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Relationship between intraocular, blood, and cerebrospinal fluid pressures: a theoretical approach

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1. Background and purpose

Intraocular pressure (IOP), arterial blood pressure (P_A), and cerebrospinal fluid (CSF) pressure have been identified as major players in several ocular pathologies, including glaucoma, central vein occlusion, and papilledema, to name a few. IOP, P_A, and CSF pressures are not independent from each other. For example, aqueous humor and CSF flows, whose mechanics contribute to establish IOP and CSF pressure levels, originate from blood flow, which is driven by P_A. As a consequence, it is difficult to experimentally isolate IOP, P_A, and CSF pressure and to disentangle their effect in pathological conditions. Here we utilize a theoretical approach to address this issue.

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2. Methods

The present mathematical model is developed to simulate fluid flow in the eyes (retina, choroid, ciliary body, and lamina cribrosa) and brain connected with a simplified description of the whole-body circulation consisting in central arteries and veins. We use an electrical circuit analog that accounts for:

1. the flows of blood and aqueous humor in the eyes;
2. the flows of blood, CSF, and interstitial fluid in the brain; and
3. lamina cribrosa biomechanics influenced by tissue pressure in the optic nerve head due to CSF within the subarachnoid space (SAS), represented by an extra ventricular compartment.

The lumped parameter circuit for the brain is adapted from the work described and validated in Lakin and Stevens[1]; the eye model originates from the approach proposed in Guidoboni *et al.*[2] for the study of retinal circulation and has been extended to account for the three ocular vascular beds (retina, choroid, and ciliary body) on the basis of the work of Kiel *et al.*[3] Finally, ocular hemodynamics is coupled with the aqueous humor dynamics as in Szopos *et al.*[4] The model takes into account the complex interaction between different biofluids in the brain and in the eye. The flow is driven by P_A, which is given as a variable input, while the venous pressure P_V is kept constant. Intracranial pressure (ICP) is the pressure in the brain compartment and CSF production rate is imposed and kept constant. IOP results from the balance between aqueous humor production and drainage, and acts as an external pressure on ocular vascular veins that are modeled as Starling resistors (they collapse when the transmural pressure is negative). The lamina cribrosa exerts a compressive stress from the combined action between IOP, CSF pressure, and scleral tension on translaminar central retinal arteries and veins segments as in Guidoboni *et al.*[2] Model parameters have been calibrated on published data. The assumptions related to the coupling between the various elements is validated: the model is used to simulate changes in IOP, CSF pressure, flow, and pressure distributions across the whole system induced by changes in P_A. Results are compared to those reported in clinical studies. In this current version of the model, time dependence and blood flow regulation are not included.

3. Results

Our model predicts relationships between IOP, P_A, and CSF pressure that are within the same range as those reported in clinical studies. Figure 1 captures the overall trend of CSF pressure variations due to changes in blood pressure and IOP, as reported in Ren *et al.*[5] Morevover, as show in Table 1, the model captures the trend of IOP variation due to changes in blood pressure, as reported by various authors.[5–9] In addition, choroidal venous pressure in the vortex veins computed by the model

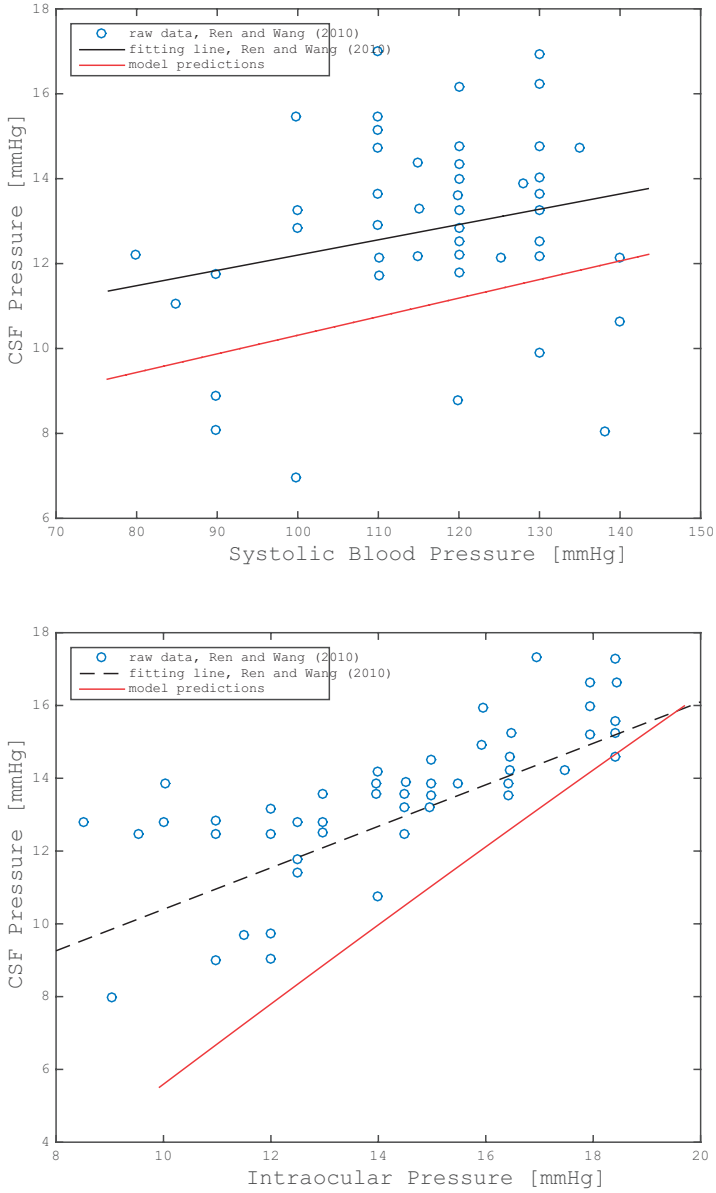

Fig. 1. (*Top*) Influence of systolic blood pressure on CSF pressure. (*Bottom*) Relationship between IOP and CSF pressure.

Table 1. Influence of systolic and diastolic blood pressures on IOP. Comparison between population-based studies and model simulations.

Source	mmHg increase in IOP/10 mmHg increase in SBP	mmHg increase in IOP/ 10 mmHg increase in DBP
Dielemans *et al.*[7]	0.23 ± 0.02	0.24 ± 0.04
Mitchell *et al.*[8]	0.28 ± 0.05	0.52 ± 0.12
Xu *et al.*[9]	-	0.39
Model Predictions	0.42	0.83

IOP: intraocular pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure

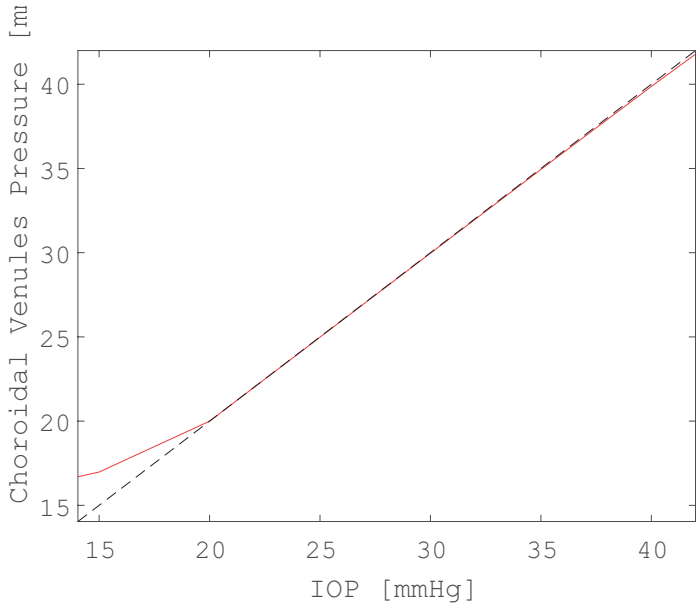

Fig. 2. Choroidal venules pressure vs IOP as predicted by the model (*red curve*). The black dashed line corresponds to equality between the two pressures.

from flow and pressure distribution within the body results to be approximately equal to IOP over a wide range of values (Fig. 2), confirming the findings by Bill.[6] Differences between model predictions and clinical data might be due to blood flow regulation (currently not included) or particular conditions of clinical studies.

4. Conclusions and future perspectives

Simulation results validate the predictive capability of the model, which provides a powerful virtual laboratory where the relationships between IOP, P_A, and CSF pressure can be assessed based on patient-specific conditions. Thus, our model may have an important clinical role as medicine is moving in the direction of individualized treatments for specific patients.

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