The fabric of the neocortex

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The neocortex is responsible for perception, cognition and action. Despite significant advances in our understanding of its structural and functional organization, its underlying computational principles remain largely unknown. The problem lies in understanding how billions of neurons communicating through trillions of synaptic connections orchestrate their activities to give rise to our mental faculties. If there are underlying principles and rules that govern this complexity, then discovering these principles could reduce the impenetrable complexity of the cortex to a manageable scale. One such principle is provided by the hypothesis that the neocortex is composed of repeating circuit motifs that contain numerous cell types wired together according to stereotypical rules which perform canonical computations. I will describe our findings so far towards our quest to determine what constitutes the elementary computational circuit motif in the neocortex, characterize its structure and function, and decipher its canonical computation(s). First, to define the component cell types we use Patch-seq, a method we developed that combines whole-cell patch-clamp recordings and single-cell RNA sequencing. Patch-seq enables linking molecularly-defined cell types to their corresponding morphological, physiological, and functional phenotypes providing a comprehensive cell types classification scheme. Second, to decipher the principles that govern the connectivity of neocortical circuits we employ multiple whole-cell patching and electron microscopy. Third, to discover the mathematical operations implemented by different cell types and the underlying canonical algorithms of cortical circuit, we use machine-learning including deep learning methods and build models from large scale neural recordings using two- and three-photon imaging.