Towards digital twins for ocular applications - a combined physics-based and data-driven approach

Vincent Chabannes[1], Christophe Prud'homme[1], **Thomas Saigre**[1], Marcela Szopos[2]

[1]Institut de Recherche Mathématique Avancée, UMR 7501 Université de Strasbourg et CNRS

[3]Université Paris Cité, CNRS, MAP5, F-75006 Paris, France

Congrès SMAI 2025

3rd June 2025

Digital twins for health: context and challenges

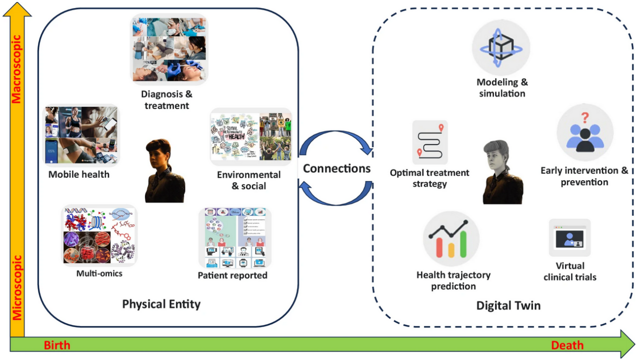


Figure 1: Digital Twins as envisioned for healthcare[a].

Definition of digital twins in precision medicine[2]

A ***digital twin*** is an *in-silico* framework that replicates a biological cell, sub-system, **organ**, or a whole organism, with a transparent **predictive model** of their relevant **causal mechanisms** and **response to interventions**.

[a] Katsoulakis, E. et al. npj Digit. Med. (2024)

[b] De Domenico *et al.* npj Digital Medicine. (2025)

Methodology

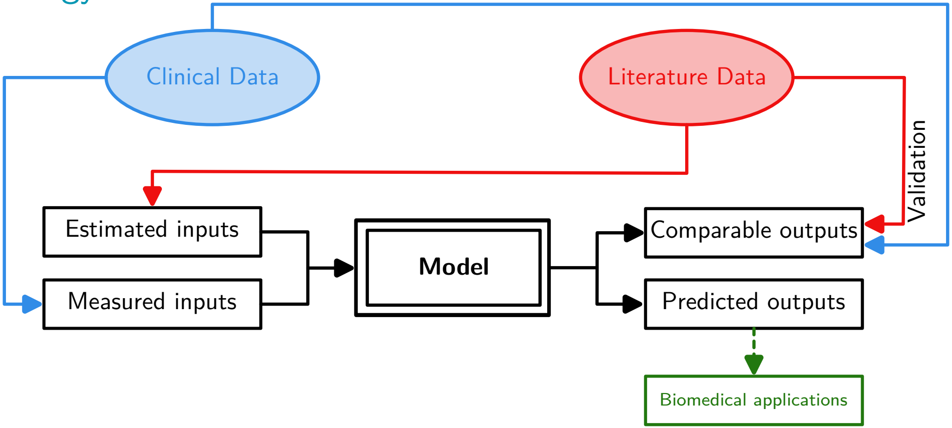
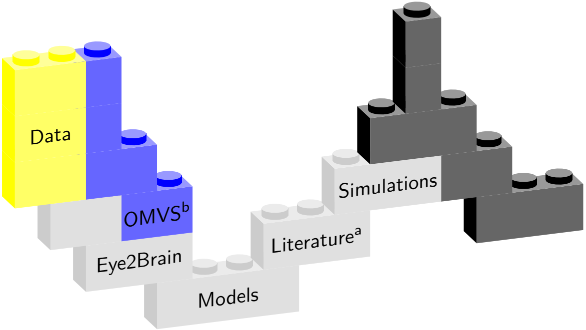


Figure 2: Methodology for the development of patient-specific models, adapted from[1].

[1] Sala *et al.* *International Journal for Numerical Methods in Biomedical Engineering*. (2023)

Aim: build a digital twin of the eye

- State-of-the-art: **digital models**[a] of the eye.
- Toward a **digital shadow**: data from **previous studies** and **measurements** to validate and enhance the models.



[a] Scott (1988), Ng et al. (2007), Dvoriashyna et al. (2019)...

[b] Sala et al. *Int J Numer Methods Biomed Eng*. (2023)

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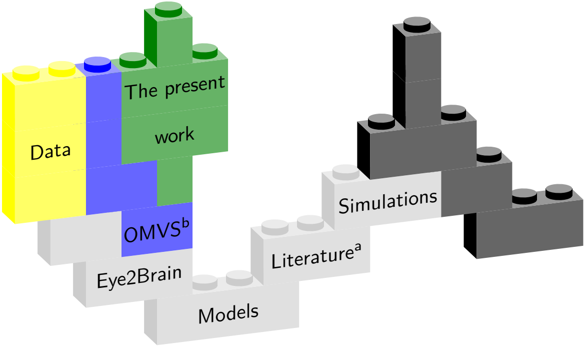

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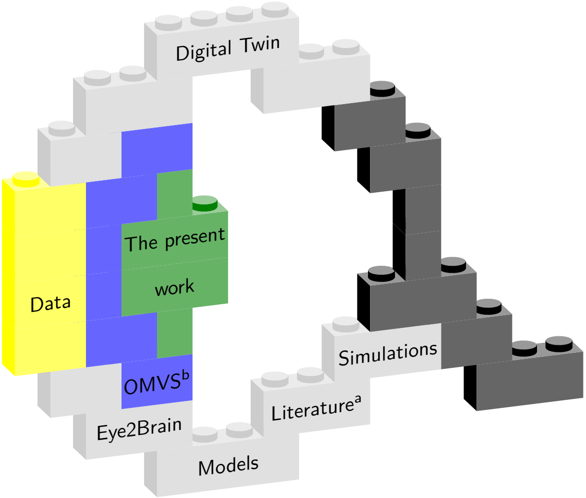
Aim: build a digital twin of the eye

- State-of-the-art: **digital models**[a] of the eye.
- Toward a **digital shadow**: data from **previous studies** and **measurements** to validate and enhance the models.
- Final goal: a **digital twin** = virtual replica of the eye, in real-time connection with the physical entity.



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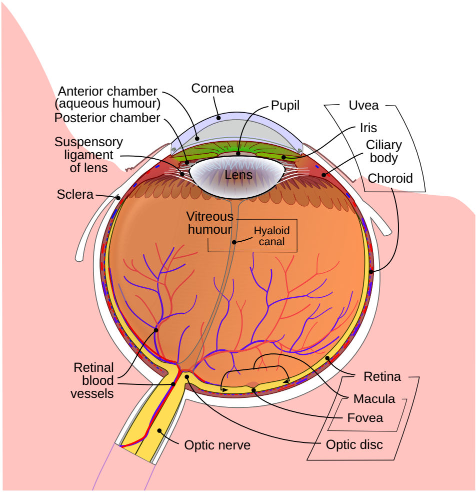
Motivation: understand ocular **physiology** and **pathology**



Rhcastilhos, from Wikipedia

- The **eye** is a complex organ, with a **multilayered structure**, numerous multiscale and multiphysics phenomena involved.
- **Measurements:** complex to perform on human subjects[a], scarce data, mostly available on surface[b].
- Present work: focus on **heat transfer** and **aqueous humor flow dynamics**.

[a] Rosenbluth & Fatt. *Exp. Eye Res.* (1977)
[b] Purslow & Wolffsohn. *Eye Contact Lens.* (2005)

Motivation: understand ocular **physiology** and **pathology**

- The **anterior chamber** (AC) is filled with **aqueous humor** (AH), whose dynamics is crucial for the ocular health[a],
- understand the **AH flow dynamics** and **heat transfer** is important for **drug distribution**[b], and **therapeutic interventions** (laser treatment, corneal cell sedimentation[c], etc.).

[a] Dvoriashyna *et al.* *Ocular Fluid Dynamics*. (2019)
[b] Bhandari. *J Control Release*. (2021)
[c] Kinoshita *et al.* *N Engl J Med*. (2018)

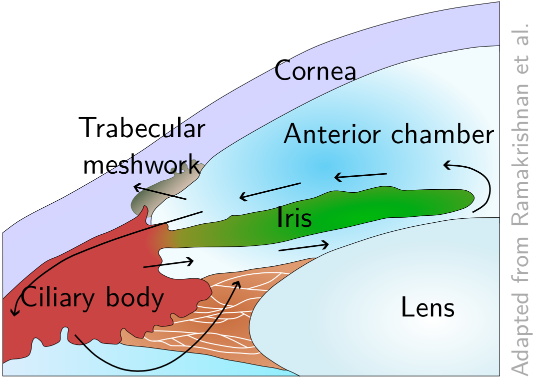
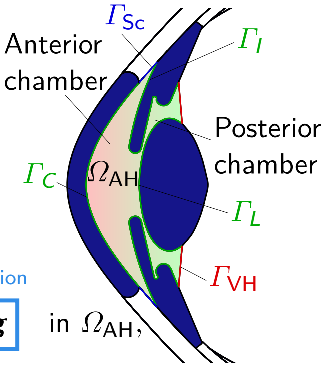


Figure 3: Production and drainage of AH in the eye.

Biophysical model[2,3]



- Incompressible fluid, constant density,
- The steady flow of the aqueous humor is governed by the Navier–Stokes equations:

$$
\begin{aligned}
&\underbrace{\boxed{\rho(\boldsymbol{u}\cdot\nabla)\boldsymbol{u} - \nabla\cdot(2\mu \boldsymbol{D}(\boldsymbol{u}) - p\boldsymbol{I})}}_{\text{Navier-Stokes equations}} = \underbrace{\boxed{-\rho\beta(T - T_{\mathrm{ref}})\boldsymbol{g}}}_{\text{Boussinesq approximation}} && \text{in } \Omega_{\mathrm{AH}},\\
&\boxed{\text{Incompressibility}} \quad \nabla\cdot\boldsymbol{u} = 0 && \text{in } \Omega_{\mathrm{AH}},\\
&\boxed{\text{Heat transfer equation}} \quad \rho C_p \boldsymbol{u}\cdot\nabla T - k_i \nabla^2 T = 0 && \text{in } \Omega = \bigcup_i \Omega_i.
\end{aligned}
$$

$+$ Boundary and Interface conditions.

[2] Scott. *Physics in Medicine and Biology*. (1988), Ng & Ooi. *Comput Methods Programs Biomed*. (2006), Li *et al.* *Int J Numer Method Biomed Eng*. (2010)...

[3] Wang *et al.* *BioMedical Engineering OnLine*. (2016), Dvoriashyna *et al.* *Mathematical Models of Aqueous Production, Flow and Drainage*. (2019)...

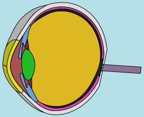
Parameter dependent model

Symbol	Name	Dimension	Baseline value	Range
T_{amb}	Ambient temperature	[K]	298	[283.15, 303.15]
T_{bl}	Blood temperature	[K]	310	[308.3, 312]
h_{amb}	Ambient air convection coefficient	$[\mathrm{W\,m^{-2}\,K^{-1}}]$	10[a]	[8, 100]
h_{bl}	Blood convection coefficient	$[\mathrm{W\,m^{-2}\,K^{-1}}]$	65[b]	[50, 110]
h_{r}	Radiation heat transfer coefficient	$[\mathrm{W\,m^{-2}\,K^{-1}}]$	6[c]	–
E	Evaporation rate	$[\mathrm{W\,m^{-2}}]$	40[c]	[20, 320]
k_{lens}	Lens conductivity	$[\mathrm{W\,m^{-1}\,K^{-1}}]$	0.4[b]	[0.21, 0.544]
k_{cornea}	Cornea conductivity	$[\mathrm{W\,m^{-1}\,K^{-1}}]$	0.58[d]	–
$k_{\mathrm{sclera}} = k_{\mathrm{iris}} = k_{\mathrm{lamina}} = k_{\mathrm{opticNerve}}$	Eye envelope components conductivity	$[\mathrm{W\,m^{-1}\,K^{-1}}]$	1.0042[e]	–
$k_{\mathrm{aqueousHumor}}$	Aqueous humor conductivity	$[\mathrm{W\,m^{-1}\,K^{-1}}]$	0.28[d]	–
$k_{\mathrm{vitreousHumor}}$	Vitreous humor conductivity	$[\mathrm{W\,m^{-1}\,K^{-1}}]$	0.603[c]	–
$k_{\mathrm{choroid}} = k_{\mathrm{retina}}$	Vascular beds conductivity	$[\mathrm{W\,m^{-1}\,K^{-1}}]$	0.52[f]	–

[a] Mapstone (1968), [b] J J W Lagendijk (1982), [c] Scott (1988), [d] Emery et al. (1975), [e] Ng et al. (2007), [f] IT'IS Foundation (2024).

Methods and computational framework

Geometrical model



Mesh generation

- 3D mesh with **$4.97 \cdot 10^6$ elements**,
- **Fine mesh refinement** in Ω_{AH}, where the coupled model is considered.

Biophysical model

$$\rho(\boldsymbol{u} \cdot \nabla)\boldsymbol{u} - \nabla(2\mu \boldsymbol{D}(\boldsymbol{u}) - p\boldsymbol{I}) = -\rho\beta(T - T_{\mathrm{ref}})\boldsymbol{g},$$
$$\nabla \cdot \boldsymbol{u} = 0,$$
$$\rho C_p \boldsymbol{u} \cdot \nabla T - k\nabla^2 T = 0.$$

Finite element solver

- Use the Feel++[1] **heatfluid** toolbox using monolithic approach and **PDE based preconditioning** for solving the **non-linear** problem,
- ✔ Model validation and verification.

[1] C. Prud'homme, *et al.* Feel++ Release V111. (2024) github.com/feelpp/feelpp

Discrete geometry: full pipeline and dataset available in GitHub [1]

- Performed with Salome meshing library, using NETGEN[2] meshing algorithm.

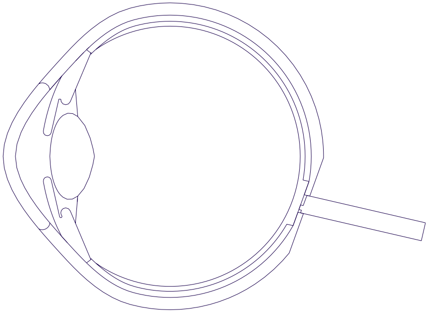


Figure 4: Geometry of the eye.

[1] V. Chabannes, C. Prud'homme, T. Saigre, L. Sala, M. Szopos, C. Trophime A 3D geometrical model and meshing procedures for the human eyeball, *Zenodo* github.com/feelpp/mesh.eye. (2024)

[2] J. Schöberl. *Computing and Visualization in Science*. (1997)

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- Performed with Salome meshing library, using NETGEN[2] meshing algorithm.
- The mesh generated by Salome is quite coarse $\longrightarrow$ refinement performed around the AC and PC.

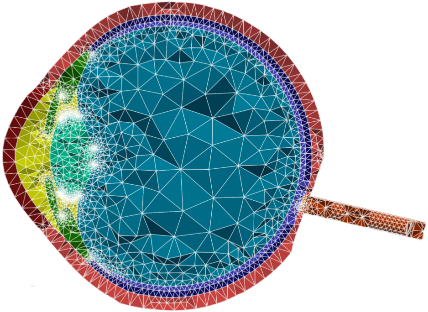

Figure 4: Original mesh, $4.64 \cdot 10^5$ tetrahedrons.

[1] V. Chabannes, C. Prud'homme, T. Saigre, L. Sala, M. Szopos, C. Trophime A 3D geometrical model and meshing procedures for the human eyeball, *Zenodo* github.com/feelpp/mesh.eye. (2024)
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- Performed with Salome meshing library, using NETGEN[2] meshing algorithm.
- The mesh generated by Salome is quite coarse $\longrightarrow$ refinement performed around the AC and PC.
- For the verification step: a family of meshes of various refinement levels is generated.

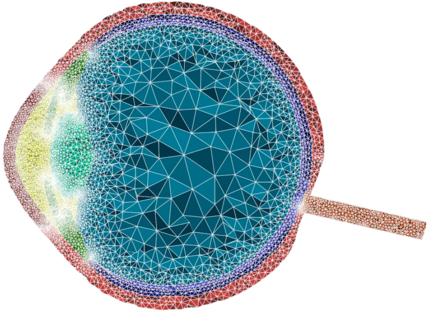


Figure 4: Mesh refined around AC and PC, $9.4 \cdot 10^5$ elements.

[1] V. Chabannes, C. Prud'homme, T. Saigre, L. Sala, M. Szopos, C. Trophime A 3D geometrical model and meshing procedures for the human eyeball, *Zenodo* github.com/feelpp/mesh.eye. (2024)

[2] J. Schöberl. *Computing and Visualization in Science*. (1997)

High Fidelity model

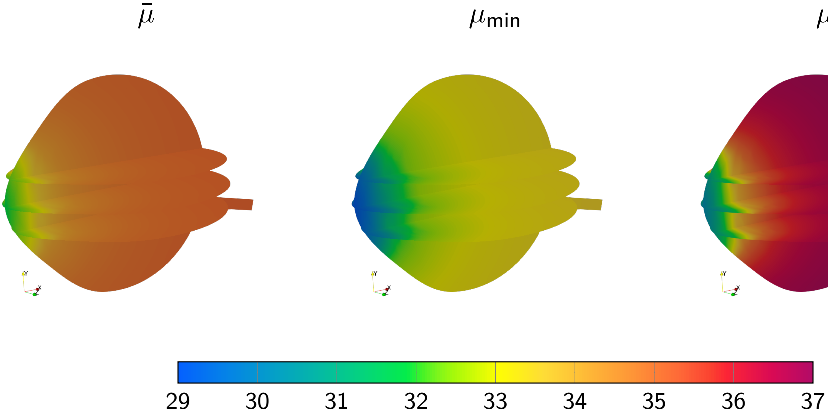
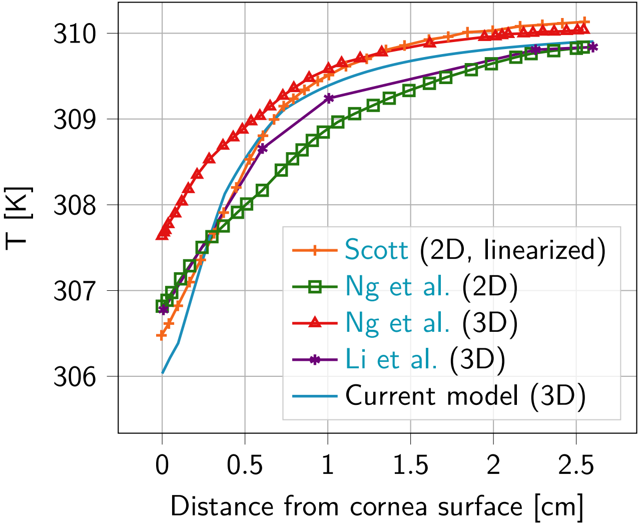
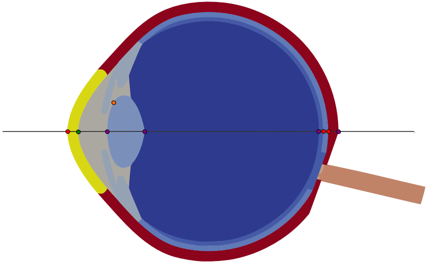


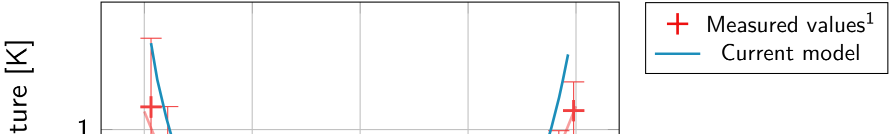
Figure 5: Distribution of the temperature [°C] in the eyeball from the linear model.

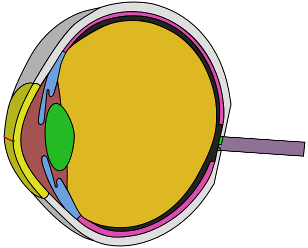
Comparison with previous **numerical** studies





Validation: **measured** values over the GCC





[1] Efron *et al.* *Current Eye Research*. (1989)

Numerical results: impact of the posture on the pressure and velocity of the AH[a]

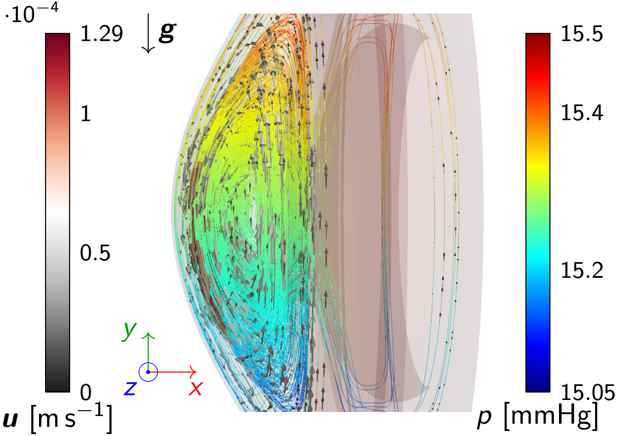


Figure 6: Standing position.

- **Recirculation** of the AH,

[a] T. Saigre *et al.* submitted. ()
[b] Wang *et al.* BioMedical Engineering OnLine. (2016)
[c] Abdelhafid *et al.* *Recent Devel. in Mathematical, Statistical and Computational Sciences*. (2021)
[d] Murgoitio-Esandi *et al.* *Translational Vision Science & Technology*. (2023)

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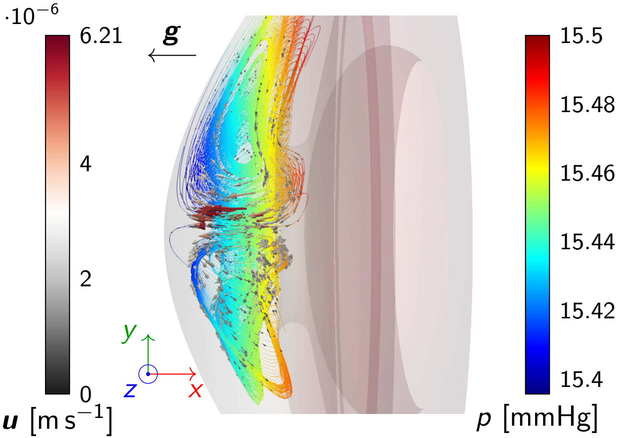

Figure 6: Prone position.

- **Recirculation** of the AH,
- Formation of a **Krukenberg's spindle**, in good agreement with clinical observations and previous studies[b,c,d]

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[b] Wang *et al.* BioMedical Engineering OnLine. (2016)

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[d] Murgoitio-Esandi *et al.* *Translational Vision Science & Technology*. (2023)

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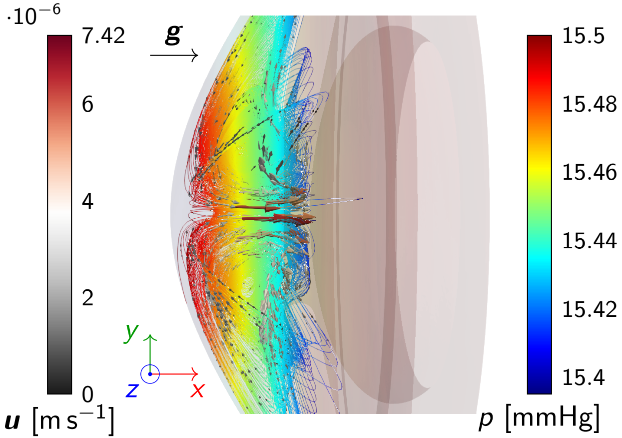

Figure 6: Supine position.

- **Recirculation** of the AH,
- Formation of a **Krukenberg's spindle**, in good agreement with clinical observations and previous studies[b,c,d]
- Fluid dynamics is **strongly influenced by the position of the patient**.

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[a] T. Saigre *et al.* submitted. ()

[b] Wang *et al.* BioMedical Engineering OnLine. (2016)

[c] Abdelhafid *et al.* *Recent Devel. in Mathematical, Statistical and Computational Sciences*. (2021)

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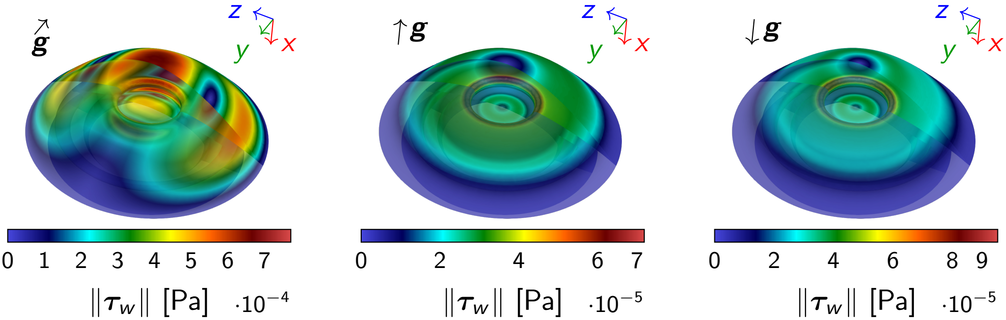
Numerical results: impact of the posture on the wall shear stress

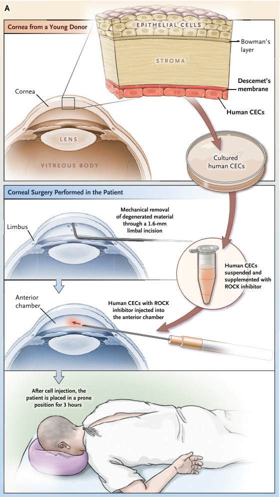


(a) Standing. (b) Prone. (c) Supine.

Figure 7: Wall shear stress distribution on the corneal endothelium for the three postural orientations.

Numerical results: impact of the posture on the wall shear stress

- **Prediction:** the WSS distribution is **impacted** by the postural orientation and the ambient temperature.
- **Clinical target:** assess the effect of ocular surface cooling on endothelial cell sedimentation in cell injection therapy.[a]
- **Optimal treatment strategy:** control the temperature to enhance the diffusion and sedimentation of the cells during treatment.[b]



Source: Kinoshita *et al.*

[a] Kinoshita *et al.* *N Engl J Med.* (2018)
[b] T. Saigre *et al.* ARVO meeting 2025. (2024)

Incorporate uncertainties

Verification, validation, and uncertainty quantification (VVUQ)

Digital twins require VVUQ to be a continual process that must adapt to changes in the physical counterpart, digital twin virtual models, data, and the prediction/decision task at hand.[1]

[1] National Academies of Sciences, Engineering, and Medicine *Foundational Research Gaps and Future Directions for Digital Twins*. (2024)

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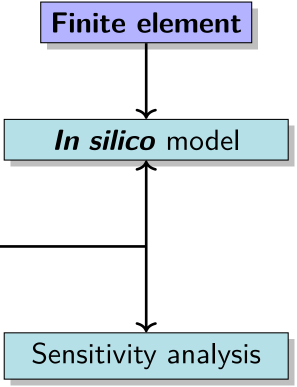

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In silico **model**

Sensitivity analysis

Prohibitive cost in 3D

[1] National Academies of Sciences, Engineering, and Medicine *Foundational Research Gaps and Future Directions for Digital Twins.* (2024)

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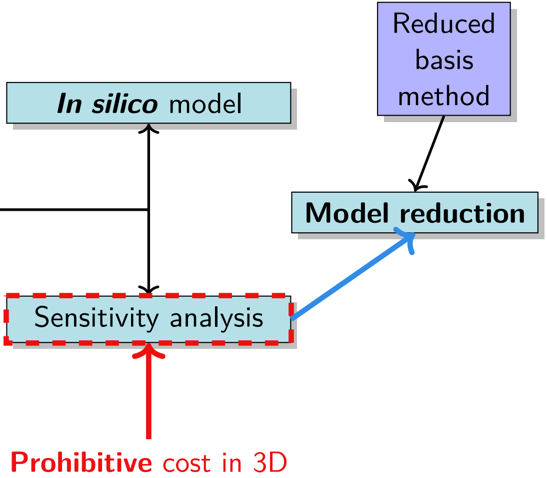

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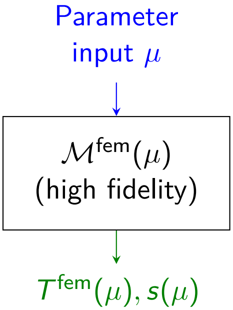
Model Order Reduction

- **Goal:** replicate input-output behavior of the high fidelity model $\mathcal{M}^{\text{fem}}$ with a reduced order model $\mathcal{M}^{\text{rbm}}$,
- with a procedure stable and efficient, here the **Certified Reduced Basis Method**[4]



[4] Prud'homme *et al.* *Journal of Fluids Engineering*. (2002)

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- with a procedure stable and efficient, here the **Certified Reduced Basis Method**[4]

$$\begin{array}{ccc}
\text{Parameter input } \mu & & \text{Parameter input } \mu \\
\downarrow & & \downarrow \\
\boxed{\mathcal{M}^{\text{fem}}(\mu) \text{ (high fidelity)}} & \Longrightarrow & \boxed{\mathcal{M}^{\text{rbm}}(\mu)} \\
\downarrow & & \downarrow \\
T^{\text{fem}}(\mu), s(\mu) & \mathcal{N} \gg N & T^{\text{rbm},N}(\mu), s_N(\mu)
\end{array}$$

[4] Prud'homme *et al.* *Journal of Fluids Engineering*. (2002)

Time of execution

Implementation in the Feel++ library.

	Finite element resolution $T^{\text{fem}}(\mu)$			Reduced model $T^{\text{rbm},N}(\mu), \Delta_N(\mu)$
	$\mathbb{P}_1$	$\mathbb{P}_2$ (np=1)	$\mathbb{P}_2$ (np=12)	
Problem size	$\mathcal{N} = 207\ 845$	$\mathcal{N} = 1\ 580\ 932$		$N = 10$
t_{exec}	5.534 s	62.432 s	10.76 s	2.88×10^{-4} s
speed-up	11.69	1	5.80	$\mathbf{2.17 \times 10^5}$

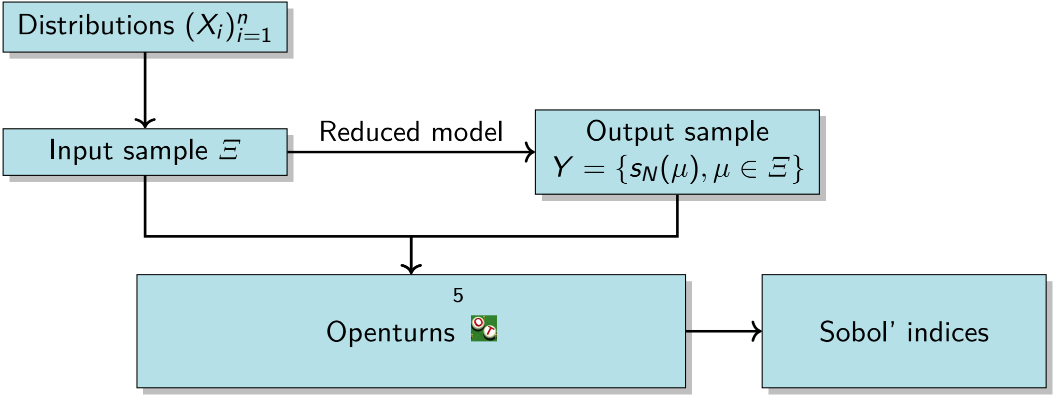
Table 1: Times of execution, using mesh `M3` for high fidelity simulations.

Stochastic sensitivity analysis

$$
\begin{tikzcd}
\boxed{\text{Distributions } (X_i)_{i=1}^n} \arrow[d] & \\
\boxed{\text{Input sample } \varXi} \arrow[r, "\text{Reduced model}"] & \boxed{\begin{array}{c}\text{Output sample}\\ Y = \{s_N(\mu), \mu \in \varXi\}\end{array}}
\end{tikzcd}
$$

[5] Baudin *et al.* *Handbook of Uncertainty Quantification*. (2016)

Stochastic sensitivity analysis



[5] Baudin *et al.* *Handbook of Uncertainty Quantification.* (2016)

Stochastic sensitivity analysis[a]

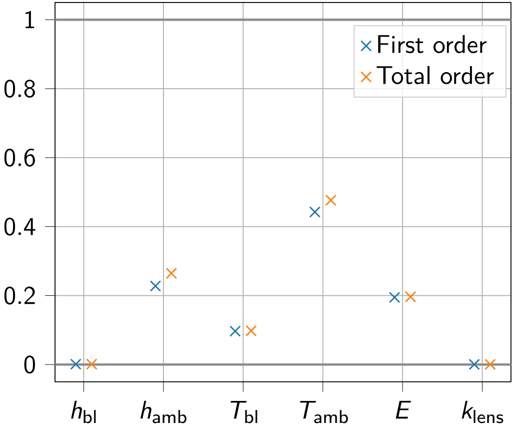
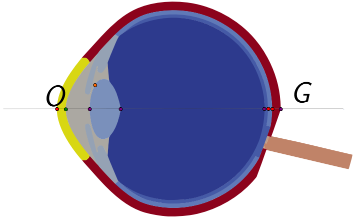


Figure 7: Sobol' indices: temperature at point O.



Temperature at the level of the **cornea**:

- **significantly** influenced by T_{amb}, h_{amb} (external factors) and E, T_{bl} (subject specific parameters) $\longrightarrow$ need for measurements/better model for these contributions,
- **minimally** influenced by k_{lens}, h_{bl} $\longrightarrow$ can be fixed at baseline value,
- **high order** interactions on T_{amb}, h_{amb}.

[a] T. Saigre *et al.* *Int J Numer Methods Biomed Eng.* (2024)

Stochastic sensitivity analysis[a]

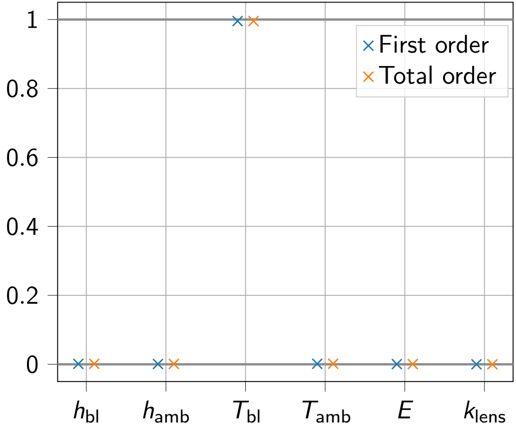
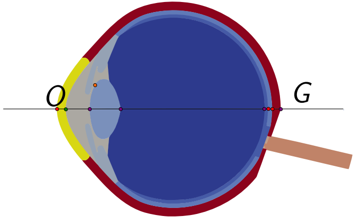


Figure 7: Sobol' indices: temperature at point G.



Temperature at the back of the eye:

- only influenced by the blood temperature.

[a] T. Saigre *et al.* *Int J Numer Methods Biomed Eng.* (2024)

Conclusion and perspectives

- **Heat transport model in the human eye:** perform FEM simulations, validation against experimental data,
- Develop a **reduced model** with **certified error bound**,
- **Sensitivity analysis:** compute Sobol' indices, highlight the impact of specific parameters on the outputs of interest.
- **Couple heat transfer with AH dynamics:** evaluate the impact of postural orientation and environmental conditions on flow and its properties.
- **Clinical application:** demonstrate that thermal modulation can improve the results of endothelial cell therapy.

Thomas Saigre et al. "Model order reduction and sensitivity analysis for complex heat transfer simulations inside the human eyeball". en. In: *International Journal for Numerical Methods in Biomedical Engineering* 40.11 (Sept. 2024), e3864

Thomas Saigre. "Mathematical modeling, simulation and reduced order modeling of ocular flows and their interactions: Building the Eye's Digital Twin". Theses. Université de Strabourg, Dec. 2024

Conclusion and perspectives

- **Enhance the model:**
  - **Geometrical model:** take into account geometrical parameters,
  - **Fluid dynamics:** incorporate the production and drainage of aqueous humor to assess their impact.
- **Study laser surgery:** integrate radiative transfer module to capture light-tissue interactions and transient thermal effects (internship and thesis of Pierre-Antoine Senger)
- Steps toward a **digital twin** of the eye:
  - incorporate patient-specific data,
  - enhance predictive modeling and personalized medical applications,
  - real time connection with the physical entity.

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Thank you for your attention!

Bibliography

[Abd+21] Farah Abdelhafid et al. "Operator Splitting for the Simulation of Aqueous Humor Thermo-Fluid-Dynamics in the Anterior Chamber". en. In: *Recent Developments in Mathematical, Statistical and Computational Sciences*. Ed. by D. Marc Kilgour et al. Vol. 343. Series Title: Springer Proceedings in Mathematics & Statistics. Cham: Springer International Publishing, 2021, pp. 489–499.

[Bau+16] Michaël Baudin et al. "OpenTURNS: An Industrial Software for Uncertainty Quantification in Simulation". In: *Handbook of Uncertainty Quantification*. Ed. by Roger Ghanem, David Higdon, and Houman Owhadi. Cham: Springer International Publishing, 2016, pp. 1–38.

[BBS20] Ajay Bhandari, Ankit Bansal, and Niraj Sinha. "Effect of aging on heat transfer, fluid flow and drug transport in anterior human eye: A computational study". en. In: *Journal of Controlled Release* 328 (Dec. 2020), pp. 286–303.

[Bha21] Ajay Bhandari. "Ocular Fluid Mechanics and Drug Delivery: A Review of Mathematical and Computational Models". en. In: *Pharmaceutical Research* 38.12 (Dec. 2021), pp. 2003–2033.

[Cha+24] Vincent Chabannes et al. *A 3D geometrical model and meshing procedures for the human eyeball*. Sept. 2024.

[Chr+24] Christophe Prud'homme et al. *feelpp/feelpp: Feel++ Release V111 preview.9*. Mar. 2024.

Bibliography

[Com+24] Committee on Foundational Research Gaps and Future Directions for Digital Twins et al. *Foundational Research Gaps and Future Directions for Digital Twins*. Place: Washington, D.C. Mar. 2024.

[De +25] Manlio De Domenico et al. "Challenges and opportunities for digital twins in precision medicine from a complex systems perspective". In: *npj Digital Medicine* 8.1 (2025). Publisher: Nature Publishing Group UK London, p. 37.

[Dvo+19] Mariia Dvoriashyna et al. "Mathematical Models of Aqueous Production, Flow and Drainage". en. In: *Ocular Fluid Dynamics*. Ed. by Giovanna Guidoboni, Alon Harris, and Riccardo Sacco. Series Title: Modeling and Simulation in Science, Engineering and Technology. Cham: Springer International Publishing, 2019, pp. 227–263.

[Eme+75] A. F. Emery et al. "Microwave Induced Temperature Rises in Rabbit Eyes in Cataract Research". en. In: *Journal of Heat Transfer* 97.1 (Feb. 1975), pp. 123–128.

[EYB89] N. Efron, G. Young, and N. A. Brennan. "Ocular surface temperature". eng. In: *Current Eye Research* 8.9 (Sept. 1989), pp. 901–906.

[ITI24] IT'IS Foundation. *Thermal Conductivity*. 2024.

Bibliography

[J J82] J J W Lagendijk. “A mathematical model to calculate temperature distributions in human and rabbit eyes during hyperthermic treatment”. In: *Physics in Medicine & Biology* 27.11 (Nov. 1982), pp. 1301–1311.

[Kat+24] Evangelia Katsoulakis et al. “Digital twins for health: a scoping review”. In: *NPJ Digital Medicine* 7.1 (2024). Publisher: Nature Publishing Group UK London, p. 77.

[Kin+18] Shigeru Kinoshita et al. “Injection of Cultured Cells with a ROCK Inhibitor for Bullous Keratopathy”. en. In: *New England Journal of Medicine* 378.11 (Mar. 2018), pp. 995–1003.

[KS10] Andreas Karampatzakis and Theodoros Samaras. “Numerical model of heat transfer in the human eye with consideration of fluid dynamics of the aqueous humour”. In: *Physics in Medicine and Biology* 55.19 (Oct. 2010), pp. 5653–5665.

[Li+10] Eric Li et al. “Modeling and simulation of bioheat transfer in the human eye using the 3D alpha finite element method (αFEM)”. In: *International Journal for Numerical Methods in Biomedical Engineering* 26.8 (2010), pp. 955–976.

[Map68] R. Mapstone. “Measurement of corneal temperature”. en. In: *Experimental Eye Research* 7.2 (Apr. 1968), 237–IN29.

Bibliography

[Mur+23] Javier Murgoitio-Esandi et al. "A Mechanistic Model of Aqueous Humor Flow to Study Effects of Angle Closure on Intraocular Pressure". In: *Translational Vision Science & Technology* 12.1 (Jan. 2023), p. 16.

[NO06] E.Y.K. Ng and E.H. Ooi. "FEM simulation of the eye structure with bioheat analysis". en. In: *Computer Methods and Programs in Biomedicine* 82.3 (June 2006), pp. 268–276.

[NO07] E.Y.K. Ng and E.H. Ooi. "Ocular surface temperature: A 3D FEM prediction using bioheat equation". en. In: *Computers in Biology and Medicine* 37.6 (June 2007), pp. 829–835.

[ON08] Ean-Hin Ooi and Eddie Yin-Kwee Ng. "Simulation of aqueous humor hydrodynamics in human eye heat transfer". en. In: *Computers in Biology and Medicine* 38.2 (Feb. 2008), pp. 252–262.

[Pru+02] C. Prud'homme et al. "Reliable Real-Time Solution of Parametrized Partial Differential Equations: Reduced-Basis Output Bound Methods". en. In: *Journal of Fluids Engineering* 124.1 (Mar. 2002), pp. 70–80.

[Pru+24] Christophe Prud'homme et al. *feelpp/feelpp: Feel++ Release V111 preview.10*. July 2024.

[PW05] Christine Purslow and James S. Wolffsohn. "Ocular Surface Temperature: A Review". en. In: *Eye & Contact Lens: Science & Clinical Practice* 31.3 (May 2005), pp. 117–123.

Bibliography

[RF77] Robert F. Rosenbluth and Irving Fatt. “Temperature measurements in the eye”. en. In: *Experimental Eye Research* 25.4 (Oct. 1977), pp. 325–341.

[RRK13] R Ramakrishnan, Shalmali Ranaut, and Mona Khurana. “Aqueous Humor Dynamics”. en. In: *Diagnosis and Management of Glaucoma*. Jaypee Brothers Medical Publishers (P) Ltd., 2013, pp. 76–76.

[Sai+] Thomas Saigre et al. “A coupled fluid-dynamics-heat transfer model for 3D simulations of the aqueous humor flow in the human eye”. In preparation.

[Sai+24] Thomas Saigre et al. *Effect of Cooling of the Ocular Surface on Endothelial Cell Sedimentation in Cell Injection Therapy: Insights from Computational Fluid Dynamics*. 2024.

[Sai24] Thomas Saigre. “Mathematical modeling, simulation and reduced order modeling of ocular flows and their interactions: Building the Eye’s Digital Twin”. Theses. Université de Strabourg, Dec. 2024.

[Sal+23] Lorenzo Sala et al. “The ocular mathematical virtual simulator: A validated multiscale model for hemodynamics and biomechanics in the human eye”. en. In: *International Journal for Numerical Methods in Biomedical Engineering* (Nov. 2023), e3791.

[Sch97] Joachim Schöberl. “NETGEN An advancing front 2D/3D-mesh generator based on abstract rules”. In: *Computing and Visualization in Science* 1.1 (July 1997), pp. 41–52.

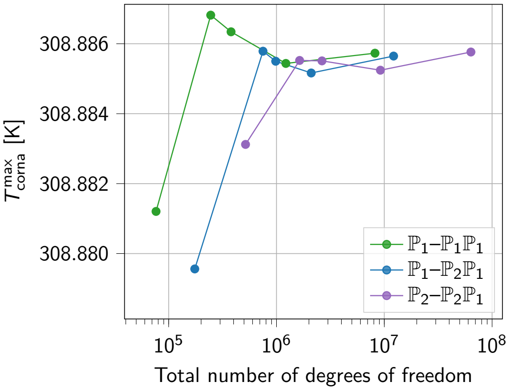
Bibliography

[Sco88] J A Scott. "A finite element model of heat transport in the human eye". In: *Physics in Medicine and Biology* 33.2 (Feb. 1988), pp. 227–242.

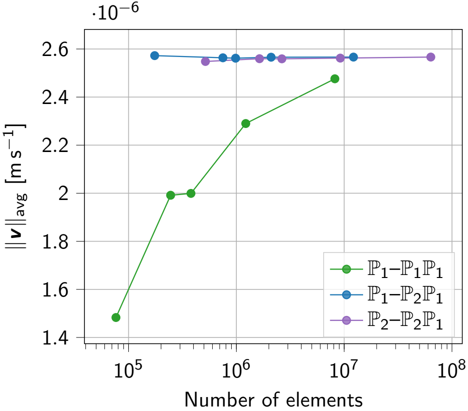
[SPS24] Thomas Saigre, Christophe Prud'homme, and Marcela Szopos. "Model order reduction and sensitivity analysis for complex heat transfer simulations inside the human eyeball". en. In: *International Journal for Numerical Methods in Biomedical Engineering* 40.11 (Sept. 2024), e3864.

[Wan+16] Wenjia Wang et al. "Fluid and structure coupling analysis of the interaction between aqueous humor and iris". en. In: *BioMedical Engineering OnLine* 15.S2 (Dec. 2016), p. 133.

Verifications and validations of the coupled heat-fluid model: mesh convergence



(a) Maximal temperature of the cornea.



(b) Mean fluid velocity.

Verifications and validations of the coupled heat-fluid model

Author	T_{amb}	No AH flow	AH flow coupled		
			Prone	Supine	Standing
Scott (2D)	293.15	306.4	–	–	–
Ooi et al. (2D)	298	306.45	–	–	306.9
Karampatzakis et al. (3D)	293	306.81	–	–	307.06
	296	307.33	–	–	307.51
	298	307.69	–	–	307.83
Current model (3D)	293	306.5647	306.56915	306.55899	306.63672
	296	307.09845	307.10175	307.09436	307.14651
	298	307.45746	307.46008	307.45432	307.49222

Verifications and validations of the coupled heat-fluid model

Position	Reference	Maximum velocity [$\mathrm{m\,s^{-1}}$]	Average velocity [$\mathrm{m\,s^{-1}}$]	Pressure [mmHg]
Supine	Wang et al.	$9.44 \cdot 10^{-4}$	$4.1 \cdot 10^{-5}$	13.50 – 13.58
	Murgoitio-Esandi et al.	$6 \cdot 10^{-5}$	n/a	n/a
	Bhandari et al.	n/a	$9.88 \cdot 10^{-6}$	n/a
	Current model	$2.59 \cdot 10^{-5}$	$3.21 \cdot 10^{-6}$	15.42 – 15.59
Standing	Wang et al.	$9.6 \cdot 10^{-4}$	$2.5 \cdot 10^{-4}$	13.50 – 13.59
	Bhandari et al.	n/a	$5.88 \cdot 10^{-5}$	n/a
	Current model	$2.76 \cdot 10^{-4}$	$5.23 \cdot 10^{-5}$	15.28 – 15.72