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Optogenetic inhibition reveals large-scale intracortical interactions during early development

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In ferret visual cortex, spontaneous activity prior to eye-opening is organized into large-scale, modular patterns in the absence of long-range horizontal projections. This correlated activity reveals endogenous networks that predict aspects of future orientation selectivity. Previous modelling works have shown that the long-range correlations observed in these networks can arise from purely locally connected neurons through multi-synaptic interactions. Here we seek to explicitly map the structure of cortical lateral interactions through localized perturbations in vivo.

We first constructed a non-linear recurrent neural network model of strongly coupled excitatory and inhibitory units with effective local heterogeneous Mexican hat connections, finding that perturbing a small region of inhibitory neurons exerts a spatially extended influence on the pattern of ongoing activity. Notably, the influence is modular, partially similar in structure to spontaneous activity, and the strength of influence depends on stimulation location.

To test these predictions, we virally expressed GCaMP6s in excitatory neurons and Chrimson-ST in inhibitory neurons in layer 2/3 of young ferret visual cortex, allowing us to optogenetically activate small regions (˜500μm diameter) of inhibitory neurons and simultaneously record widefield calcium activity.

In line with model predictions, local optogenetic inhibitory perturbations propagate through the entire network and induce a reorganization of activity even in areas up to 2mm away from stimulation site. The degree of disruption to the structure of correlations in activity depends on the perturbation location, and can be predicted from stimulation site's overlap with the leading spontaneous principal components (PCs). The variance in optogenetically-perturbed activity patterns only partially overlaps with spontaneous activity space, suggesting a different activity manifold with local disruption.

Our results are consistent with the presence of strongly coupled E and I networks in early cortex, and demonstrate that network behaviour is an emergent property with local activity exerting specific and global influences

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