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Emulating Diurnal Variation in the Retinal Vasculature Using Machine Learning and a Physiology-based Mathematical Model

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Abstract

Purpose : Physiology-enhanced modeling and data analytics provide a quantitative assessment of risk factors for primary open angle glaucoma (POAG), including hemodynamic biomarkers within the retinal vasculature. Obtaining accurate values of the diurnal

variation of these variables, however, is a significant challenge. Here, a novel machine learning (ML)/statistical surrogate approach based on a mechanistic model of the retinal circulation capable of generating hemodynamic response to time-varying clinically-measurable inputs is presented.

Methods : Intraocular pressure (IOP), heart rate (HR), and systolic and diastolic blood pressures (SBP, DBP) were used as individualized inputs for a mathematical model of retinal circulation, providing 8 hemodynamic outputs based on mechanisms of vascular physiology. An extreme learning machine (ELM) model was then used to emulate the outputs of the mathematical model. Diurnal variations of IOP throughout the wake/sleep cycle as presented for “older healthy” patients in Mosaed et al. (2005) were considered (Fig.1). The ML model was incorporated into a Gaussian time-series framework that accounts for model and input errors. The highly efficient yet flexible ELM yielded nearly instantaneous distributions of hemodynamic outputs given sequences of IOP, HR, SBP, and DBP.

Results : The ELM produced excellent out-of-sample fits for the emulated outputs ($R^2 > 0.998$). Fig. 2 shows the simulated diurnal distributions for model-estimated BP in the central retinal artery (P_{cra}), arterioles (P_{art}), venules (P_{ven}), and the central retinal vein (P_{crv}); resistances in the central retinal artery (R_{cra}), arterioles (R_{art}), venules (R_{ven}), and the central retinal vein (R_{crv}); and total retinal blood flow (Q). The distributions show significant variation during the sleep phase in all hemodynamic outputs except R_{ven} .

Conclusions : ML/statistical surrogate models in combination with physiology-based mathematical modeling provide a testbed and a translational toolset to rapidly emulate distributions of retinal hemodynamic variables throughout the diurnal period using widely available clinical markers as inputs, showing potential to identify individualized risks in POAG eyes and ultimately guide tailored treatment plans.

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Diurnal variations of IOP throughout the wake/sleep cycle

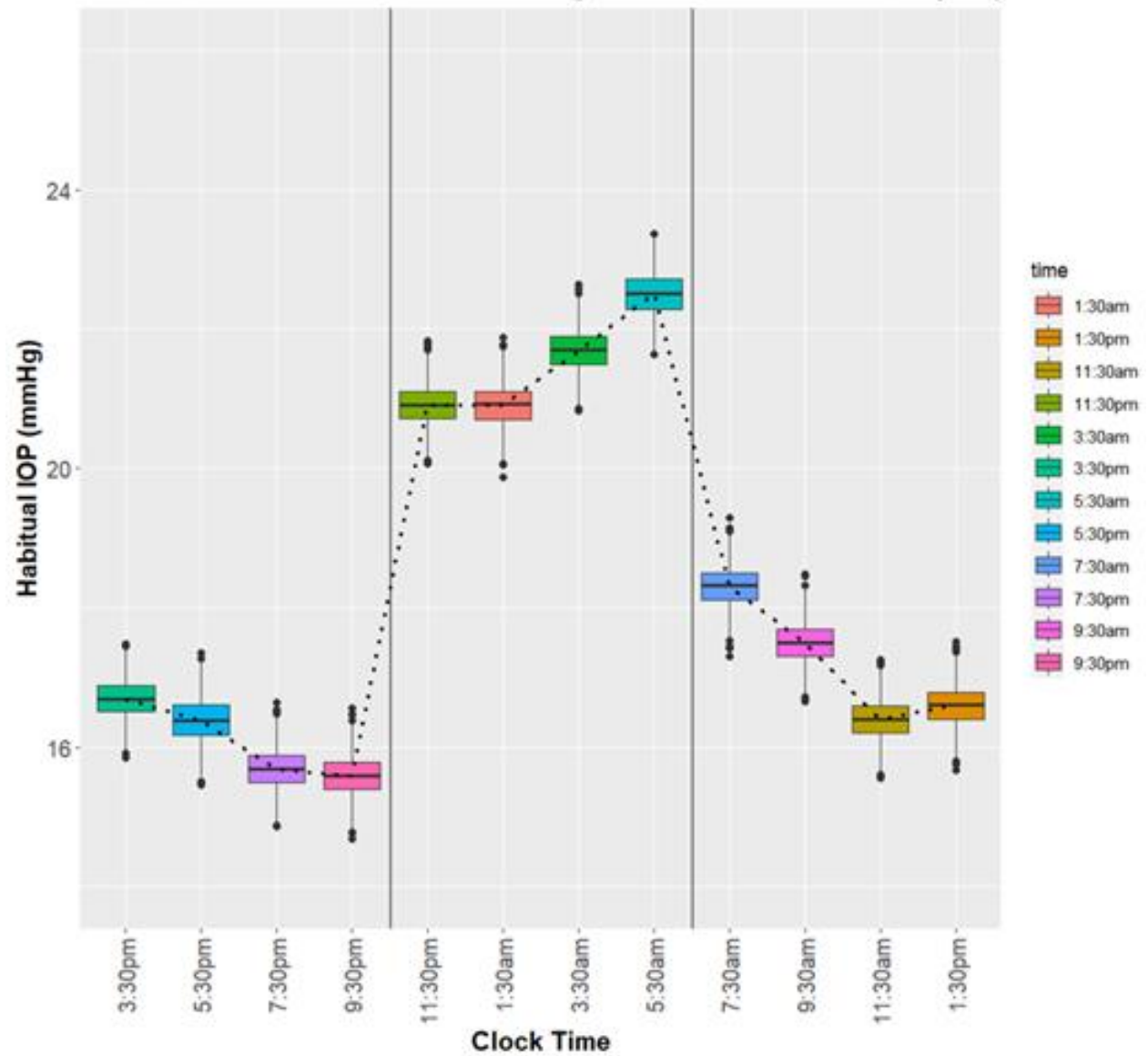


Figure 1. Diurnal variations of IOP based on Mosaed et al (2005).

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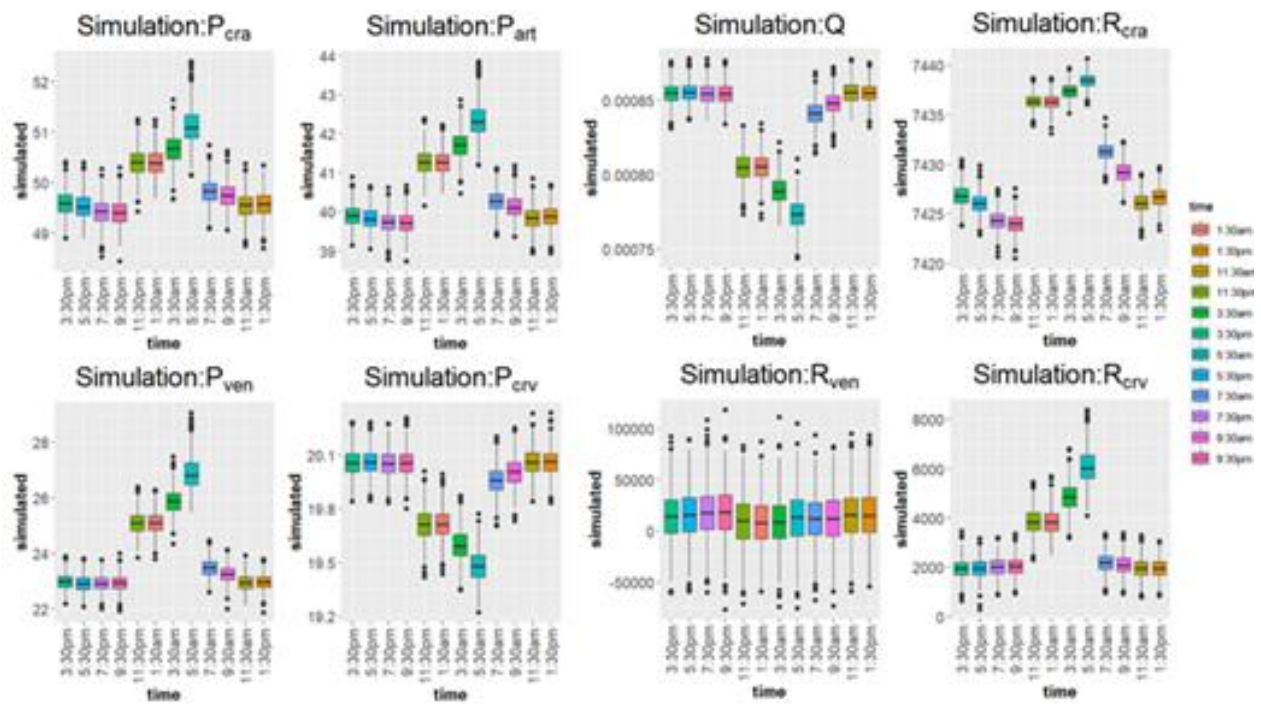


Figure 2. Simulated distributions of the hemodynamic variables obtained from the model.

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