Functional connectivity analysis in cortical microcircuits: what it can teach us about the architecture of multi-neuronal processing

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In the first part of my talk, I will discuss how functional connectivity analysis in cortical microcircuits can help us understand properties of multi-neuronal computations along the cortical column. Although the work I describe was performed in the mouse, parallel experiments can be performed in other species including primates. In time, such experiments will help to reveal how different aspects of the algorithmic architecture of cortical computations manifest along various branches of the mammalian evolutionary tree.

We used two-photon imaging to record from granular and supragranular layers in mouse primary visual cortex (V1) under spontaneous firing conditions and applied an extension of the spike time tiling coefficient (STTC; introduced by Cutts and Eglen J Neurosci 2014) to map the functional connectivity architecture between pyramidal neurons within and across layers. A significant fraction of intra- and inter-layer pyramidal pairs exhibit statistically significant functional connections, extending to distances ~1mm or more. Neurons with similar tuning functions exhibit a significant bias towards higher inter-neuronal correlations, as expected; however, this bias is weak, suggesting the constitution of functionally connected neuronal ensembles remains largely promiscuous. First-order degree of connectivity groups of individual pyramidal neurons determine the hub structure of area V1 columns, revealing strong small-world characteristics and network robustness in all layers examined. The probability of firing of layer-2/3 pyramidal neurons as a function of co-firing activity across their layer-4 first-order “partners” (their “putative input” group) conform well to ReLU functions, reaching up to probability one for some units. Interestingly, L2/3 neurons with different L4 degrees of connectivity behave differently with respect to information transmission, and with respect to how they couple to internal state modulations, reminiscent of “choroists" vs “soloists" (Okun et al. Nature 2015). Overall, information transmission is best viewed as proceeding from neuronal ensemble to neuronal ensemble; we identified candidate ensembles in layer 4 and layer 2/3 and demonstrated that they exhibit high sensitivity, precision, and specificity for L4 to L2/3 activity transmission. A tentativehypothesis is proposed under which such information encoding ensembles may be regulated by a small number of individual interneurons. In sum, functional connectivity analysis under spontaneous activity conditions reveals a modular neuronal ensemble architecture within and across granular and supragranular layers of mouse primary visual cortex. Furthermore, modules with different degrees of connectivity appear to obey different rules of engagement and communication across the area V1 columnar circuit.

In the second part of my talk, I plan to discuss the crucial role that primate disease models promise to play in bridging the gap between basic research and clinical applications in human medicine. With their genetic, physiological, and anatomical similarities to humans, primates offer a valuable platform for studying complex neuronal circuit diseases and testing potential treatments. Over time primate models will prove to be an invaluable tool for understanding disease mechanisms and for predicting the human response to promising therapeutic interventions. By everaging primate models, researchers can enhance the translational relevance of preclinical studies, ultimately leading to improved outcomes in human health.