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Response to "Merchant and Heys, Effects of Variable Permeability on Aqueous Humor Outflow, Applied Mathematics and Computation 196 (2008) 371–380"

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We read with great interest the recent article by Merchant and Heys. While we believe that the authors have effectively formulated a porous media flow model describing how heterogeneous permeability may elevate the hydraulic resistance of this medium, we have serious concerns about how this model applies to the specific problem of aqueous humor flow through the juxtacanalicular connective tissue (JCT), as described by Merchant and Heys.

We have three major concerns. These are:

- The authors analyzed a single, largely unrepresentative image of the JCT obtained at an unphysiological state of zero intraocular pressure. Furthermore, they extrapolate their results from a section of the JCT that was approximately 1.3 μm thick to the entire 10 μm thickness of the JCT.
- The author's assessment of the effects of heterogeneity on flow through this porous medium ignored the most significant heterogeneity of the tissue: large, micron-sized open spaces devoid of matrix structure that are present in the very same quick-freeze/deep-etch (QFDE) image data set [1] that the authors used for their analysis. These open spaces, being at least 10-times larger than the matrix pores analyzed in their study, would effectively eliminate any meaningful resistance predicted from their porous media analysis. Similar arguments apply to the basement membrane of the endothelium that is believed to be discontinuous [1–4], and these discontinuities would eliminate a large fraction of the predicted resistance from the current study.
- While the authors indicated that they addressed the depth-of-field correction necessary for these images, we are puzzled as to how they could have done this. QFDE images visualize structures down to variable depths into the replica, and this depth-of-field can strongly influence the predicted flow resistance by 10-fold or more [5] unless stereological correction is performed [6]. Moreover, depth-of-field is non-constant across images and often varies within individual images, and it must therefore be determined locally using stereo images. Our previous assessment of depth-of-field in the JCT for the very same image analyzed by the authors ranged from 53–82 nm, but this decreases significantly in the basement membrane region. Thus, we are at a loss as to how the depth-of-field correction could have been done correctly. Our own assessment of the flow resistance in the JCT region (away from the basement membrane) is 5-fold smaller than the author's reported values for the homogeneous permeability case.

In conclusion, we agree with Merchant and Heys that a heterogeneous porous medium might well have a different flow resistance than does a homogeneous medium even if their average porosities are similar. However, porous media analysis is statistical by its very nature, and use of 2-D images to determine the permeability of a porous medium requires a sufficient number of images to justify use of the theory, particularly when applied to such a heterogeneous tissue as the JCT.

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