

Theoretical predictions of metabolic flow regulation in the retina

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Reviewer #1

We thank the reviewer for careful reading of the manuscript and helpful comments. In response, we have modified the manuscript as follows. The reviewer's comments are in italics.

MAJOR ISSUES:

1. Page 4, top. The authors make reference to a previous paper in which the model used in the numerical computations was proposed and illustrated. From the synthetic model description provided in the present manuscript, however, it is not clear where does the temporal dependence of the model solution come from, as Figure 2 does not include capacitive elements in the electrical representation. The clarity of the presentation will certainly be improved if such dependence (which leads, as stated, to solving a system of ODEs) is shortly justified and described.

We thank the reviewer for this comment. In the Methods section (please see the blue text on pages 3-4), we have included a more complete description of the solution algorithm that is used to solve this coupled model. We have also explained the appearance of an ODE even though the model does not include capacitive elements.

2. Page 6. Model predictions of venous saturation appear to be in contrast with measured data. The impact of the contribution will certainly be improved if an attempt of motivating model failure is indicated. In particular, it might be interesting to consider the question of whether such a failure is to be connected with the choice of assuming R_{4a} and R_{4b} to be constant, in contrast with the biophysically ascertained property of veins to be collapsible.

We thank the reviewer for this suggestion. We have added text to the Discussion (blue text, Pages 6-7) that describes the role of the model limitations in yielding a model-predicted value of venous saturation that is not consistent with experimental results. In particular, we have noted that the inability of this model to differentiate between the inner and outer retina affects the predicted venous saturation levels. In addition, we acknowledge that model does not include a Starling resistor description of the veins. However, we note that the inclusion of a Starling resistor would not have much influence on the model predictions for changes in tissue oxygen demand since the Starling resistor effect is more relevant for changes in the level of transmural pressure difference, and here the level of the external pressure (IOP) and of the input pressure (P_{in}) are held constant.

MINOR ISSUES:

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We have implemented this change.

page 4:

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