlation[1], little change in the network's firing rate, and a decrease in the duration of up & down states[2].

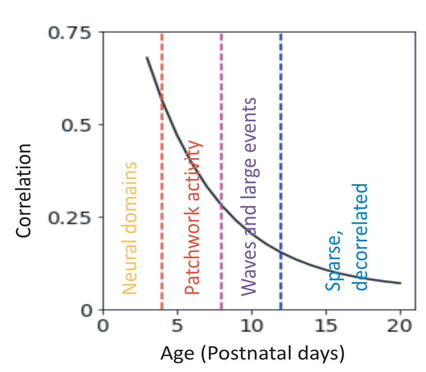


Mouse cortical activity at postnatal days 9 and 14. Data from Portera-Cailliau lab

What are the neural mechanisms underlying decorrelation?

Through computational modeling, we investigated the effects of increasing excitatory and inhibitory connection strengths[3], as well as excitatory excitability, on firing rate and correlation.

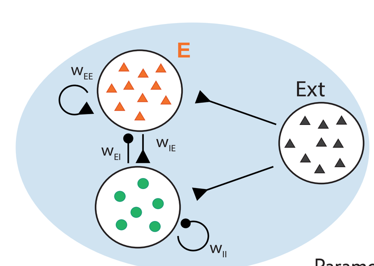
We explored both rate and spiking models of the cortex. The spiking model gave insights into spike train patterns on a shorter time scale, while the rate model allowed for exploration of up/down states on a longer time scale.



1. DECORRELATION IS DRIVEN BY INCREASED INHIBITION IN NON-SPATIAL SPIKING MODEL

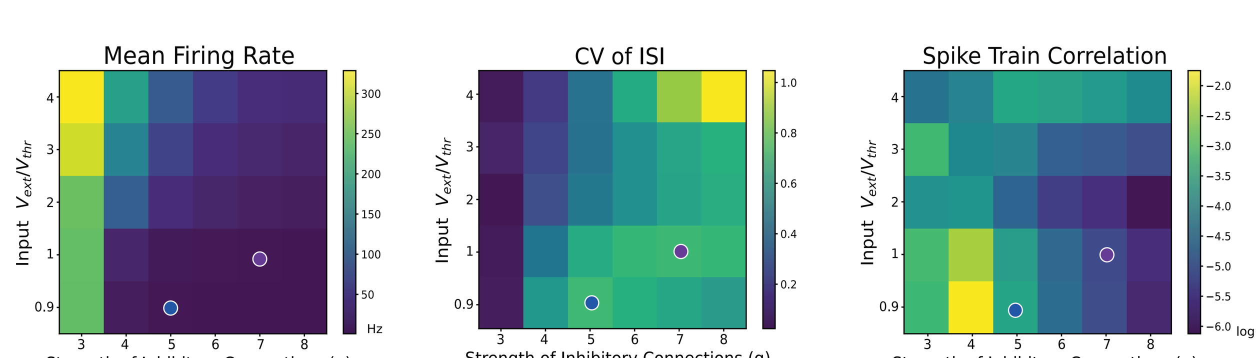
Two population spiking model with random, sparse connectivity

$$\tau_i \frac{dv_i}{dt} = -v_i + \sum_i w_{ij}\tau_i \sum_k \delta\left(t - t_j^k - D_{ij}\right)$$

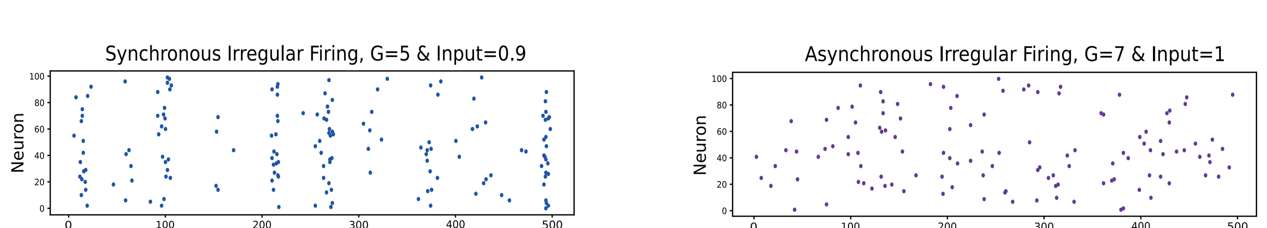


Parameters and equations adapted from Brunel[4]

Manipulation of inhibitory connection and feedforward input strengths



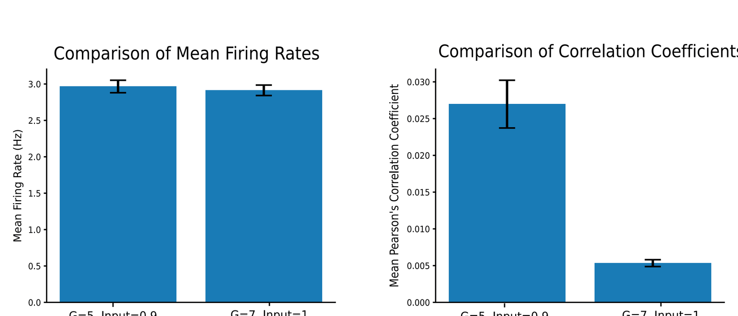
Firing rate, regularity of spike occurences (mean coefficient of variation of interspike intervals), and synchrony (Pearson's correlation coefficient) measured across a range of parameters. Realistic, irregular systems are marked by a high CV (>0.3). Synchronous activity is characterized by high spike train correlation and oberved in both regular and irregular firing regimes. ● indicates parameter set used to generate figures below.



Increased inhibition is sufficient to drive decorrelation within biologically realistic constraints

In neonatal rodents, cortical firing rate does not change dramatically during development.

We identified a case in which increasing the strength of inhibitory connections was sufficient to drive a decrease in spike train correlation while firing rate remained constant.

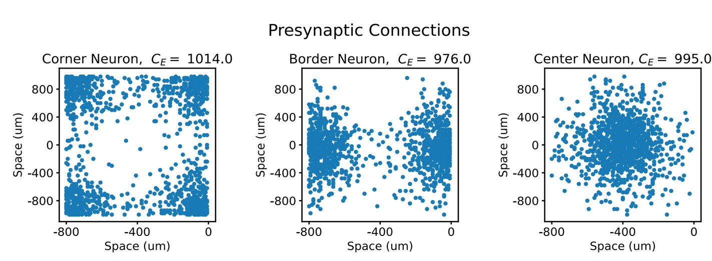


2. STRONG EXCITATION SUPPORTS SYNCHRONOUS WAVES IN SPATIAL SPIKING MODEL

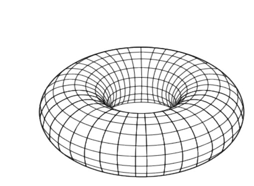
We adapted the spiking model such that neuronal connections were spatially organized, such that the probability of connection decays with distance.

Spatial Network Parameters

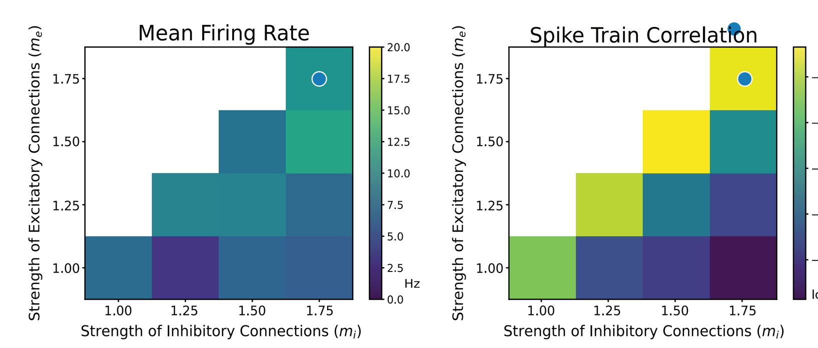
Parameter	Excitatory Population	Inhibitory Population
Number of Neurons	10,000	10,000
Connections per Neuron	1,000	1,000
Area of Simulated Space	4 mm^2	4 mm^2
Connection Scale	0.266 mm	0.230 mm
Max. Connection Probability	0.7	1



A torus was chosen as a mathematical approximation of the spatial structure in the cortex



Increasing recurrent excitation drives synchronous activity

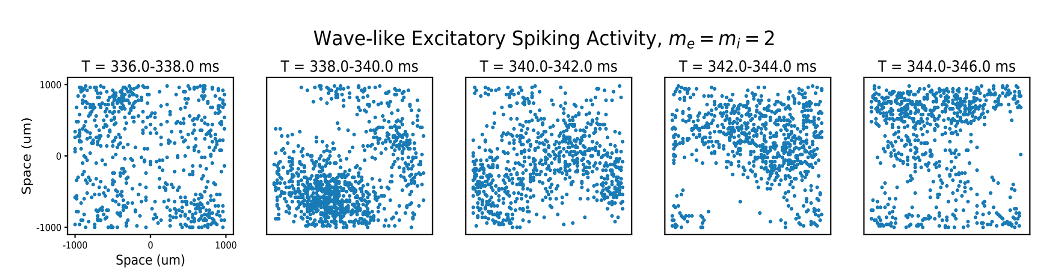


Effect of recurrent excitatory and inhibitory connection strengths on correlation in spatially organized system.

Firing rate was normalized by changing input strength within the range 0.8-1.4.

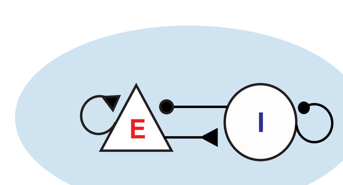
● indicates parameter set used to generate figure below

Strongly connected balanced systems support wave-like actvity during synchronous events



Wave-like activity was observed for balanced and nearly balanced systems with strong excitation and inhibition. A localized input was applied for 100 ms to the center of the system to drive spiking activity.

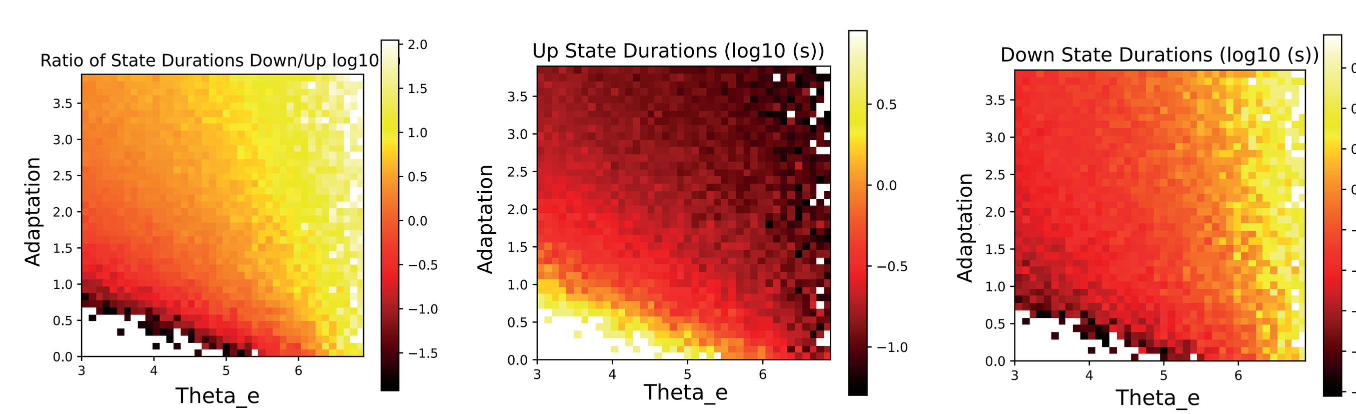
3. DECORRELATION IS NOT DRIVEN BY EXCITABILITY ALONE IN POPULATION RATE MODEL



$$\tau_e \frac{dE}{dT} = -E + \phi(W_{ee}E - W_{ei}I - a + \epsilon_E(t) - \theta_e)$$
$$\tau_i \frac{dI}{dT} = -I + \phi(W_{ie}E - W_{ii}I + \epsilon_I(t) - \theta_i)$$
$$\tau_a \frac{da}{dT} = -a(t) + B * E$$

Equation based on Jercog et. al (2017) Elife

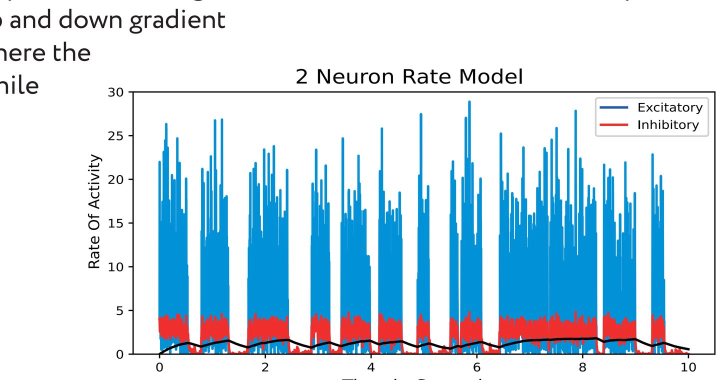
E and I are the average rate of firing activity in the excitatory and inhibitory neuron populations. The rate of change in activity is a function of synaptic weights strengths (Wee, Wei, Wie, Wii), intrinsic adaptation (a), and a threshold level of synaptic input required to initiate activity (theta_e).



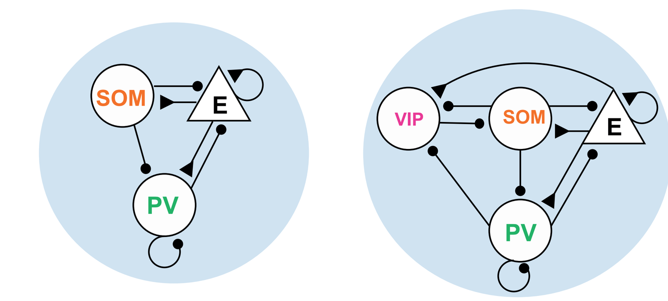
We looked at how changes in excitability (theta_e) affect up/down duration in early developmental stages, where the excitability of excitatory neurons decreases, we first replicated Jercog's[2] analysis and then examined points that had an increased excitability threshold.

Change in adaptation strength and excitation threshold tend to have an opposite effect on the duration of up states versus down states due to the similar, but opposite duration gradient in the chosen threshold-adaptation parameter space. A subtle difference in the up and down gradient curvature, however, does create a limited space where the ratio of down to up durations remains the same while durations decrease.

Initial findings suggest that increasing theta_e does not significantly reduce up and down state durations while maintaining ratio and average firing rate, indicating excitability alone likely isn't the main driver of decorrelation during development.



4. INCREASED EXCITATION AND INHIBITION CAN LEAD TO SHORTER UP/DOWN STATES IN MULTIPLE CELL MODEL



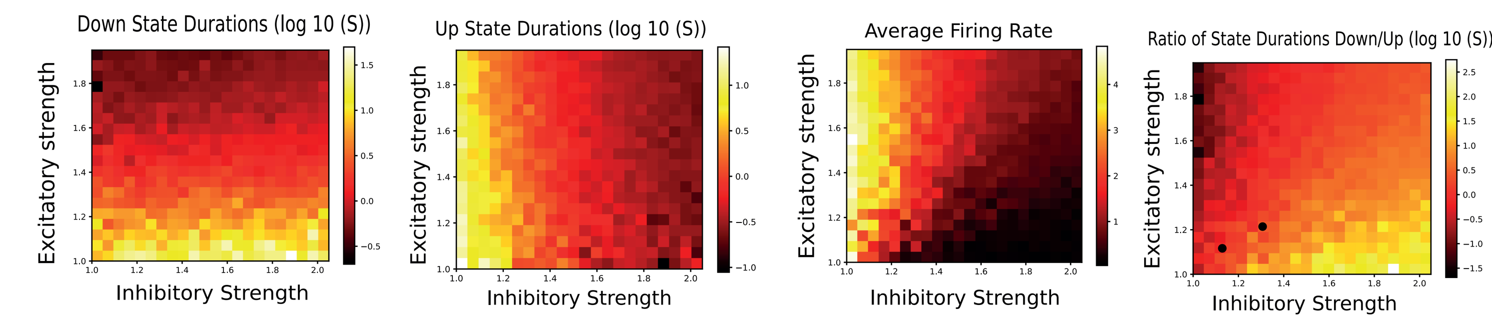
$$\tau_e \frac{dE}{dT} = -E + g_e(W_{ee}E - W_{ep}P - W_{es}S - a + \epsilon_E(t) - \theta_e)_+$$
$$\tau_p \frac{dP}{dT} = -P + g_p(W_{pe}E - W_{pp}P - W_{ps}S + \epsilon_P(t) - \theta_p)_+$$
$$\tau_s \frac{dS}{dT} = -S + g_s(W_{se}E - W_{sv}V + \epsilon_S(t) - \theta_s)_+$$
$$\tau_v \frac{dV}{dT} = -V + g_v(W_{ve}E - W_{vp}P - W_{vs}S + \epsilon_V(t) - \theta_v)_+$$
$$\tau_a \frac{da}{dT} = -a + B * E$$

Inhibitory Neurons
- Somatostatsin expressing neurons (SOM)
- Vasoactive intestinal polypeptide expressing neurons (VIP)
- Parvalbumin fast-spiking interneurons (PV)

Addition of Somatostatin expressing neurons (SOM), Parvalbumin fast-spiking interneurons (PV) and Vasoactive intestinal polypeptide expressing neurons (VIP).

SOM, VIP and PV neurons are types of inhibitiory neurons with different properties.

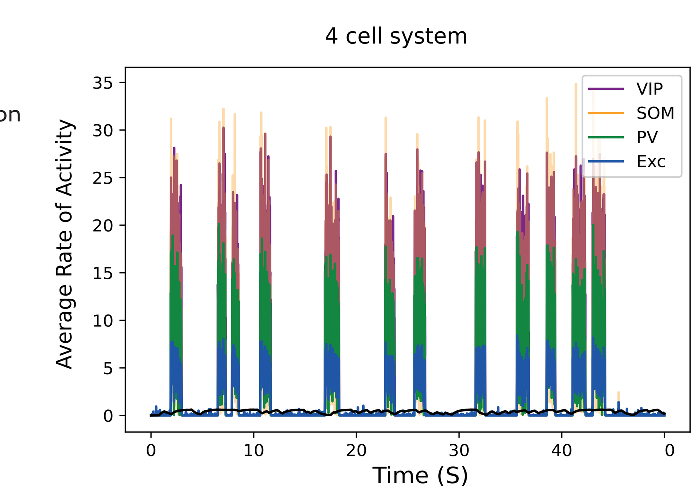
Manipulation of all excitatory and all inhibitory connections in a 3 cell model.



Increasing the strength of excitatory synapses and inhibitory synapses can decrease the duration of up and down while maintaining the average firing rate in a initial simulations. Trajectories that lead to shorter up and down durations, also correspond to a slight decrease in UP state firing rate and a minimal decrease in the down to up ratio, consistent with experimental observations. (Wee = 5, Wep = 0.5, Wes = 0.5, Wpe = 10, Wpp = 1, Wps = 1, Wse = 4., sigma = 2.5, B = 0.)

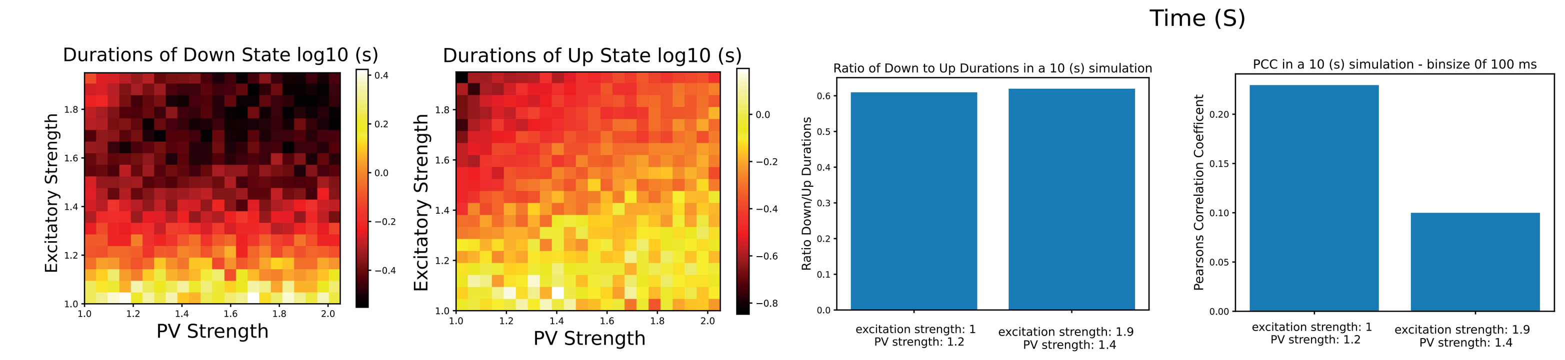
Identification of 4 Cell Synaptic Weights

We were able to identify synaptic weights that yielded up state firing rates that matched roughly experimental firing rates based on and matched known connectivity, in a four cell system.



Manipulation of Excitatory Strengths and PV Strength

Increasing PV strength (including recurrent strength) and excitatory strength led to a more analogous gradient of durations. Notably, the reinforcement of specific inhibitory connections, exerts a substantial influence over alterations in state durations. (Wee=5.5, Wep=0.5, Wsp=0.5, Wpe = 18, Wpp=1, Wps=2, Wse = 8, Wsv=1, Wve=16,Wvp=2, Wvs=1, sigma = 2.5, B = 0)



CONCLUSIONS

1. We developed a sparsely connected spiking model of the cortex. For a biologically realistic set of parameters, we found that increasing the strength of inhibitory connections decreased spike train correlation without changing the system's firing rate.
2. We modified the spiking model to have spatially organized connectivity. This model supported traveling waves and high spike train correlation when excitatory and inhibitory connections were both strong and balanced.
3. We developed a two cell rate model based on Jercog et al.[2] Within biological constraints, we found an increase in excitability alone could not elicit a decrease in up and down state durations while maintaining firing rate and duration ratios.
4. To create a more representative rate model, we incorporated VIP and SOM inhibitory neurons found in the neocortex. Increasing the strength of excitatory and inhibitory connections could decrease global fluctuations and decrease correlation.

References:

1. Golshani et al., J Neurosci. 2009
2. Jercog et al. Elife. 2017
3. Micheva et al., J Comp Neurol. 1996
4. Brunel, J Comput Neurosci. 2000
5. Romero-Sosa et al., J Neurosci. 2021

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