Spatial structure and organization of nonlinear subunits in primate retina

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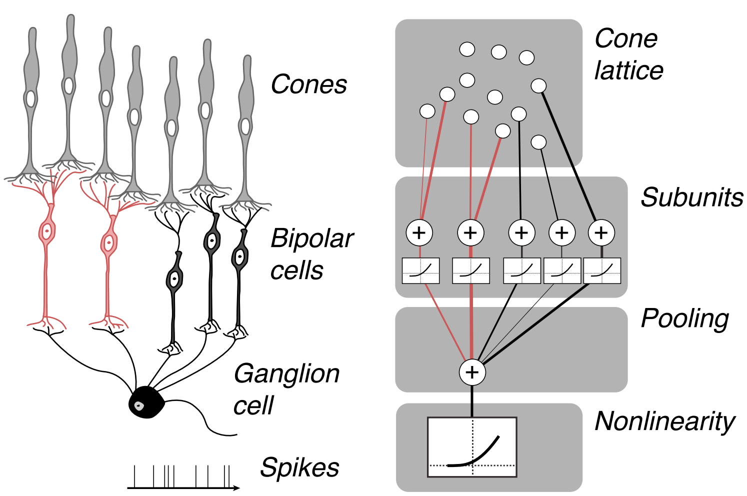
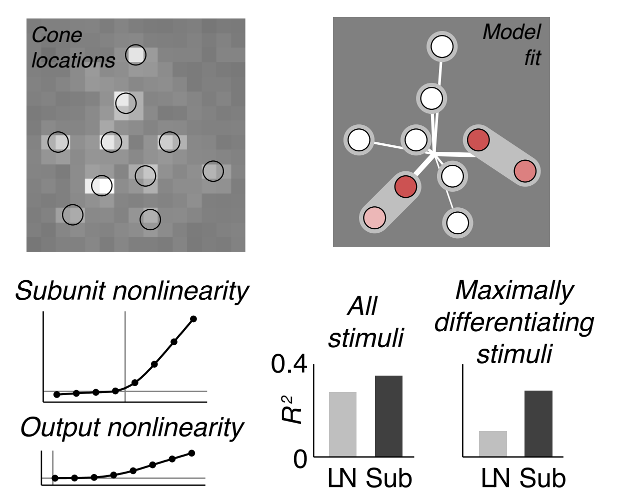
Sensory processing is commonly described using hierarchical cascades of linear and nonlinear operations. For example, in the primate retina, several types of retinal ganglion cells (RGCs) exhibit nonlinear responses to spatially-structured stimuli that can be explained by "subunits" within the receptive field -- localized filters with rectified outputs (Victor and Shapley, 1979). These subunits are hypothesized to reflect the function of bipolar cells that convey cone photoreceptor signals to RGCs, but their structure and function remain incompletely understood. We developed a novel approach to understand subunit computations in the retinal circuitry at single-cell resolution.

Multi-electrode recordings and high-resolution stimuli were used to record from populations of identified RGCs in isolated primate retina while stimulating individual cones. Responses were fitted with a model consisting of two linear-nonlinear stages. The first stage consists of subunits that linearly combine signals from groups of cones followed by a nonlinearity. The second stage is a weighted sum of subunit responses followed by a final output nonlinearity. The assignment of cones to subunits was inferred using a greedy search for assignments that maximized response likelihood. Estimates of weights at both stages, as well as a smooth parameterization of the subunit nonlinearity, were obtained using block coordinate ascent on likelihood.

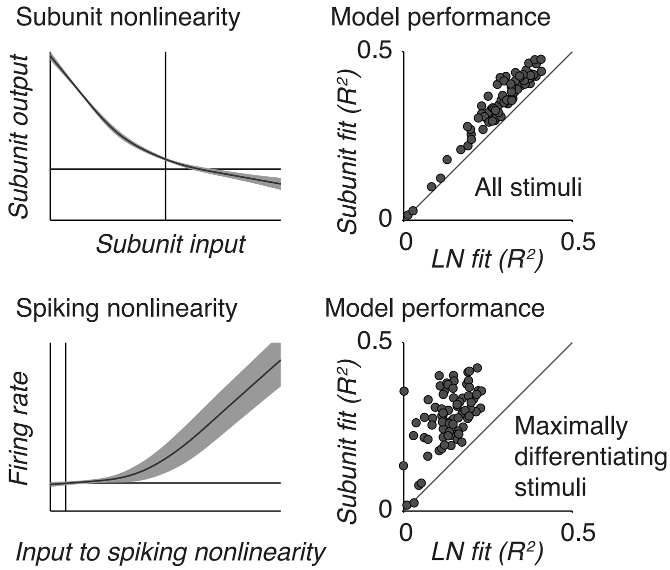
Fitted subunits for ON and OFF midget RGCs revealed varying degrees of rectification. Subunits typically included 1-3 cones, and convergence varied with eccentricity as predicted from anatomical data. The improvement in explained variance of RGC responses was typically 10-20% over a standard linear-nonlinear model for white noise stimuli, but much larger for noise segments that maximally differentiated the models. Additional validation was performed with repeated white noise, sinusoidal gratings, and targeted stimulation of selected pairs of cones. The results provide a picture of nonlinear signaling and circuitry in RGC populations at cellular resolution.



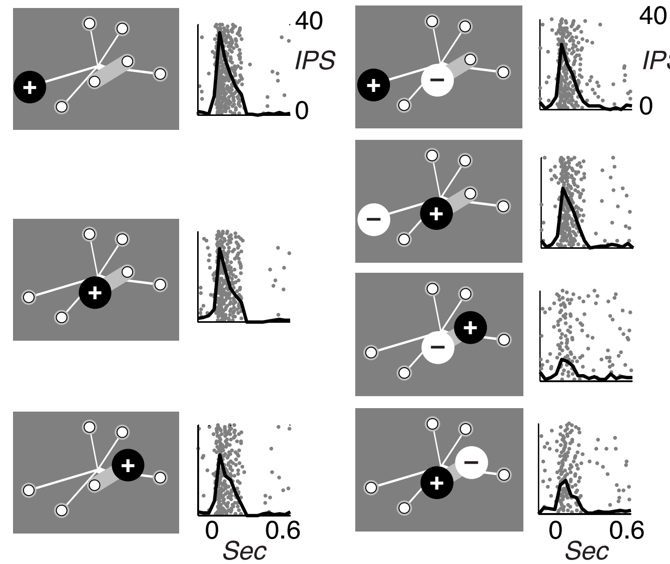
Anatomy and functional model. (Left) Anatomically, each type of primate midget ganglion cell receives input from only one type of bipolar cell, and at mid-peripheral eccentricities, there is convergence at both layers of the circuit. (Right) Our functional model consists of two stages of linear integration followed by point-wise nonlinearity. We assume that each cone provides input to only one subunit.



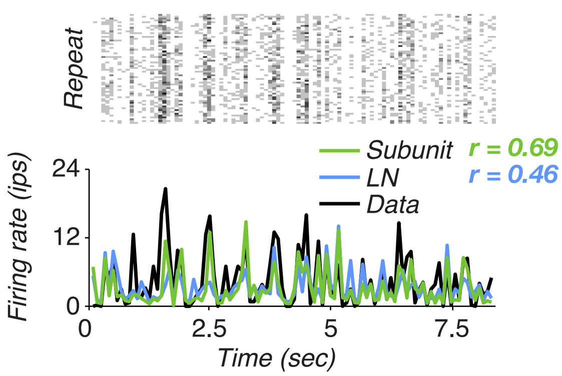
Example fit for an ON midget RGC. (Left) White noise characterization identifies cone locations. (Right) Gray regions indicate subunits, line thickness, weighting from subunits to RGC, and color shading, cone weights. (Bottom) Recovered spline nonlinearities, cross-validated performance on all noise stimuli, and on a subset that maximize differences in model prediction.



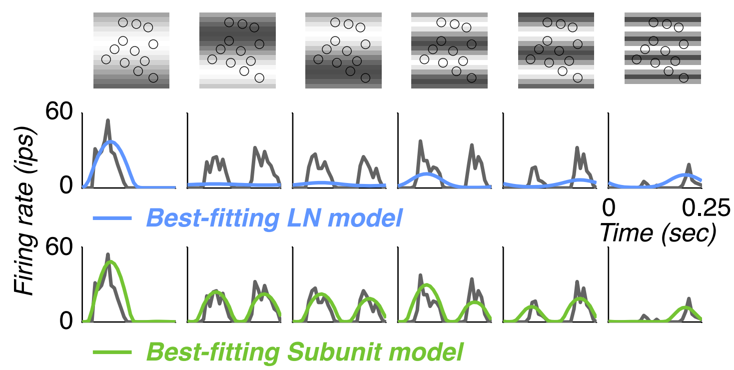
Summary of fits to a population of OFF midget RGCs. (Left) Average recovered nonlinearities, gray shaded region indicates 1 s.d. across 78 RGCs. (Top right) Cross-validated performance for subunit and LN models for all white noise stimuli. (Bottom right) Performance for the 20% of stimuli that maximally differentiated the predictions of the two models.



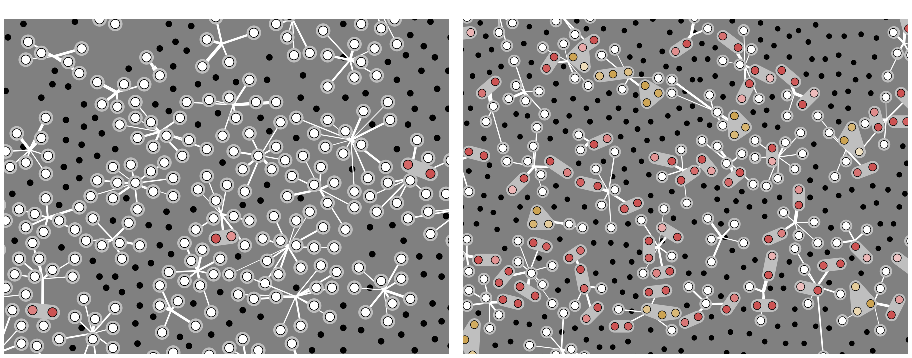
Targeting stimuli to validate model fits. (Left) Responses of a single OFF midget RGC to decrements of light presented to three individual cones. (Right) Responses of the same cell to increments and decrements of light presented to pairs of cones. Signals cancelled, yielding reduced responses, for pairs within, but not across, the identified subunits.

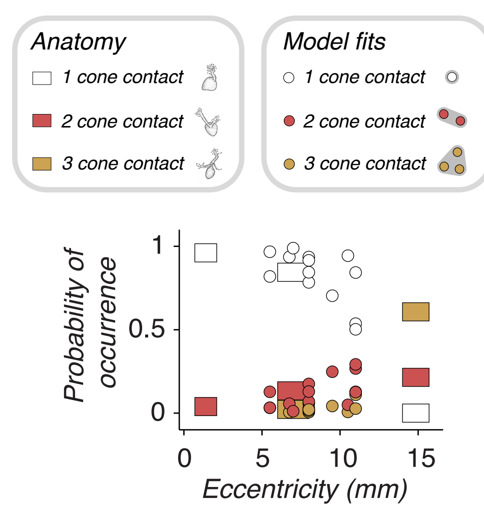


Responses to repeated noise. (Top) An OFF midget RGC responds reliably to repeated presentations of spatially unstructured white noise. (Bottom) The average response is better predicted by the subunit model than a linear-nonlinear model.



Responses to gratings. An OFF midget RGC exhibits frequency doubled responses to a contrast-modulated sinusoidal grating. This characteristic nonlinear property of RGCs is predicted by the subunit model but not the LN model.





Subunits in RGC populations. Model fits for multiple RGCs, from retinas at two different eccentricities: 6.75 mm (left), and 9.5 mm (right). (Far right) Across multiple retinas, the occurrence of subunits / bipolars with different numbers of cone contacts is consistent between functional and anatomical measurements (from Wässle et al., 1994).