Inferring hidden structure in multi-layered retinal circuits

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Sensory circuits contain multiple cell layers that successively shape neural response properties. Traditionally, understanding the sensory code at a given layer involves building quantitative encoding models that directly map stimulus to response at that layer. However, between stimulus and response often lie multiple intervening layers of circuitry that are neither simultaneously recorded nor explicitly modeled. Excluding such layers limits both biophysical interpretations and computational capacity of encoding models, obscuring our ability to understand how neural circuits give rise to perception.

This problem already occurs in the retina, where signals flow from photoreceptors through bipolar and amacrine cells to ganglion cells. We approximate these transformations with successive stages of linear filtering and nonlinear thresholding, thus modeling the retina as a two layer linear-nonlinear (LN) model, or LN-LN model. We asked whether the parameters of LN-LN models fit to retinal ganglion cells would learn structure resembling properties of the intervening, unrecorded retinal circuitry. To answer this, we developed novel computational methods for learning LN-LN models with very little data. In contrast to previous work, we make no assumptions about the number of hidden first-layer subunits or the structure of subunit nonlinearities.

Using these new methods, we find that LN-LN models yield a better description of the retinal response, demonstrating robust improvement (~53%) in prediction performance over single layer LN models. Moreover, we find a striking resemblance between spatiotemporal filters learned in the model's first layer, and quantitative properties of bipolar cell receptive fields measured experimentally using intracellular recording. These results suggest that our methods for learning LN-LN models are sufficient to uncover biophysical mechanisms underlying nonlinear response properties of the sensory code.

In general, our methods simultaneously infer properties of unrecorded neurons feeding into a population of recorded neurons, from which significant insights into multi-layered sensory computation may be extracted.