SPATIAL STRUCTURE AND ORGANIZATION OF NONLINEAR SUBUNITS IN PRIMATE RETINA

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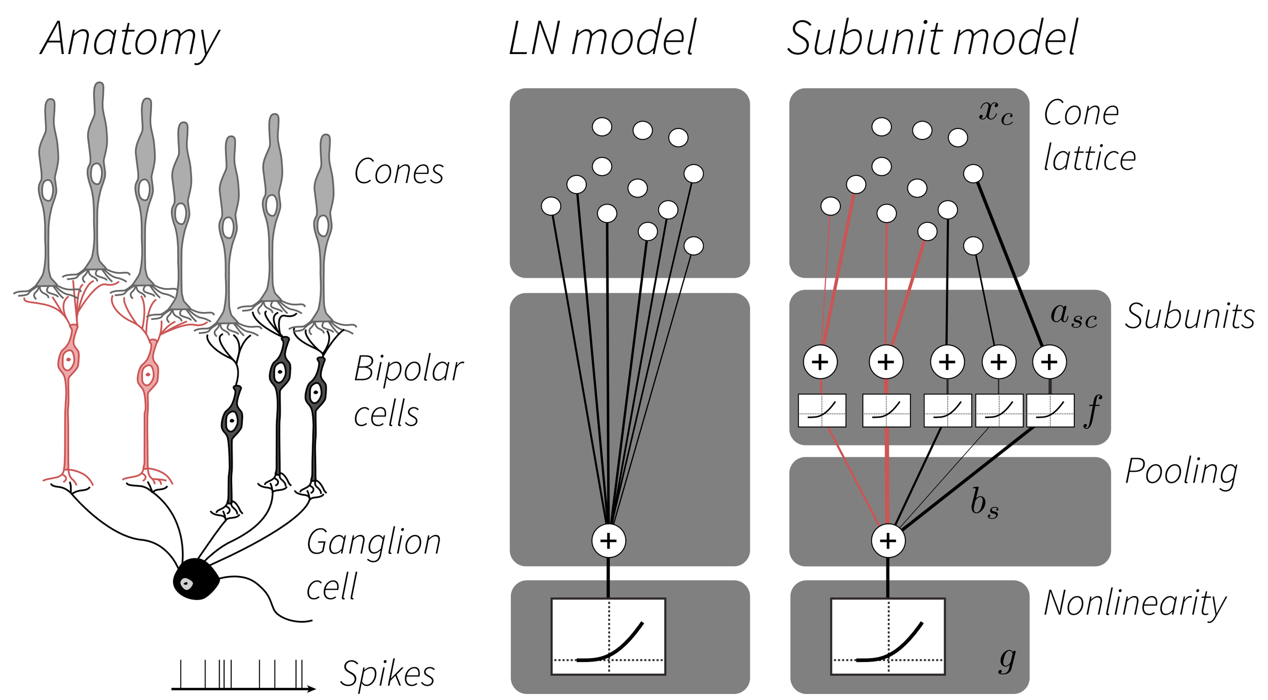
INTRODUCTION



How do ***circuit*** elements give rise to ***functional*** response properties of retinal ganglion cells?

Anatomically, retinal ganglion cells (RGCs) are at the third stage of a hierarchical circuit containing two feed-forward stages of convergence and nonlinear transduction.

Functionally, spatial nonlinearities have been characterized in the responses of many RGC types, and modeled as nonlinear "subunits" within the receptive field (Hochstein and Shapley, 1976; Victor and Shapley, 1979). Subunits are thought to reflect bipolar cell circuitry (Demb et al., 2001; Crook et al., 2008), but it is challanging to directly record from this interneuron layer.

Computationally, the roles of many RGC types are influenced by subunits – e.g. detection of fine-grained patterns and spatial invariance – but quantitative models of subunit structure in terms of the elements of the circuit, especially at the population level, are lacking.

We measured spiking responses in large populations of midget RGCs by recording from isolated retinas using a multi-electrode array. We presented high-resolution visual noise stimuli, and fit a hierarchical model to describe the measured RGC responses. Given the complete input and output of the circuit, we infer properties of the interneuron computation, and our findings are consistent with properties of bipolar cells.

APPROACH TO FITTING

Output nonlinearity · *Subunit nonlinearity* · *Binary assignment (cones to subunits)*

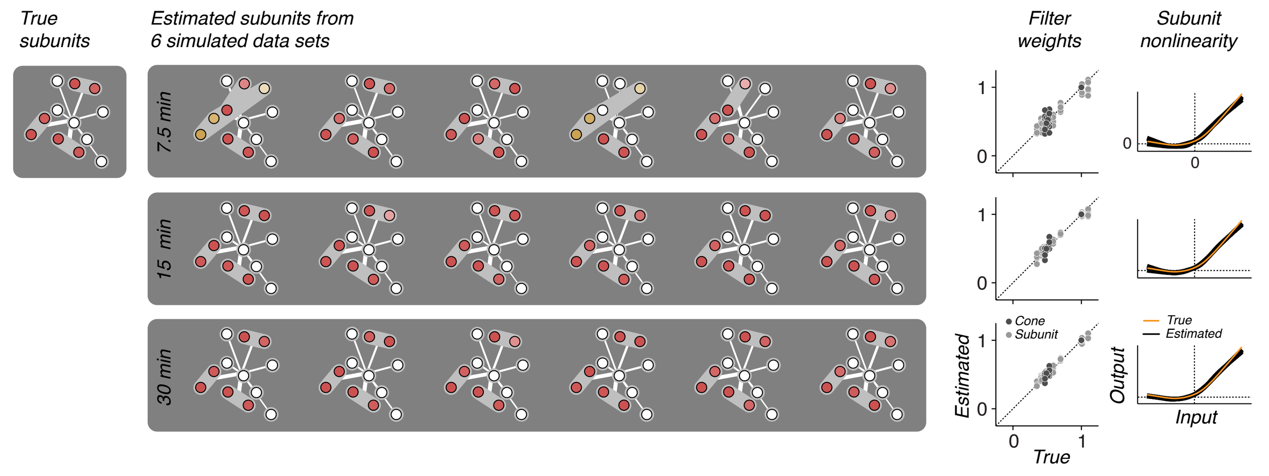
$$r(t) = g\left(\sum_s b_s f\left(\sum_c I_{cs} a_{cs} x_c(t)\right)\right)$$

Predicted RGC firing rate · *Subunit weights* · *Cone weights* · *Cone input*

Model choices
- Subunits do not overlap
- Cone weights are positive
- Nonlinearities are splines
- Poisson spiking

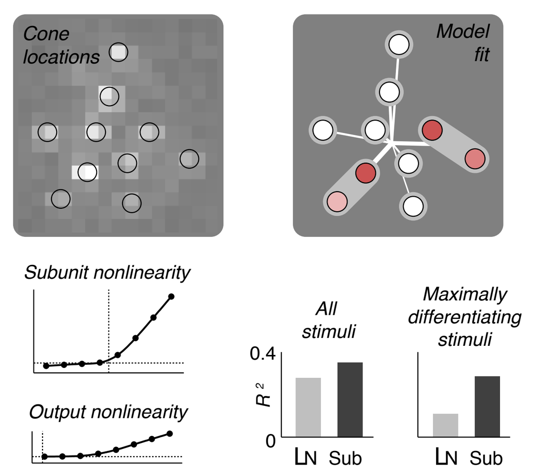
Model fitting
- Block coordinate ascent on likelihood to estimate cone weights, subunit weights, and nonlinearities
- Greedy search over assignment matrices

Recovering subunits in simulation



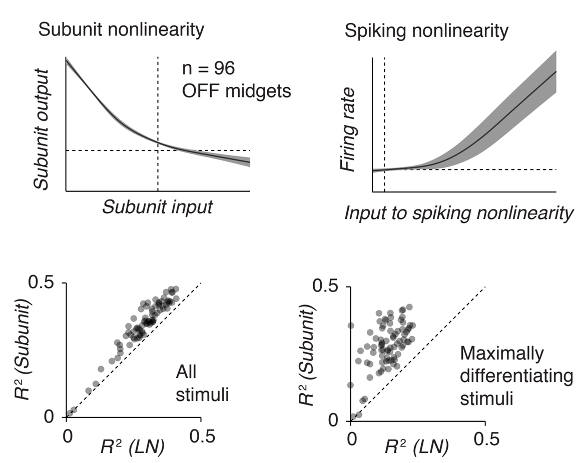
MODEL FITS

Single ON midget RGC

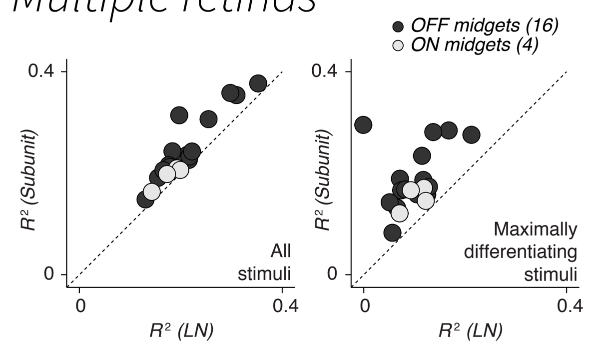


Punctate spots of light within the receptive field indicate cone locations, and allow us to transform the stimulus from pixel space to cone space. For most midget RGCs, the model recovers an accelerating subunit nonlinearity, with subunits of 1, 2, or 3 cones. Cross-validated improvement in explained variance is ~10-20%. If we only consider stimuli for which the models differ in their predictions, it exceeds 50%. Improvement is driven more by the subunit nonlinearity than by the cone-to-subunit assignments.

Single retina summary

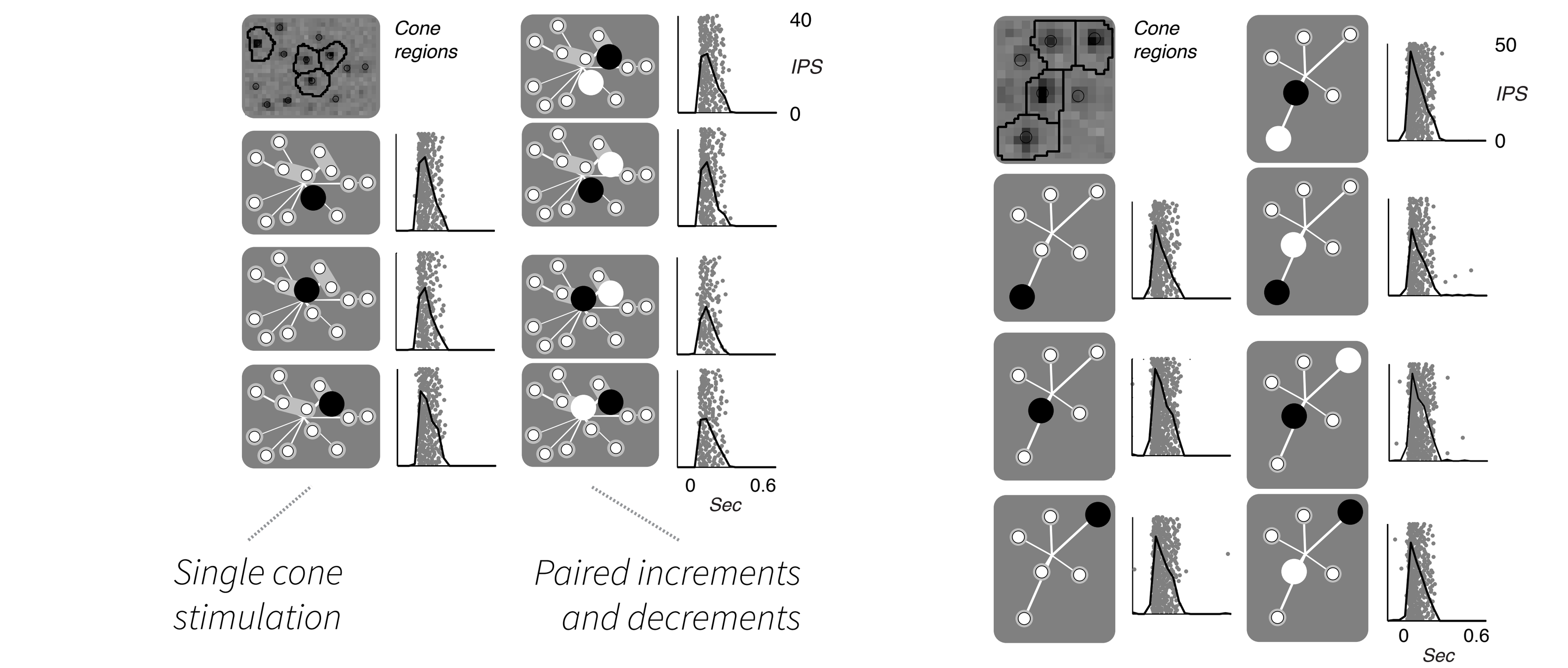


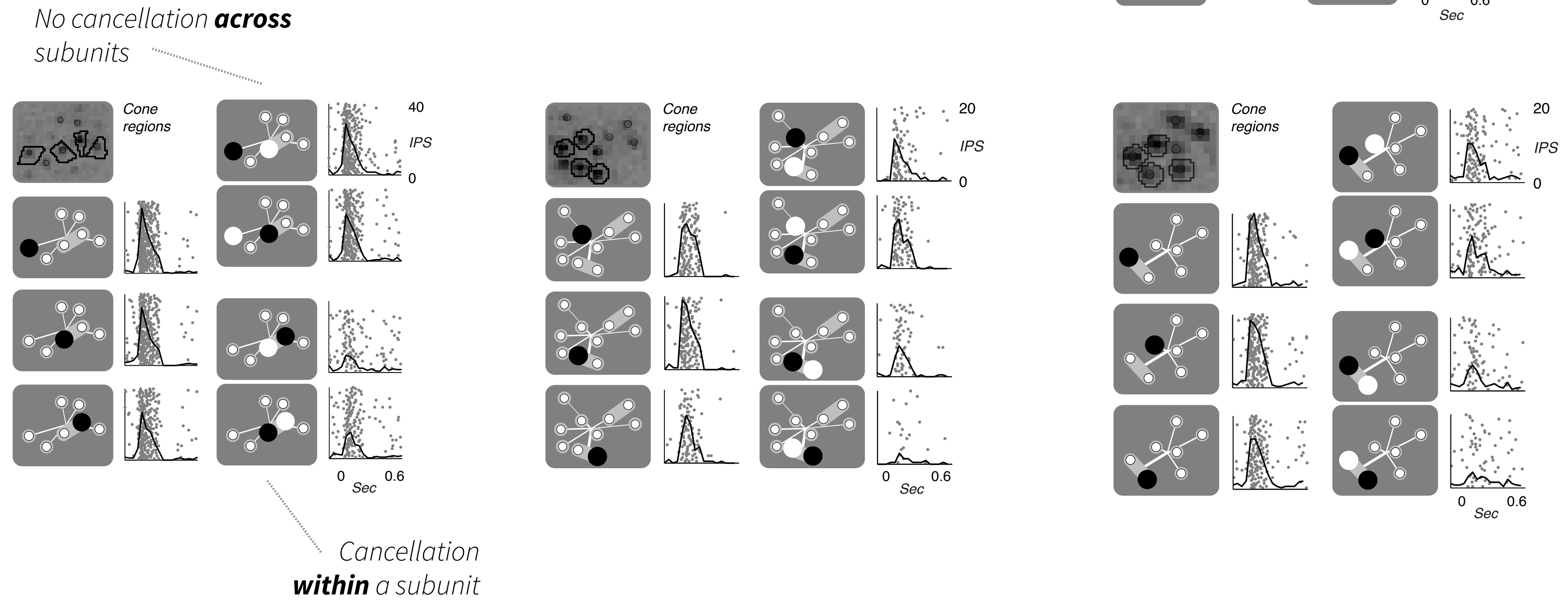
Multiple retinas



CONFIRMING SUBUNIT STRUCTURE WITH TARGETED STIMULI

We use an online targeted experiment to more directly test the recovered subunit structure. The subunit model predicts that cone signals combine linearly within subunits, and nonlinearly across subunits. Rapid parallelization allows us to fit the model to complete populations online. Stimulating individual cones provides a baseline level of response. Paired increments and decrements within a subunit should cancel responses more than paired increments and decrements to cones across subunits.

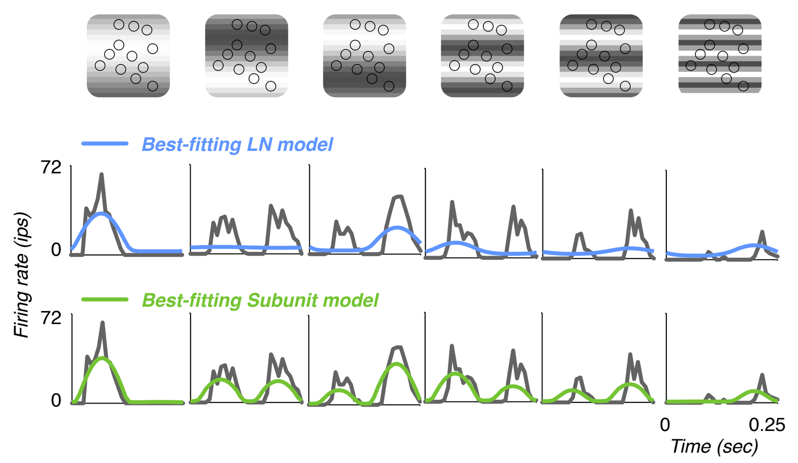




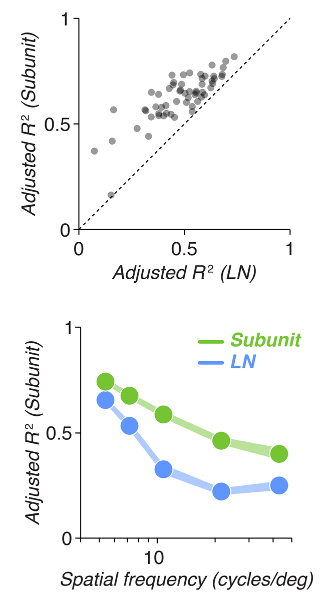
VALIDATING WITH GRATINGS

Midget RGC responses to contrast-modulated sinusoidal gratings exhibit "frequency doubling". The subunit model predicts frequency doubling but the LN model does not. Subunit model improvement is greatest at high spatial frequencies.

Example cell



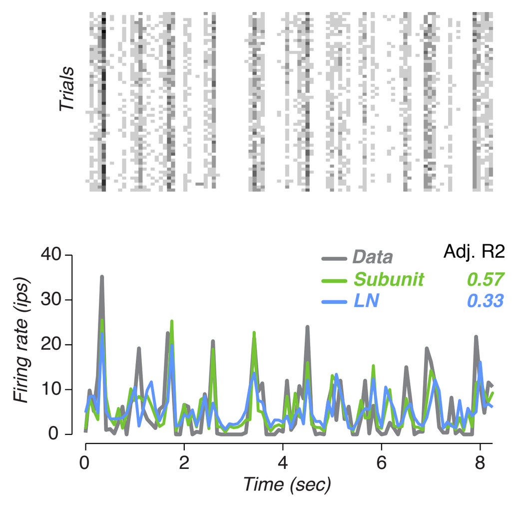
Population



VALIDATING WITH NOISE

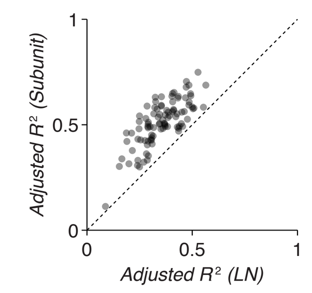
Example cell

The same 8-second sequence of noise was presented 50 times.

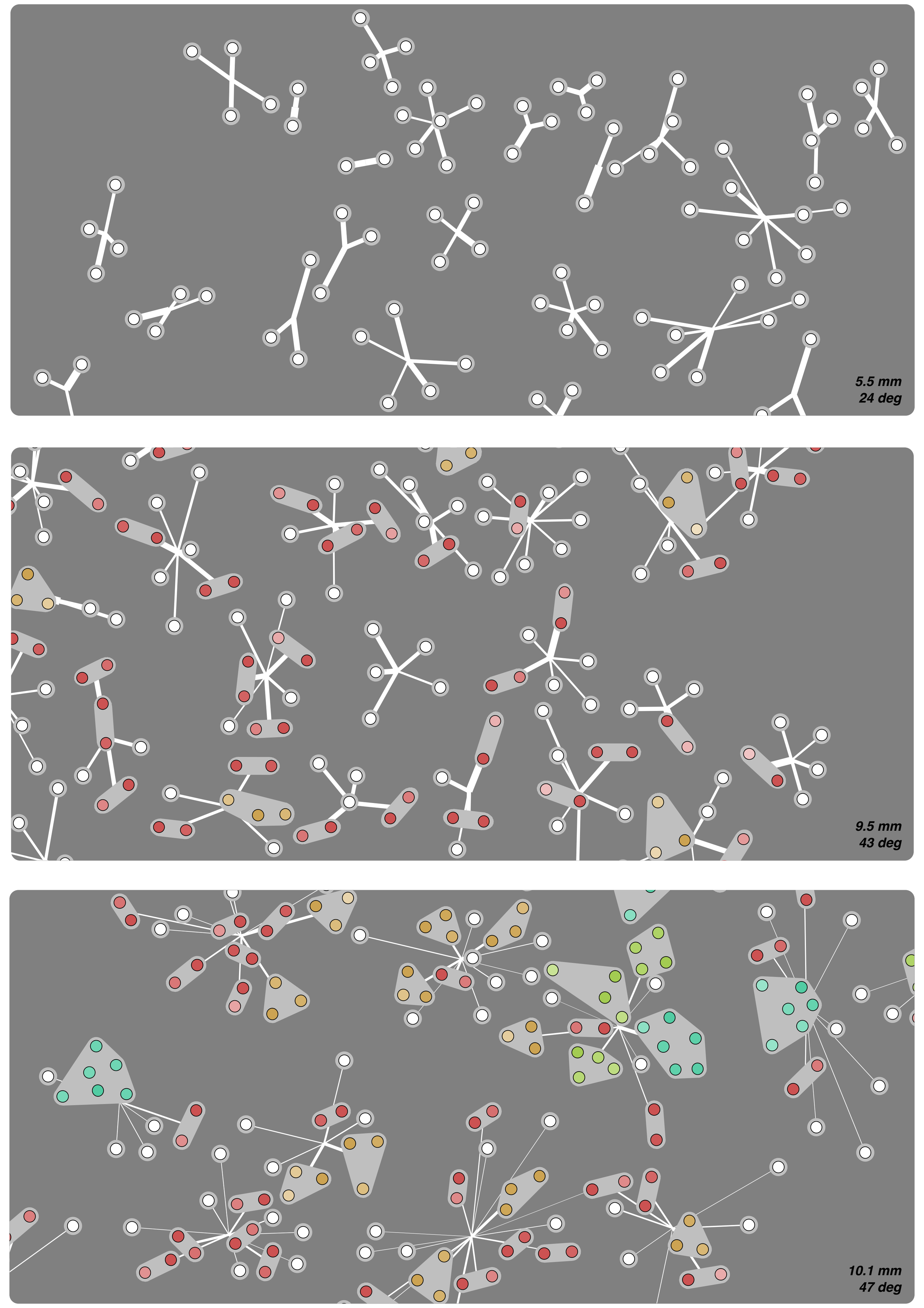


The subunit model captures more than 50% of the explainable variance on average, and outperforms the LN model by 40-50%.

Population



SUBUNITS VARY WITH ECCENTRICITY



Across multiple retinas, the relative fractions of 1, 2, and 3-cone subunits in the model fits approximately match anatomical predictions, and vary as expected with eccentricity.