Revision

1 Response to the Editor

2 Response to reviewer-1

2.1 Overall comment

Comment: *This is a very well written paper in which authors provide an extensively constrained and validated model of midget retinal ganglion cell mosaics across the retina. They provide sufficient detail and open source code for reproducibility, which is commendable and should be the standard for computational studies. Overall the contribution and the quality of the work justifies publication in the Journal of Computational Neuroscience.*

Response: Thank you very much. We worked hard on this paper, and we are happy that the work is clearly presented and appreciated.

2.2 Major comment

Comment: *The only serious concern I have is situating the model in the context of state of the art retina models. The authors overwhelmingly reference studies of the ISETBio platform, and provide minimal comparison to other modeling efforts. The introductory sentence of the abstract summarizes this issue well: "Accurate image-computable models of retinal ganglion cell (RGC) mosaics across the retina do not currently exist."*

At least two such models come to mind: Ly et al. (2025), Kornprobst et al. 2009. I do not question the contributions of this work beyond the current state-of-the-art, but at a minimum these two models are sufficiently close to the present study to warrant a thorough explanation how this model is different and where it advances beyond these models. I haven't done further in-depth literature review on other 'large-scale' retinal models, but I am rather sure there are more to be found. I would strongly urge authors to perform such a review and thoroughly position their model against prior work.

Response: Nicolas to review suggested papers and do a literature review.

2.3 Minor comments

Comment–1 : *I couldn't find where authors demonstrate that the sampled cone mosaic follows an anatomical cone-eccentricity distribution (Curcio et al. 1990)?*

Response: A comparison between the model's cone density variation with eccentricity and that of Curcio is depicted in Reviewer Figure 1.

Comment–2 : *Is there some quantitative physiological grounding for the exponents chosen at different eccentricities for the supra-gaussian distribution? If no such experimental data exists, it should be apparent from the text.*

Response: There is no quantitative physiological grounding of the exponents. Our intent with varying the exponent was to bridge the degree of RF overlap that has been established in the periphery (Refs) with the zero RF overlap in the fovea, where midget RF centers receive a single cone input.

Comment–3 : *"Finally, in the macaque experiments of Croner & Kaplan, stimulus orientation was not optimized to match any orientation bias in the RF of macaque mRGCs (Lisa Croner, personal communication), whereas in the simulated experiments, stimulus orientation was matched to the cell's visual-space referred orientation bias, which results in the smallest possible estimate of RF center size."*
- Why don't the authors test showing randomly oriented gratings and show that this is a significant contributing factor?

Response: Following the reviewer's suggestion, we characterized spatial transfer functions of model neurons using gratings of random orientations. We then fitted the DoG model to the computed STFs and characterized, as a function of eccentricity from 1 to 8 degrees along the nasal meridian, the fitted models' Rc, as well as the ratios of surround to center radii, (Rs/Rc) and surround to center integrated sensitivity, $(KsRs/(KcRc)^2$. The results of this analysis are summarized in Reviewer Figure 1. Panels A1, B1, and C1 depict the variation with eccentricity in the fitted models' Rc, Rs/Rs, $(KsRs/(KcRc)^2$, respectively, for STF measurements with gratings that matched each cell's preferred visual space-referred orientation. Panels A2, B2, and C2, depict the same results for STF measurements with gratings of random orientation for each cell. Note that the distribution of the Rc parameter is widened somewhat (A2 vs A1) and model cells are now closer to population of macaque mRGCs. Also note that the distribution of Rs/Rc is less sharply peaked, better approximating the distribution of Rs/Rc in the macaque (B2 vs B1). The $(KsRs/(KcRc)^2$ distribution is also somewhat less sharply peaked (C2 vs C1). This analysis shows that the mismatched orientation contributes, but is not the only factor responsible

for the deviation from the macaque data, and suggests that other factors, such as inadequately refracted physiological optics in the fovea and parafoveal, residual eye movements, corneal edema, or a combination of these factors, might be responsible for this discrepancy.

Comment–4 : *"The second in vitro study we validated our synthetic mRGCs against, is that of Field et al.[15]" ... - is this validation purely qualitative? Did the authors perform some form of statistical testing to show that they indeed match experimental RF center/surround size in this case?*

Response: Yes, the reviewer is correct. This is purely qualitative. Nicolas working on some statistical testing.

Comment–5 : *3.6.1 How did the authors choose the Gaussian noise level for the CSF analysis? Do the conclusions hold for different noise levels?*

Response: The variance of the applied Gaussian noise was selected arbitrarily. In future versions of the model, we plan to add physiologically realistic levels of Gaussian noise based on macaque mRGC recordings (e.g. Croner et al, 1993).

Should we do different noise levels to answer his second question?

2.4 TYPOS

Typo–1 : *page 7: "which are dealt with in the nest stage."*
Response: Fixed.

Typo–2 : *page 8: "Figsures 4B and 4C depict mosaics synthesized as ϕ decreases to 0.5 and 0.0,"*
Response: Fixed.

Typo–3 : *page 16: "which requites re-computing the surround pooling functions."*
Response: Fixed.

3 Response to reviewer-2

3.1 Overall comment

Comment: *This paper develops and test a biologically realistic model of the retinal mosaic of ganglion cells. This model is part of a much larger retina model, which is a heroic and important effort and fits well in the ¿ JCNS remit. Overall, it is a very well presented paper, the writing is clear and the graphics enlightening.*
Response: Thank you very much. We worked hard on this paper, and we are happy that

the work is clearly presented and appreciated.

Comment: *I only have a few remarks/suggestions. p17 1st sentence misses an "A"*
Response: Corrected.

Comment: *On p15 and 19, K and R sometimes have subscript sometimes not (Kc vs K_c)*
Response: Fixed these issues on P15 and p19, as well as in a few other places

Comment: *The use of bold and capital letters for symbols is*
Response: This sentence is incomplete. Not sure what the reviewer had in mind here.

Comment: *In the Methods section, refer forward to the Apendices for the interested reader.*
Response: Added references to the various Appendices.

Comment: *How are weights defined? Are they relative to the total ? (Ie. summing up to 1)*
Response: Cone weights to the RF center have a maximal value of 1.0. In model cells where there is zero RF overlap, all center cone weights are set to 1.0. In model cells with non-zero RF overlap, cone weights have a Gaussian distribution, with a maximum of 1.0. Text was added in Section 2.2 to clarify this.

Cone weights to the RF surround are computed so as to achieved the desired ratios of visual space - referred surround to center radii and surround to center integrated sensitivities. In the computation of the model cell's composite response (Equation 4), we normalize with respect to the sum of the pooling weights of the cones supplying the RF center, as described in Section 2.5