Supplementary Material

Numerical modeling of therapeutic lens drug delivery in the anterior human eye for the treatment of primary open-angle glaucoma (POAG)

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Assumptions used for heat transfer modeling

1. There is steady-state temperature distribution in all the domains of the eye.
2. AH velocity ($\vec{v}$) is present only inside AC and PC of the eye and is responsible for heat transfer due to natural convection inside them. In all other domains of the eye, the primary mode of heat transfer is via conduction.
3. Q_{met} and Q_{blood} are significant only inside iris and sclera of the eye since they are the only vascular components of the eye.[1]

Assumptions used for drug transport modeling

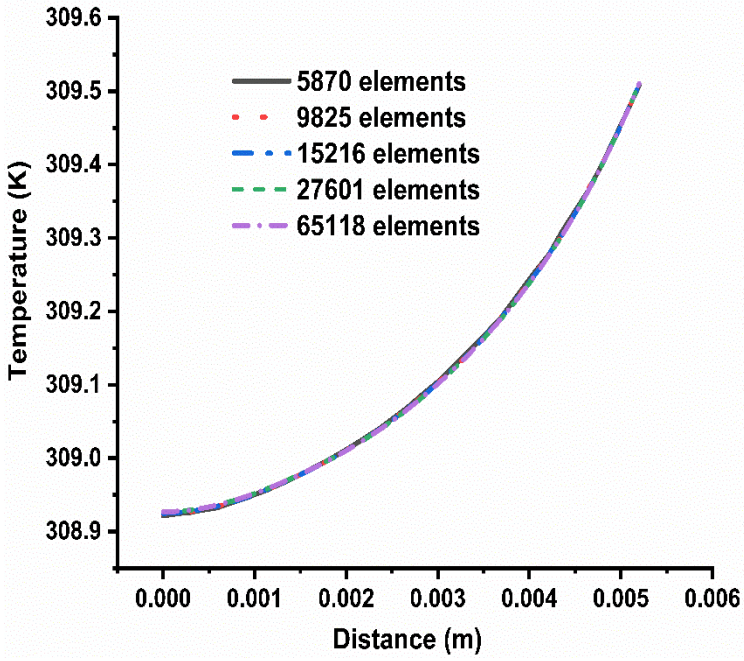
1. The drug transport equation (Equation (13) in the manuscript) has been solved in all the domains of the eye except the vitreous chamber. This is because the objective of the current study is to simulate the drug transport through the therapeutic lens in the anterior segment of the eye for the treatment of POAG, which is an anterior segment eye disease. Further, when the drug is administered through the corneal route, there is almost negligible diffusion in the vitreous part of the eye that has also been shown experimentally by Ahmed et al. [2,3] *in vivo*.
2. The convection term ($\vec{v} \cdot \nabla C$) in equation (13) is absent for all the domains of the eye except AC, PC and TM. This is because there is no AH flow in all the domains of the eye except AC, PC and TM.

Mesh convergence study

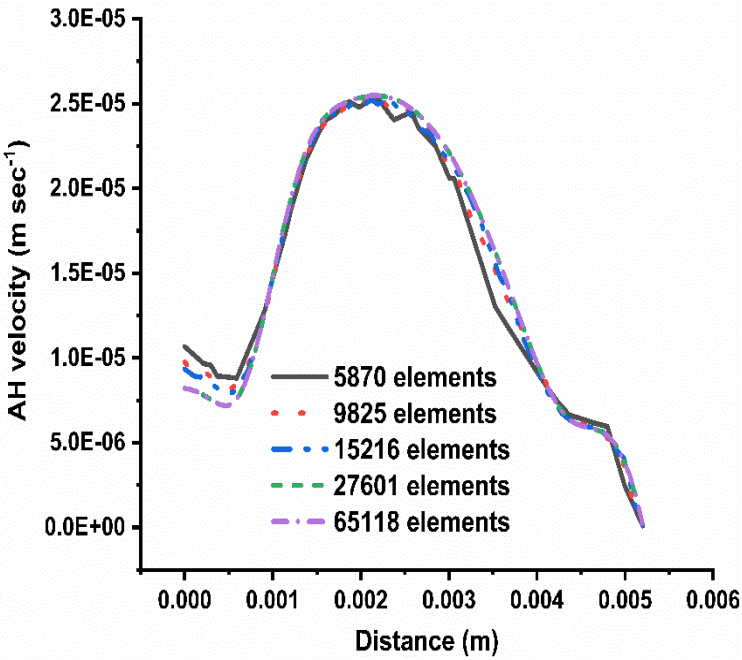
Before the final simulation study, proper mesh convergence has been performed to ensure that the simulated results (temperature, AH velocity field and drug concentration) are independent of the change in mesh densities. Since the main activity (convection and diffusion) occurs inside the AC of the eye, therefore, mesh convergence has been examined along a cut line in AC of the eye, which is shown in Figure S1(a Mesh convergence has been achieved by systematically decreasing the maximum element size in the AC from 1 mm to 0.0573 mm. Further, the maximum element size was kept the same in all the eye domains as was kept in AC at each convergence step apart from the vitreous chamber (in which drug concentration is not being solved). This has been done to avoid any discontinuity in the drug concentration between different eye domains and to accurately capture the physical phenomenon.

Figures S1(b)-(d) show line plots depicting temperature, AH velocity and drug concentration values for different mesh elements plotted along the cut line. It can be observed from Figure S1(b) that temperature is least sensitive to mesh, whereas AH velocity and drug concentration have been found to converge at 27601 mesh elements (Figures S1(c)-(d)). No change in AH velocity and drug concentration values was found between 27601 and 65118 mesh elements. Apart from the cut line, we have also analyzed the average drug concentration in AC at all the time points for different number of mesh elements (Figure S1(e)). It can be observed that no change in average drug concentration happens between 27601 and 65118 mesh elements.

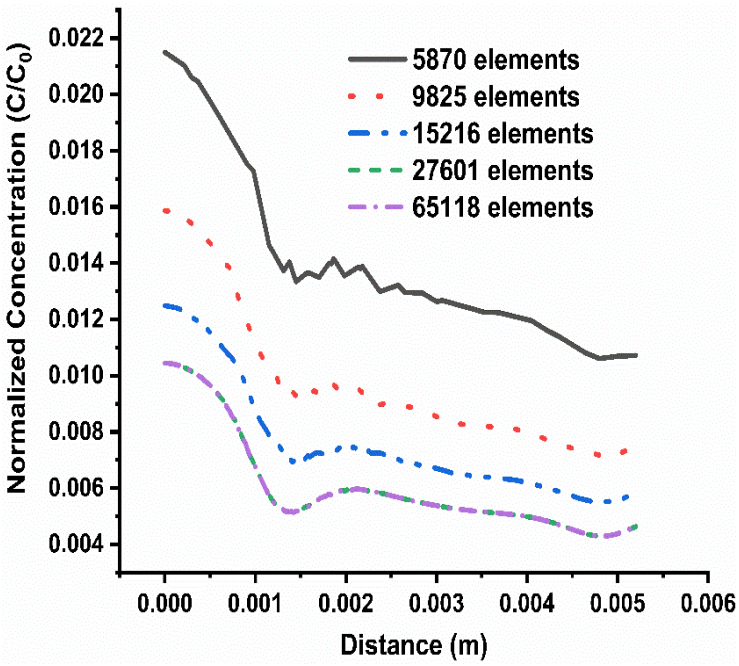
(a)



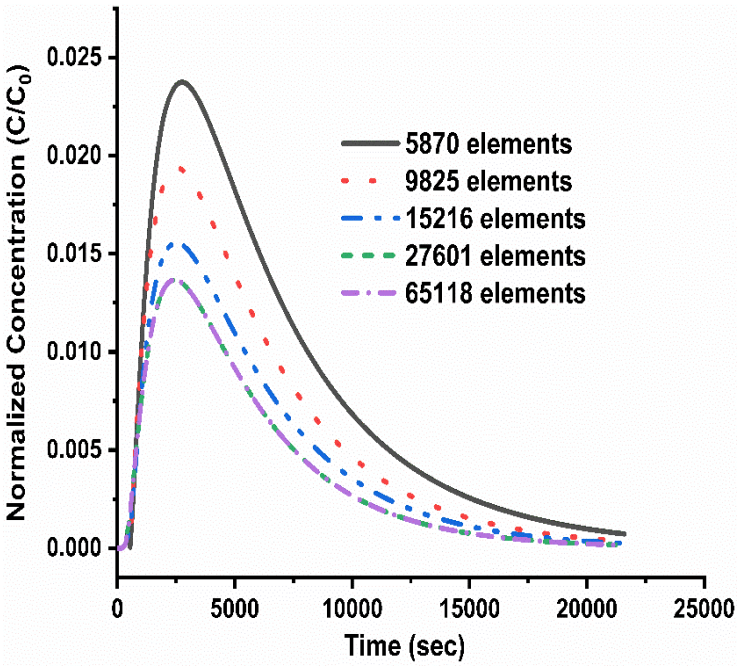
(b)



(c)



(d)



(e)

Figure S1. (a) Cut line (red color) in the AC along which mesh convergence study plots have been shown for an up-facing eye with therapeutic lens. Mesh convergence study along the cut line for (b) Temperature, (c) AH velocity, (d) Drug concentration at 2 hours and (e) Average drug concentration in AC for different mesh elements.

Therefore, the final study for the 2D axisymmetric case consisted of 27601 mesh elements at which all the parameters (temperature, AH velocity and drug concentration) converged. The final mesh for the 3D horizontal eye with a similar meshing strategy consisted of 1.62 million mesh elements. The final mesh for the 2D axisymmetric (up-facing) human eye has been shown in Figure S2.

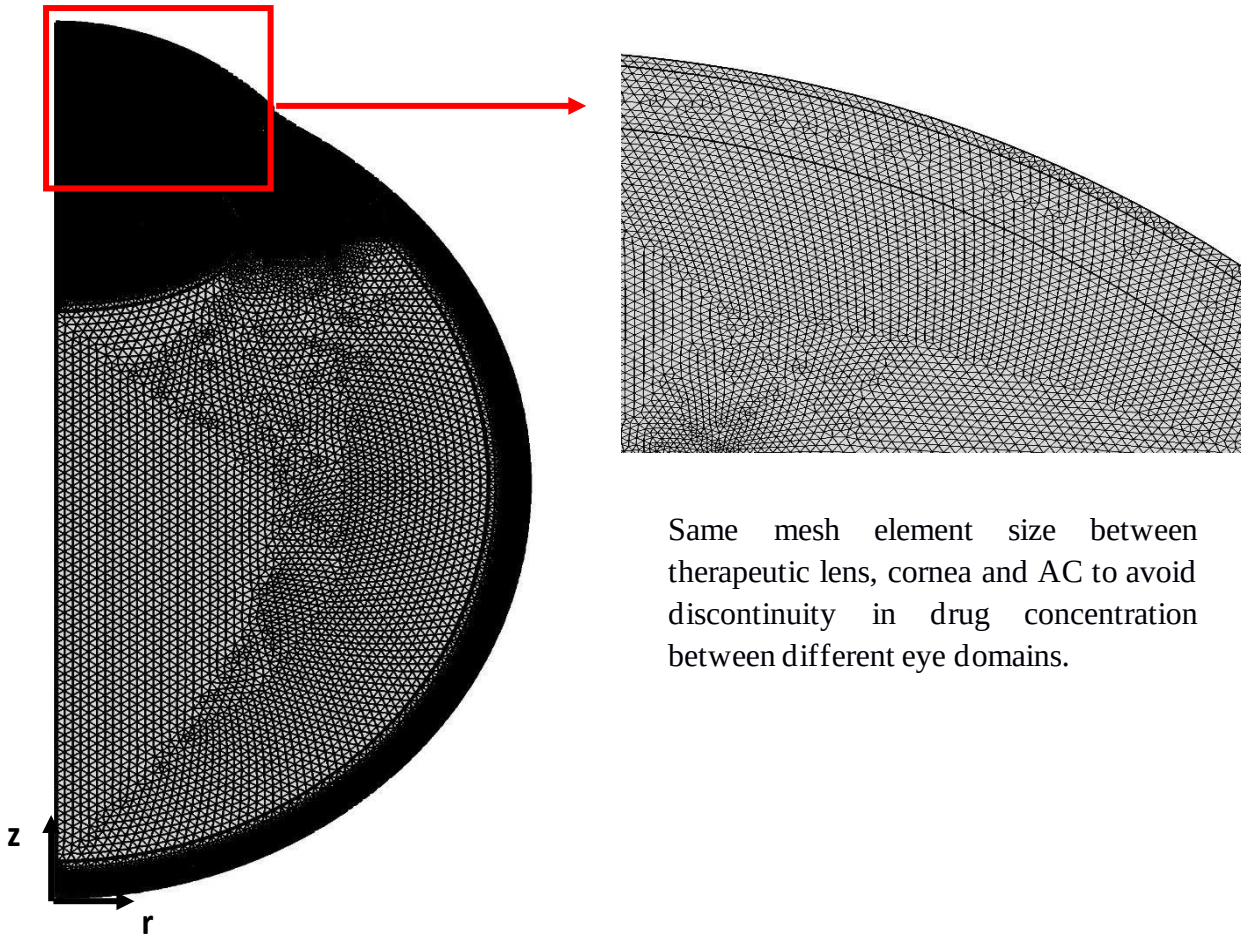
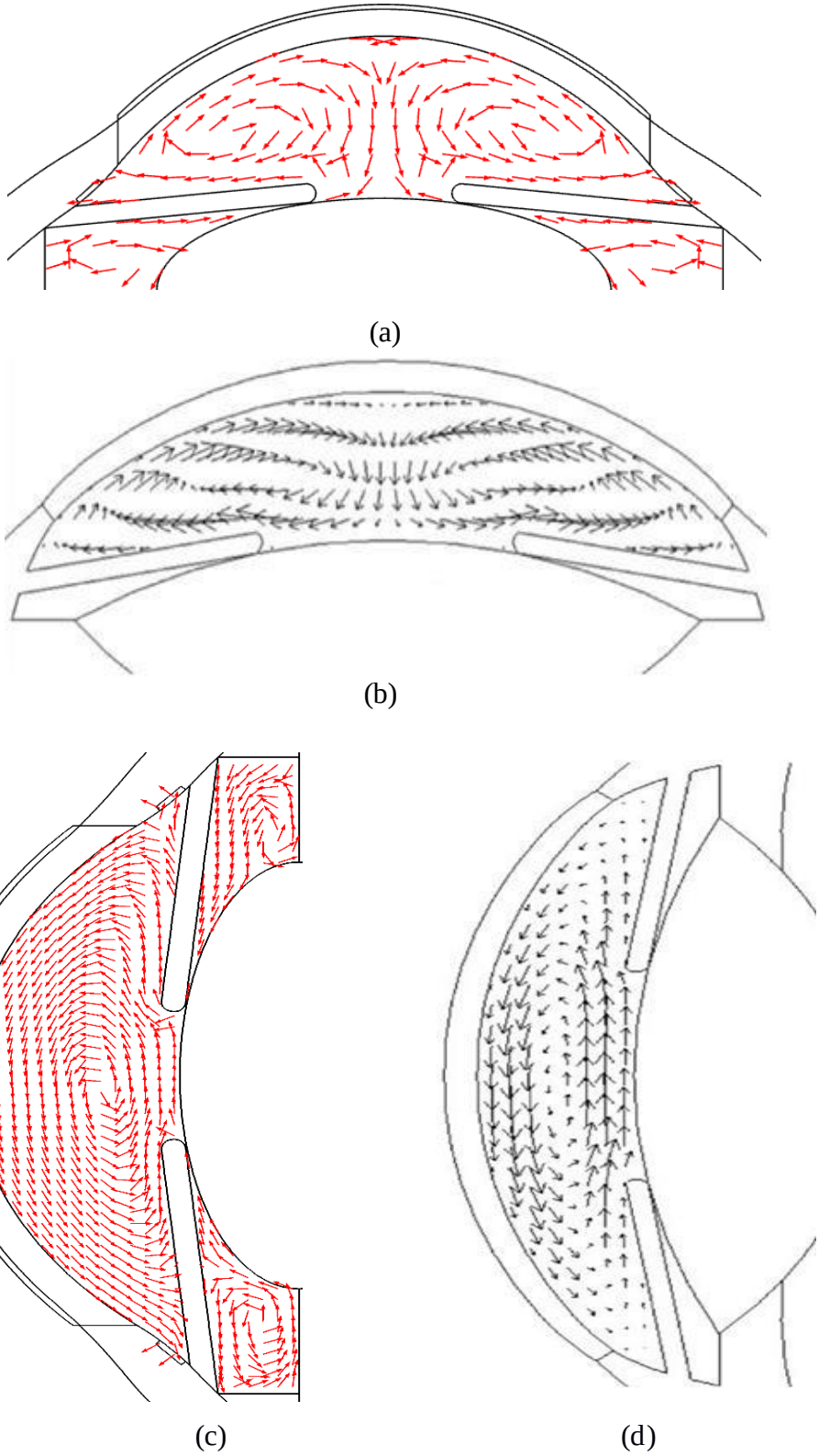


Figure S2. Final mesh for 2D axisymmetric (up-facing eye) (gravity parallel to eye optical axis).

Validation of AH results in up-facing and horizontal-facing eye

The AH velocity in an up-facing eye (Figure S3(a)), as well as the horizontal facing eye (Figure S3(c)) was validated with the one reported by Ooi et al. [4] (Figure S3(b) and 3(d)). An excellent qualitative agreement was observed between the two. Further, the order of AH magnitude in an

up-facing eye and the horizontal-facing eye (our results) was also observed to be the same as reported by Loke et al. and Zhang et al.[5,6] for other drug delivery modes as well.



(a)

(b)

(c)

(d)

Figure S3. Comparison of simulation results of AH velocity distribution in the (a) up-facing eye and (c) horizontal-facing eye (at y = 0 plane) in our simulation and from Ooi et al. 2008 ((b) and (d)).

References

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4. Ooi EH, Ng EYK. Simulation of aqueous humor hydrodynamics in human eye heat transfer. *Comput Biol Med* 2008; 38: 252–262.
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