Chapter 21

Digital Twins of the Retina: A Computational Framework for Personalised Microvascular Health Assessment

Wahbi K. El-Bouri[1,2]* and Rémi J. Hernandez[1,2]

[1]Department of Cardiovascular and Metabolic Medicine, Institute of Life Course and Medical Sciences, University of Liverpool, UK

[2]Liverpool Centre for Cardiovascular Science, University of Liverpool & Liverpool Heart and Chest Hospital, UK

Abstract

Digital twins of the retina have the potential to personalise treatment options for individuals. This study presents a computational framework for generating digital twins of retinal vasculatures, simulating haemodynamics and transit times, on an individual basis. Starting with optical coherence tomography angiography (OCTA) and fundus photographs, we developed a pipeline to segment the retinal vasculature, virtually recreate it and run blood flow simulations tailored to each individual.

Digital twins of six eyes were created, and blood flow was solved through the networks, demonstrating variability between individuals. Simulations were validated against literature data for blood flow and blood velocity distributions. Diseases such as diabetic retinopathy and retinal vein occlusion were simulated for each case, demonstrating variable risk between individuals.

Our framework enables computation of microvascular haemodynamic metrics that are challenging to measure directly. In particular, mean transit times and transit time heterogeneity—important markers of microvascular health in other organs—were derived from the digital twins. This proof-of-concept demonstrates the potential of computational frameworks as tools to explore associations between microvascular ageing, disease, and retinal health. Future integration with real-time imaging devices could allow live-streamed feedback and personalised risk prediction, strengthening the translational impact of this approach.

Keywords: *Retinal Digital Twins, Haemodynamic Simulations, Diabetic Retinopathy, Retinal Biomarkers, Personalised Healthcare*

Introduction

The retina is one of the few places in the human body where the microvasculature can be visualised non-invasively. Retinal health reflects not only ocular function but also systemic vascular conditions, including diabetes, hypertension, and neurodegenerative disorders[1]. Early detection and monitoring of microvascular changes can provide valuable insights for preventing vision loss and assessing overall cardiovascular risk.

[1]J. Chua et al., "Optical coherence tomography angiography of the retina and choroid in systemic diseases." *Progress in Retinal and Eye Research*, 103 (November 2024): 101292.

However, current clinical assessments rely largely on qualitative grading or global averages, overlooking inter-individual variability in microvascular topology and function.

Digital twins (virtual replicas of biological systems) are gaining traction across medicine. In cardiology, orthopaedics, and oncology, digital twins have been used to simulate organ function, predict disease progression, and optimise therapies[2,3,4]. Yet their application in ophthalmology is still in its infancy[5,6,7]. We hypothesised that creating digital twins of the retina could capture individual-specific vascular structures and haemodynamic patterns, providing a foundation for personalised diagnostics and treatments.

This chapter presents an image-based computational framework for constructing retinal digital twins from optical coherence tomography angiography (OCTA) and fundus images. By modelling blood flow and red blood cell movements, we aimed to (i) demonstrate variability across individuals, (ii) validate simulations against existing literature, (iii) explore disease conditions such as diabetic retinopathy, and (iv) investigate microvascular health markers, particularly mean transit time and heterogeneity.

Methods

Generating the Retinal Digital Twins

Six individuals were chosen: 4 from the open-source DRIVE dataset[8] and 2 from an in-house dataset[9]. These images were a combination of colour fundus photographs and optical coherence tomography (OCT), augmented with en-face OCTA. The vessel networks were segmented from these images, with Voronoi tessellations representing the three-layered capillary bed connected.

For each individual, 20 capillary beds were generated due to the inability to visualise them in the imaging; thus, each individual had 20 twins with the same retinal morphology, except for the central capillary beds. The segmentation process is visualised in Figure **1**.

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[2]J. Corral-Acero et al., "The 'Digital Twin' to enable the vision of precision cardiology." *European Heart Journal* 41 no. 48 (December 2020): 4556–64.

[3]M.C. Dean et al., "Leveraging digital twins for improved orthopaedic evaluation and treatment." *Journal of Experimental Orthopaedics* 11 no. 4 (November 2024): e70084.

[4]U.S. Asghar and C. Chung, "Application of digital twins for personalized oncology." *Nature Reviews. Cancer* 25 no. 11 (November 2025): 823–25.

[5]R.J. Hernandez et al., "Advancing Treatment of Retinal Disease through in Silico Trials." *Progress in Biomedical Engineering (Bristol, England)* 5 no. 2 (2023): 22002.

[6]R.J. Hernandez et al., "Linking Vascular Structure and Function: Image-Based Virtual Populations of the Retina." *Investigative Ophthalmology and Visual Science* 65 no. 4 (April 2024): 40.

[7]E. Brown et al., "Physics-Informed Deep Generative Learning for Quantitative Assessment of the Retina," *Nature Communications* 15 no. 1 (2024).

[8]J. Staal et al., "Ridge-based vessel segmentation in color images of the retina." *IEEE Transactions on Medical Imaging* 23 no. 4 (April 2004): 501–09.

[9]R.J. Hernandez et al., "AI and the Eye – Integrating Deep Learning and in Silico Simulations to Optimise Diagnosis and Treatment of Wet Macular Degeneration," *medRxiv* (2024).

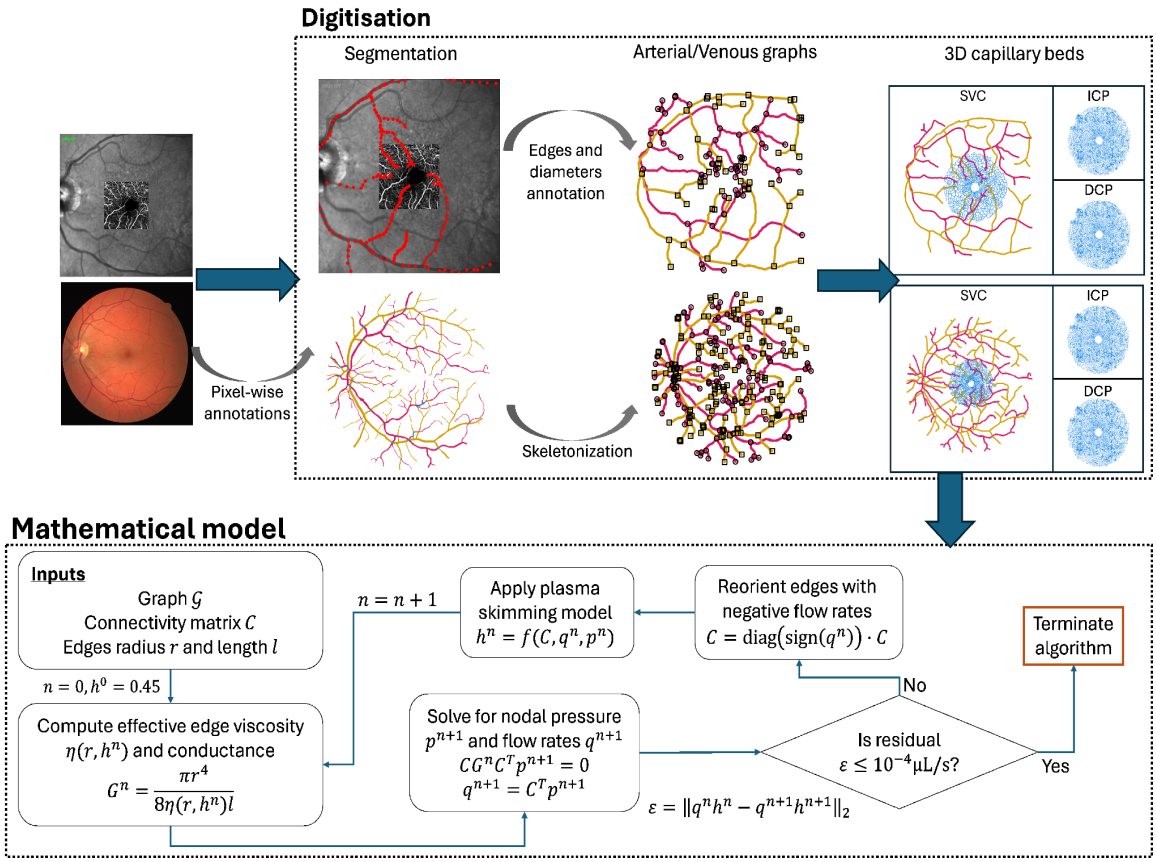

Figure 1: Summary of the framework to create digital twins, including the plasma skimming and blood flow model.

Simulating Blood Flow

The model assumes Poiseuille flow:

$$\Delta p = \frac{8\eta(r,h)Lq}{\pi r^4}$$

where q is the volumetric blood flow, r and L the vessel radius and length, and Δp the pressure drop between the ends of the vessel. The use of an effective viscosity term $\eta(r,h)$ as a function of vessel radius and discharge haematocrit (h) accounts for the non-Newtonian behaviour of blood and the Fåhræus-Lindqvist effect. A plasma skimming model, to simulate the uneven distribution of red blood cells at bifurcations in the network, is also introduced. The blood flow algorithm is shown in Figure **1**.

Results

Digital Twins of Health Eyes

Six digital twins of healthy eyes were developed, as shown in Figure **2**. Total retinal blood flow through the eyes was 43.28 ± 12.19 µL/min, similar to what has been measured *in vivo* in the retina (30 – 50 µL/min)[10]. Transit times of red blood cells were also computed, with mean transit times (MTT) across

[10]V. Doblhoff-Dier et al., "Measurement of the total retinal blood flow using dual beam Fourier-domain Doppler optical coherence tomography with orthogonal detection planes," *Biomedical Optics Express* 5 no. 2 (January 2014): 630–42.

the 6 twins ranging from 4.8 s to 9.9 s, which compare well with the measured MTT of 4.9 ± 1.9 s[11]. As such, we validate the blood flow through the digital twins.

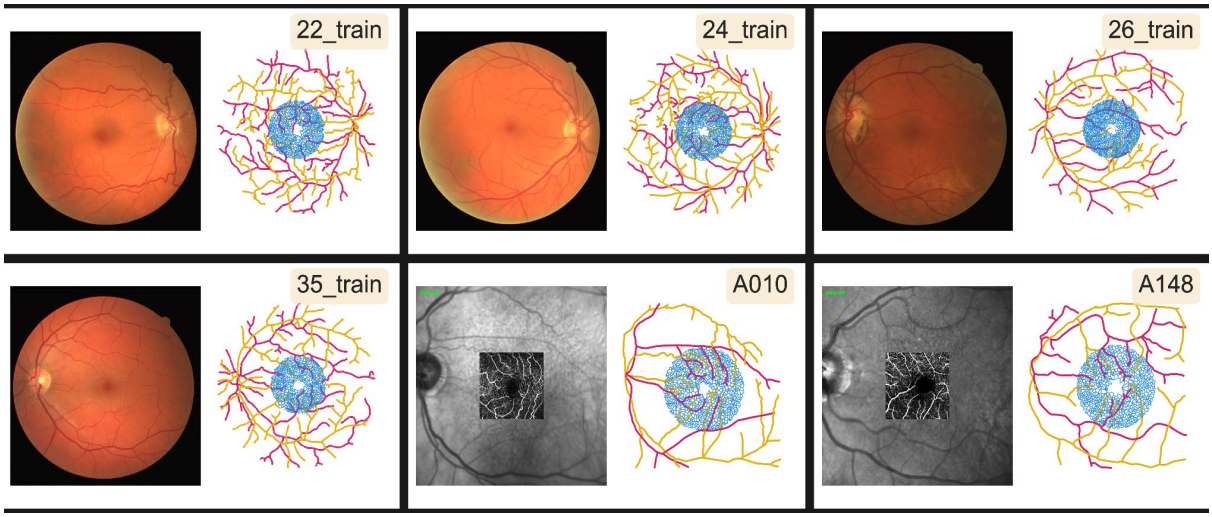

Figure 2: Example of 6 generated digital twins. The graph of the vasculature is shown next to the generated vascular graph. Arteries (in red) and veins (in orange) are digitised from the segmentation. Capillaries (in blue) are randomly generated with Voronoi tessellation.

Diabetic Retinopathy and *in silico* Biomarkers

Diabetic retinopathy affects the blood vessels of the retina. One aspect of this disease is capillary rarefaction. As such, we implemented a diabetic retinopathy model to simulate the advancement of diabetic symptoms through random capillary removal. We simulate an intermediate case by removing 2% of vessels and an advanced case by removing 5% of vessels. An example of blood pressure maps for one individual at different stages of the disease is shown in Figure **3**.

Discussion

We also sought to discover whether mean transit time (MTT) and capillary transit time heterogeneity (CTH) could be used as *in silico* biomarkers of different stages of disease. As shown in Figure **4**, there is a clear shift in each individual towards longer MTT and CTH as the disease progresses, suggesting its potential for early detection of diabetic retinopathy.

Personalised Retinal Healthcare

Our findings highlight the potential of retinal digital twins to inform personalised approaches in ophthalmology. By capturing patient-specific vascular structures and haemodynamics, digital twins go beyond population-based averages and open avenues for risk stratification tailored to individuals. In particular, physics-informed simulations of blood flow, and potentially oxygen transport, can provide further insight into disease impact for individuals and can help tailor personalised treatment.

[11]G. Bjärnhal et al., "Analysis of mean retinal transit time from fluorescein angiography in human eyes: Normal values and reproducibility," *Acta Ophthalmologica Scandinavic*a 80 no. 6 (December 2002): 652–55.

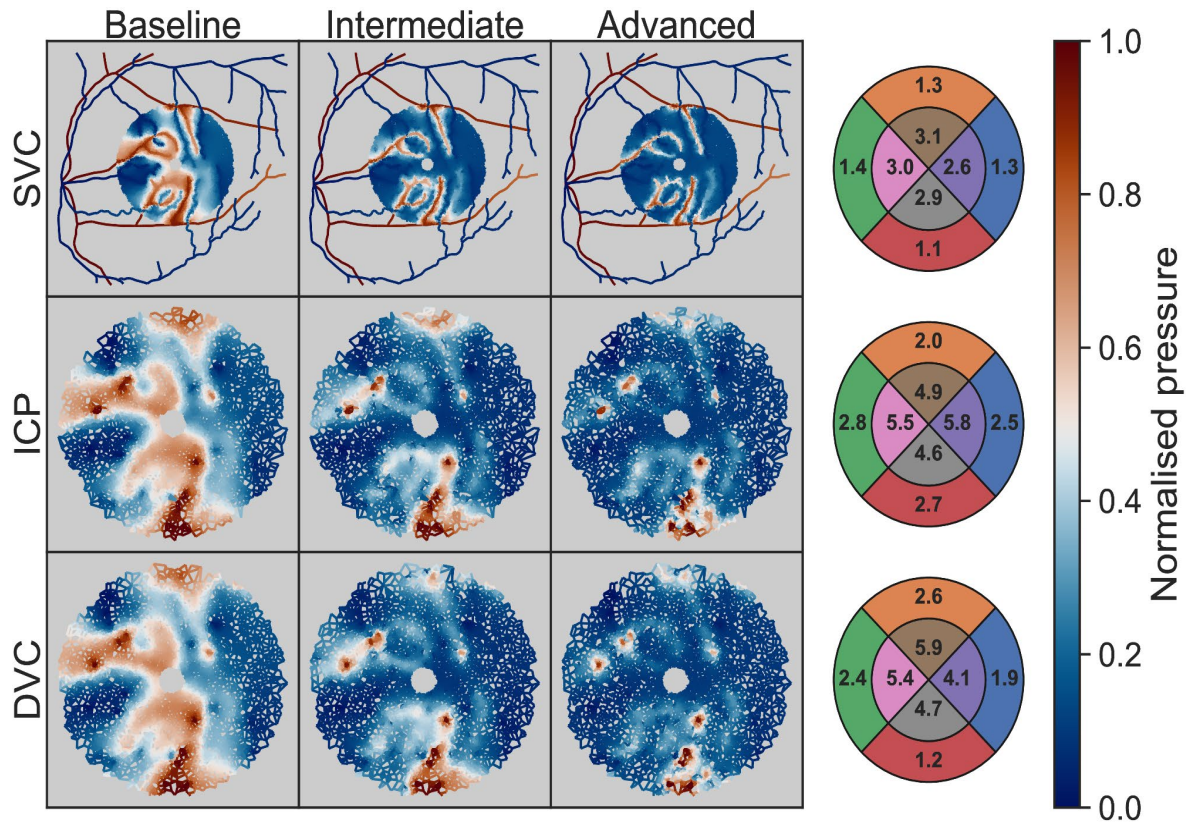

Figure 3: Blood pressure changes with diabetes in one digital twin. From left to right, capillary rarefaction increases from the baseline conditions to the advanced stages. Pie charts show the percentage of lost capillary area between healthy and intermediate diabetic stages (outer ring) and between the healthy and advanced diabetic stages (inner ring).

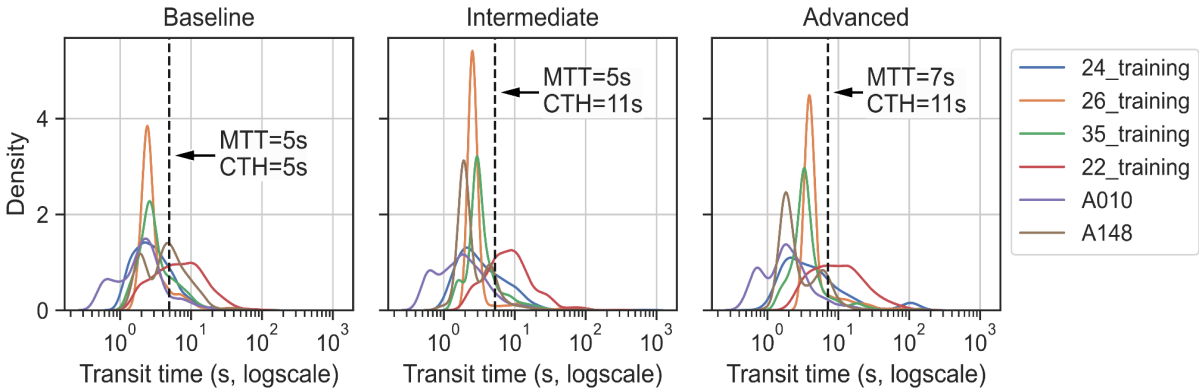

Figure 4: Plot of the probability density functions of transit times with the advancement of diabetic symptoms. Each line corresponds to a single digital twin. The vertical dashed line shows the means of MTT and CTH among the six individuals plotted.

Clinical Implications

MTT and CTH are established markers of pathology in cerebral and cardiovascular research[12]. We have demonstrated the potential of these markers to detect disease in silico, potentially extending their use in ophthalmology as indicators of retinal microvascular health. If validated in larger cohorts, these

[12]L. Østergaard, "Blood Flow, Capillary Transit Times, and Tissue Oxygenation: The Centennial of Capillary Recruitment." *Journal of Applied Physiology* 129 no. 6 (2020): 1413–21.s

metrics could provide early warning signals for diseases such as diabetic retinopathy or glaucoma, enabling pre-emptive interventions.

Translational Potential

One of the strengths of this framework is its compatibility with existing imaging modalities. OCTA and fundus photography are already widely available in clinical settings. Integrating our pipeline with these devices could enable near real-time generation of digital twins. This would provide clinicians with immediate haemodynamic insights, including MTT and CTH biomarkers, alongside routine imaging.

'Real-time' Retinal Digital Twins

The proper definition of an engineering digital twin includes a real-time stream of information from the real world to the virtual one, which the digital twin can update. In medicine, due to the fundamental constraints of real-time monitoring of patients, it has not been feasible to provide that live stream of information to the digital twin. However, the retina, of all the organs, is arguably one of the easiest to image, allowing for repeat scans to be taken with enough frequency to allow for a longitudinal digital twin to be built up. We are currently working towards this through our study at the St Paul's Eye Centre, Liverpool, where we are collecting repeat scans of patients over 3 years. This will eventually allow us to build a longitudinal digital twin, which, if integrated into imaging platforms, would provide instant feedback, enabling ophthalmologists to explore disease trajectories virtually.

Limitations

This proof-of-concept is limited by a small sample size and simplified boundary conditions. Disease models, such as that for diabetic retinopathy, remain stylised and do not account for biochemical processes such as angiogenesis or vessel remodelling. Moreover, direct in vivo flow validation was unavailable for individuals in our dataset (validation was done at the population level). Larger studies with multimodal validation are required.

Conclusions

We presented a computational framework to generate digital twins of the retinal vasculature from OCTA and fundus images. The model reproduced literature-consistent haemodynamics, revealed inter-individual variability, and simulated disease scenarios with personalised outcomes. Importantly, it enabled the derivation of perfusion markers such as MTT and CTH, which may serve as new retinal biomarkers of microvascular health.

Digital twins represent a promising tool for personalised ophthalmology, bridging imaging data with computational modelling. Future work will focus on real-time device integration, scaling to larger cohorts, and linking retinal twins to systemic models of ageing and disease

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