Toward digital twins for ocular applications: mathematical modeling, simulation and order reduction

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

[1]Institut de Recherche Mathématique Avancée, UMR 7501 Université de Strasbourg et CNRS
[2]Université Paris Cité, CNRS, MAP5, F-75006 Paris, France

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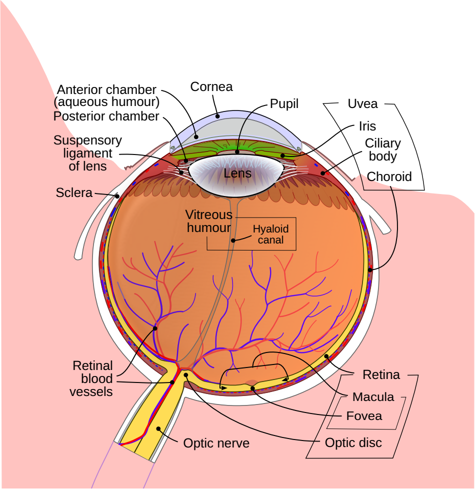
18th June 2025

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.).

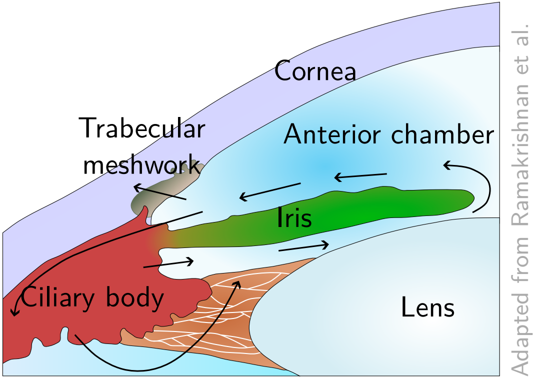
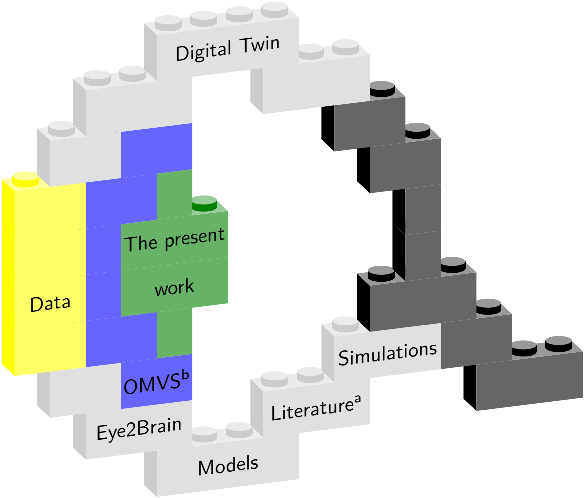


Figure 1: Production and drainage of AH in the eye.

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

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.



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

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

Methodology

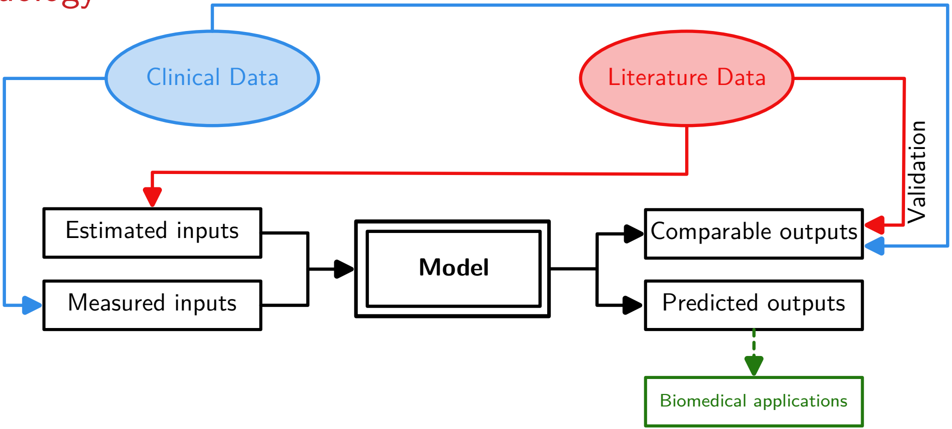
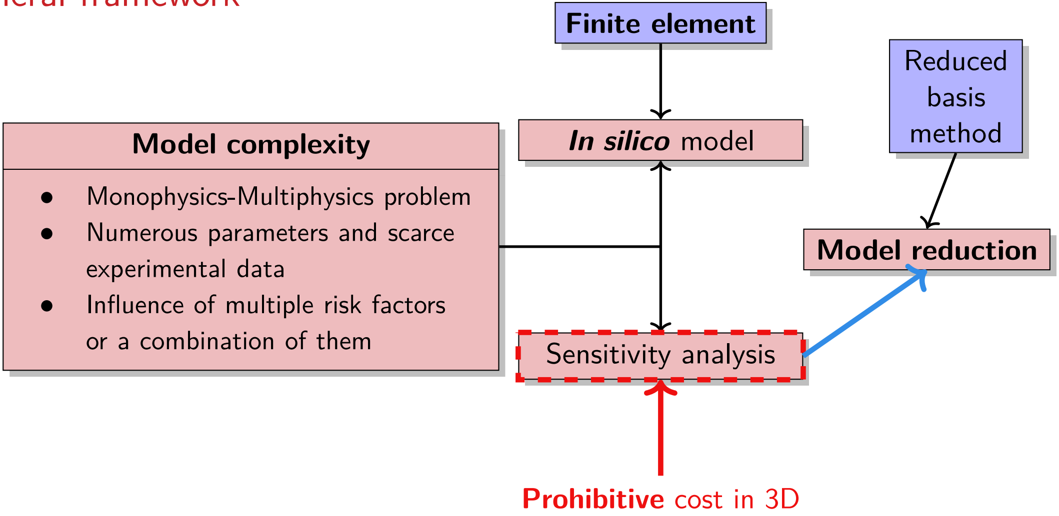


Figure 2: Methodology for the development of patient-specific models, adapted from[a].

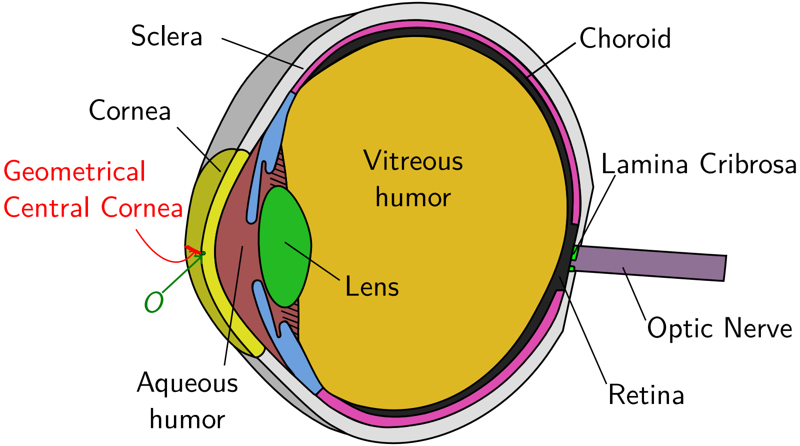
[a] Sala *et al.* *International Journal for Numerical Methods in Biomedical Engineering*. (2023)

General framework



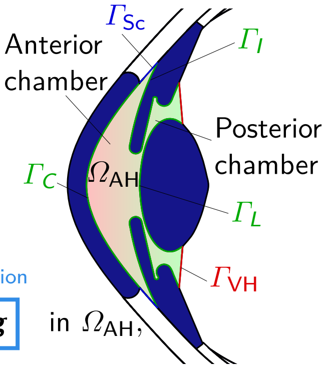
Mathematical modeling of heat transfer and aqueous humor flow mechanisms in the eye

Geometrical model[a]



[a] Sala *et al.* The ocular mathematical virtual simulator: A validated multiscale model for hemodynamics and biomechanics in the human eye. *Int J Numer Method Biomed Eng.* (2023)

Biophysical model[a,b]



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

Navier-Stokes equations — Boussinesq approximation

$$\rho(\boldsymbol{u}\cdot\nabla)\boldsymbol{u} - \nabla\cdot(2\mu\underline{\underline{\boldsymbol{D}}}(\boldsymbol{u}) - p\underline{\boldsymbol{I}}) = -\rho\beta(T - T_{\text{ref}})\boldsymbol{g} \quad \text{in } \Omega_{\text{AH}},$$

Incompressibility

$$\nabla\cdot\boldsymbol{u} = 0 \quad \text{in } \Omega_{\text{AH}},$$

Heat transfer equation

$$\rho C_p \boldsymbol{u}\cdot\nabla T - k_i\nabla^2 T = 0 \quad \text{in } \Omega = \bigcup_i \Omega_i.$$

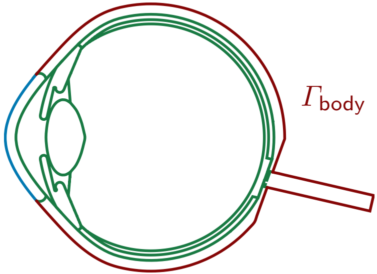
$+$ Boundary and Interface conditions.

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

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

Biophysical Model: Boundary Conditions

- Interface conditions: $\begin{cases} T_i = T_j, \\ k_i(\nabla T_i \cdot \boldsymbol{n}_i) = -k_j(\nabla T_j \cdot \boldsymbol{n}_j) \end{cases}$
  over $\partial\Omega_i \cap \partial\Omega_j$.
- Robin condition on Γ_{body}: $-k_i \dfrac{\partial T}{\partial \boldsymbol{n}} = h_{\text{bl}}(T - T_{\text{bl}})$.
- Neumann condition on Γ_{amb}:
  $-k_i \dfrac{\partial T}{\partial \boldsymbol{n}} = h_{\text{amb}}(T - T_{\text{amb}}) + \sigma\varepsilon(T^4 - {T_{\text{amb}}}^4) + E$.
- Conditions on velocity:
  $\boldsymbol{u} = \boldsymbol{0}$ on $\Gamma_C \cup \Gamma_I \cup \Gamma_L \cup \Gamma_{\text{VH}} \cup \Gamma_{\text{Sc}}$.



[a] Scott. *Physics in Medicine and Biology*. (1988)

Biophysical Model: Boundary Conditions

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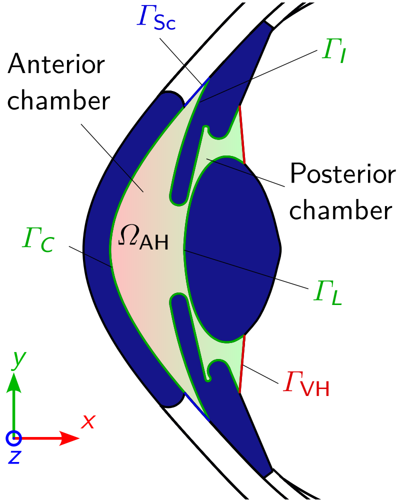
  over $\partial\Omega_i \cap \partial\Omega_j$.
- Robin condition on Γ_{body}: $-k_i \dfrac{\partial T}{\partial \boldsymbol{n}} = h_{\text{bl}}(T - T_{\text{bl}})$.
- Linearized Neumann condition[a] on Γ_{amb}:
  $$-k_i \frac{\partial T_i}{\partial \boldsymbol{n}} = h_{\text{amb}}(T - T_{\text{amb}}) + h_{\text{r}}(T - T_{\text{amb}}) + E,$$
  with $h_{\text{r}} = 6\,\text{W}\,\text{m}^{-2}\,\text{K}^{-1}$.
- Conditions on velocity:
  $\boldsymbol{u} = \boldsymbol{0}$ on $\Gamma_C \cup \Gamma_I \cup \Gamma_L \cup \Gamma_{\text{VH}} \cup \Gamma_{\text{Sc}}$.



[a] Scott. *Physics in Medicine and Biology*. (1988)

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	$[W\,m^{-2}\,K^{-1}]$	10[a]	[8, 100]
h_{bl}	Blood convection coefficient	$[W\,m^{-2}\,K^{-1}]$	65[b]	[50, 110]
h_r	Radiation heat transfer coefficient	$[W\,m^{-2}\,K^{-1}]$	6[c]	–
E	Evaporation rate	$[W\,m^{-2}]$	40[c]	[20, 320]
k_{lens}	Lens conductivity	$[W\,m^{-1}\,K^{-1}]$	0.4[b]	[0.21, 0.544]
k_{cornea}	Cornea conductivity	$[W\,m^{-1}\,K^{-1}]$	0.58[d]	–
$k_{sclera} = k_{iris} = k_{lamina} = k_{opticNerve}$	Eye envelope components conductivity	$[W\,m^{-1}\,K^{-1}]$	1.0042[e]	–
$k_{aqueousHumor}$	Aqueous humor conductivity	$[W\,m^{-1}\,K^{-1}]$	0.28[d]	–
$k_{vitreousHumor}$	Vitreous humor conductivity	$[W\,m^{-1}\,K^{-1}]$	0.603[c]	–
$k_{choroid} = k_{retina}$	Vascular beds conductivity	$[W\,m^{-1}\,K^{-1}]$	0.52[f]	–
ε	Emissivity of the cornea	[–]	0.975[a]	–

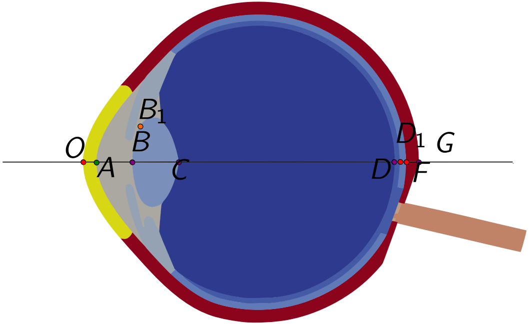
[a] Mapstone (1968), [b] J J W Lagendijk (1982), [c] Scott (1988), [d] Emery et al. (1975), [e] Ng et al. (2007), [f] IT'IS Foundation (2024).

Parameters and output of interest

- Geometrical parameters may play a role[a], but not considered in this work.
- **A parameter:** we set $\mu = (T_{\text{amb}}, T_{\text{bl}}, h_{\text{amb}}, h_{\text{bl}}, E, k_{\text{lens}})$ in $D^{\mu} \subset \mathbb{R}^6$.
- $\bar{\mu} \in D^{\mu}$ is the ***baseline value*** of the parameters.

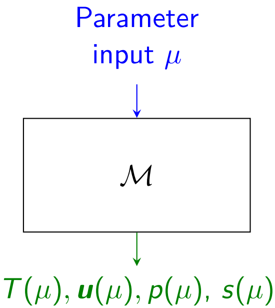
[a] Bhandari. *J Control Release*. (2021)

- Locations of interest based on literature[b,c,d]:



[b] Scott. *Physics in Medicine and Biology*. (1988)
[c] Ng & Ooi. *Comput. Biol. Med.* (2007)
[d] Li *et al.* *Int J Numer Method Biomed Eng*. (2010)

Summary



Model $\mathcal{M}_{\text{HF}}(\mu)$

- **Heat transfer** in the whole eye,
- coupled with AH **fluid dynamics** in the AC and the PC.

Model $\mathcal{M}_{\text{H}}(\mu)$

- Simplified version of $\mathcal{M}_{\text{HF}}(\mu)$.
- **Heat transfer** in the whole eye, with
- linearized radiative conditions.

Full order computational framework

Discrete geometry

- Performed with Salome meshing library, using NETGEN[a] meshing algorithm.
- The full pipeline to generate the mesh is available on GitHub[b].

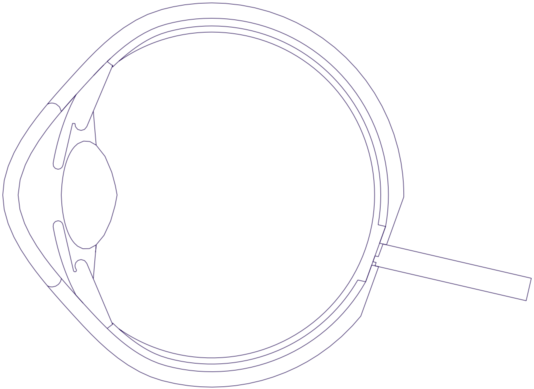


Figure 3: Geometry of the eye.

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

[b] V. Chabannes, C. Prud'homme, T. Saigre, *et al.* *A 3D geometrical model and meshing procedures for the human eyeball.* (2024) github.com/feelpp/mesh.eye

Discrete geometry

- Performed with Salome meshing library, using NETGEN[a] meshing algorithm.
- The full pipeline to generate the mesh is available on GitHub[b].
- The mesh generated by Salome is quite coarse.

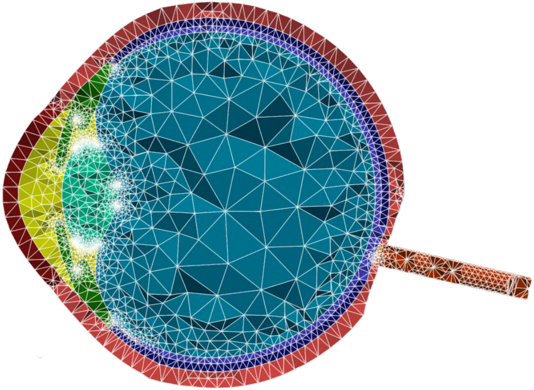


Figure 3: Original mesh M, $4.64 \cdot 10^5$ tetrahedrons.

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

[b] V. Chabannes, C. Prud'homme, T. Saigre, *et al.* *A 3D geometrical model and meshing procedures for the human eyeball.* (2024) github.com/feelpp/mesh.eye

Discrete geometry

- Performed with Salome meshing library, using NETGEN[a] meshing algorithm.
- The full pipeline to generate the mesh is available on GitHub[b].
- The mesh generated by Salome is quite coarse.
- We refine the mesh around the AC and PC.
- For the verification step, we generate a family of meshes of various refinement.

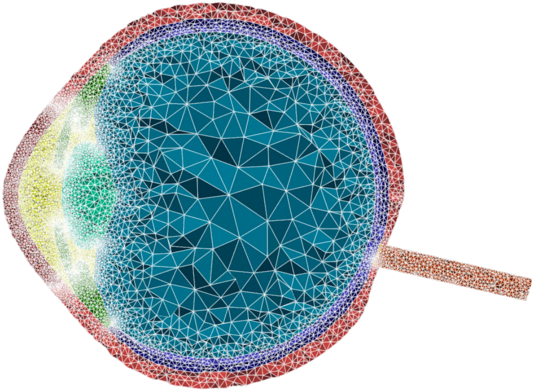


Figure 3: Mesh refined around AC and PC `Mr`, $9.4 \cdot 10^5$ elements.

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

[b] V. Chabannes, C. Prud'homme, T. Saigre, *et al.* *A 3D geometrical model and meshing procedures for the human eyeball.* (2024) github.com/feelpp/mesh.eye

Mesh adaptation and refinement

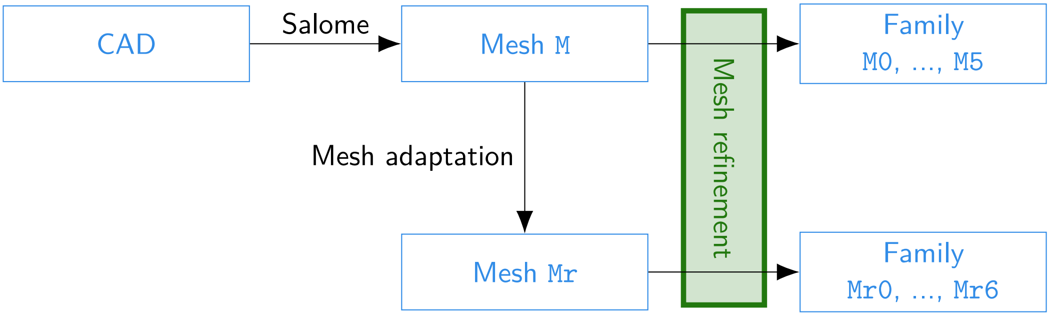


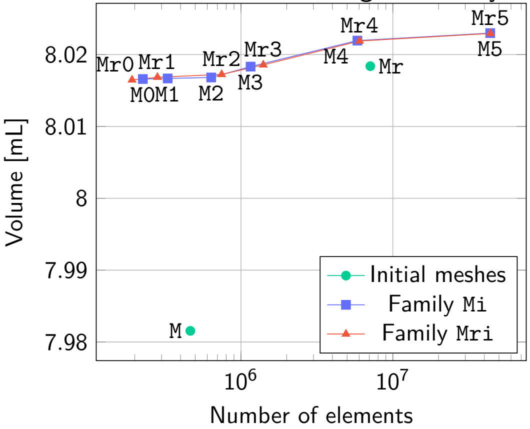
Figure 4: Pipeline to generate the geometry and mesh families.

- All the meshes are available in an open-source repository[a].

[a] T. Saigre *et al.* *Mesh and configuration files to perform coupled heat+fluid simulations on a realistic human eyeball geometry with Feel++*. (2024)

Verification steps: preservation of the volume

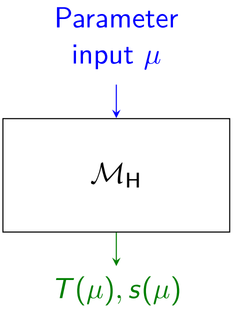
- Solve a Laplacian problem with manufactured solution and compare convergence with the FEM theory.
- Perform a mesh convergence study to ensure the mesh is well refined.



- The volume tends toward a constant value, around 8.02 mL.
- The geometric model overestimates this value, but still remains in an acceptable physiological range[a].

[a] Heymsfield *et al.* *Anatomy & Physiology*. (2016)

Continuous and discrete problem $\mathcal{M}_\mathrm{H}$



We set $V := H^1(\Omega)$.

Problem considered

Given $\mu \in D^\mu$, evaluate the output of interest

$$s(\mu) = \ell(T(\mu); \mu),$$

where $T(\mu) \in V$ is the solution of

$$a(T(\mu), v; \mu) = f(v; \mu) \quad \forall v \in V.$$

The bilinear form $a(\cdot, \cdot; \mu)$ and the linear form $f(\cdot; \mu)$ are defined by the variational formulation of the problem.

Continuous and discrete problem $\mathcal{M}_{\mathrm{H}}$

We set $V := H^1(\Omega)$

Para
inp

$\mathcal{M}$

$T^{\mathrm{fem}}(\mu), s(\mu)$

$$a(T, v; \mu) = f(v; \mu),$$

with:

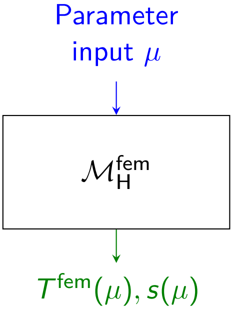
$$a(T, v; \mu) := k_{\mathrm{lens}} \int_{\Omega_{\mathrm{lens}}} \nabla T \cdot \nabla v \,\mathrm{d}x + \sum_{i \neq \mathrm{lens}} k_i \int_{\Omega_i} \nabla T \cdot \nabla v \,\mathrm{d}x +$$

$$\int_{\Gamma_{\mathrm{amb}}} [h_{\mathrm{amb}} T + h_r T]\, v \,\mathrm{d}\sigma + \int_{\Gamma_{\mathrm{body}}} h_{\mathrm{bl}} T v \,\mathrm{d}\sigma$$

$$f(v; \mu) := \int_{\Gamma_{\mathrm{amb}}} [h_{\mathrm{amb}} T_{\mathrm{amb}} + h_r T_{\mathrm{amb}} - E]\, v \,\mathrm{d}\sigma + \int_{\Gamma_{\mathrm{body}}} h_{\mathrm{bl}} T_{\mathrm{bl}} v \,\mathrm{d}\sigma.$$

The bilinear form $a(\cdot, \cdot; \mu)$ and the linear form $f(\cdot; \mu)$ are defined by the variational formulation of the problem.

Continuous and discrete problem $\mathcal{M}_{\mathrm{H}}$



We set $V := H^1(\Omega)$. Denote by $V_h \subset V$ a finite-dimensional subspace of V of dimension $\mathcal{N}$.

High-fidelity model

Given $\mu \in D^{\mu}$, evaluate the output of interest

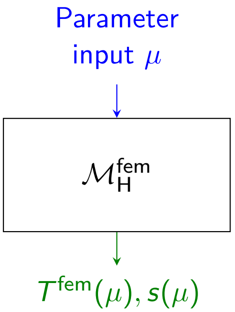
$$s(\mu) = \ell(T^{\mathrm{fem}}(\mu); \mu),$$

where $T^{\mathrm{fem}}(\mu) \in V_h$ is the solution of

$$a(T^{\mathrm{fem}}(\mu), v; \mu) = f(v; \mu) \quad \forall v \in V_h.$$

The bilinear form $a(\cdot, \cdot; \mu)$ and the linear form $f(\cdot; \mu)$ are defined by the variational formulation of the problem.

Continuous and discrete problem $\mathcal{M}_{\mathrm{H}}$



High fidelity resolution

Input: $\mu \in D^{\mu}$,

- Construct $\underline{\underline{\boldsymbol{A}}}(\mu)$, $\boldsymbol{f}(\mu)$ and $\boldsymbol{L}_k(\mu)$,
- Solve $\underline{\underline{\boldsymbol{A}}}(\mu)\boldsymbol{T}^{\mathrm{fem}}(\mu) = \boldsymbol{f}(\mu)$,
- Compute outputs $s(\mu) = \boldsymbol{L}_k(\mu)^T \boldsymbol{T}^{\mathrm{fem}}(\mu)$.

Output: Numerical solution $\boldsymbol{T}^{\mathrm{fem}}(\mu)$ and outputs $s(\mu)$.

High Fidelity model $\mathcal{M}_{\mathrm{H}}^{\mathrm{fem}}$

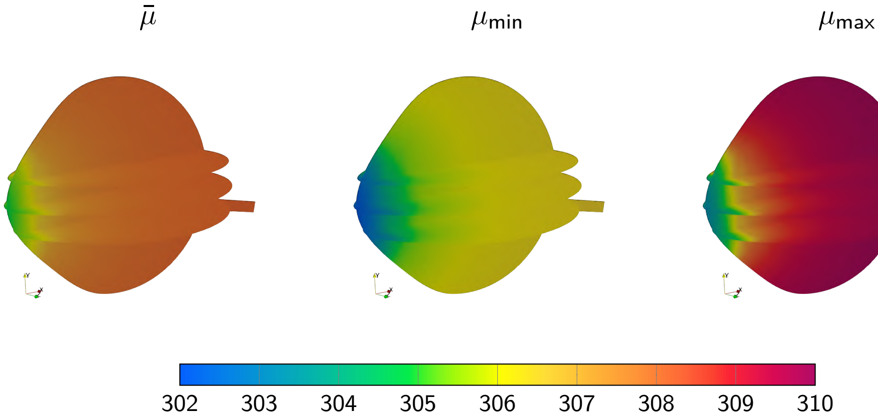
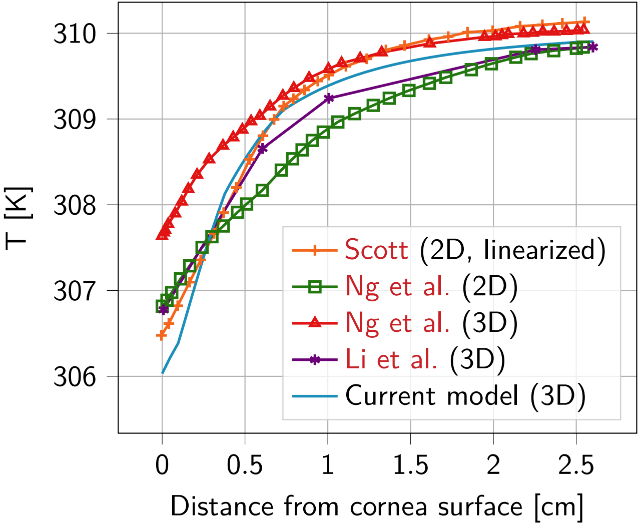
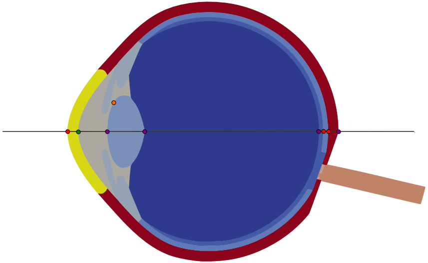


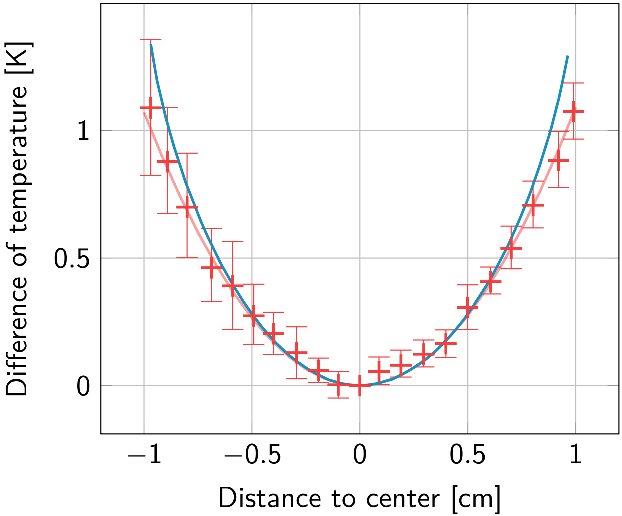
Figure 5: Distribution of the temperature [K] in the eyeball from the linear model.

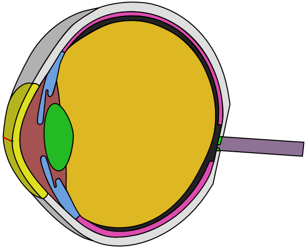
Comparison with previous **numerical** studies





Validation: **measured** values over the GCC



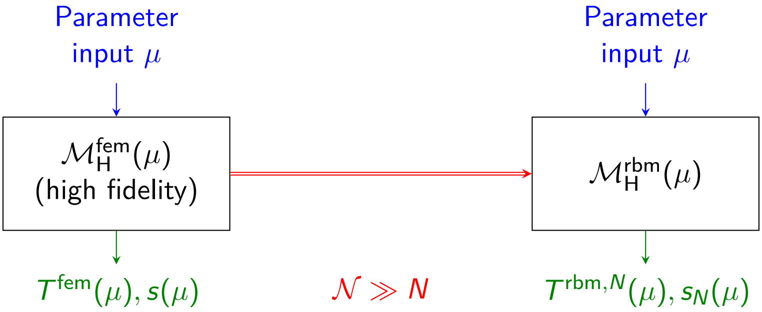


[a] Efron *et al.* *Current Eye Research.* (1989)

Reduced order computational framework

Model Order Reduction

- **Goal:** replicate input-output behavior of the high fidelity model $\mathcal{M}_{\mathrm{H}}^{\mathrm{fem}}$ with a reduced order model $\mathcal{M}_{\mathrm{H}}^{\mathrm{rbm}}$,
- with a procedure stable and efficient.



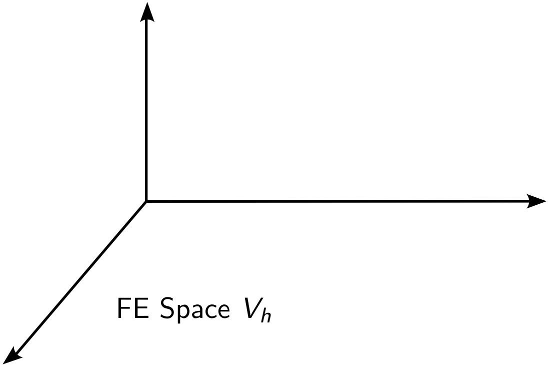
Model Order Reduction

Mathematical and numerical methods for model order reduction:

- Proper orthogonal decomposition[a]
- Certified Reduced Basis method[b]
- Non-Intrusive Reduced Basis[c]
- Machine learning techniques, such as Physics-Informed Neural Networks[d]

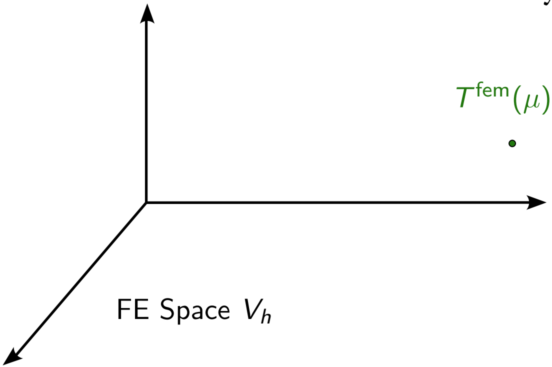
[a] Kerschen *et al.* *Nonlinear Dynamics*. (2005)
[b] Prud'homme *et al.* *Journal of Fluids Engineering*. (2002)
[c] Chakir & Maday. *Comptes Rendus Mathématique*. (2009)
[d] Raissi *et al.* *Journal of Computational Physics*. (2019)

Reduced basis method[a]



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

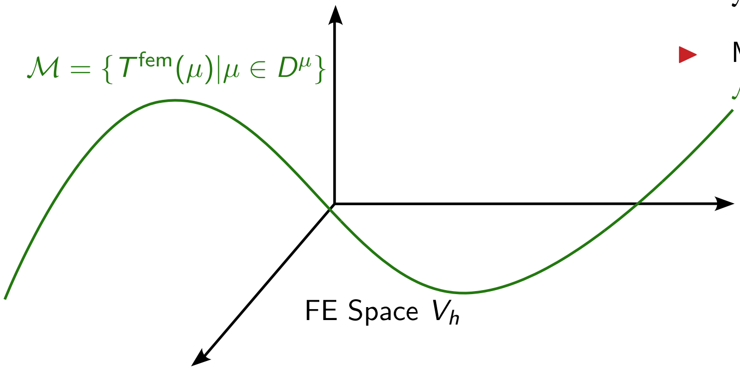
Reduced basis method[a]



- High fidelity model: $\mathcal{M}_{\text{H}}^{\text{fem}} : \mu \mapsto T^{\text{fem}}(\mu)$

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

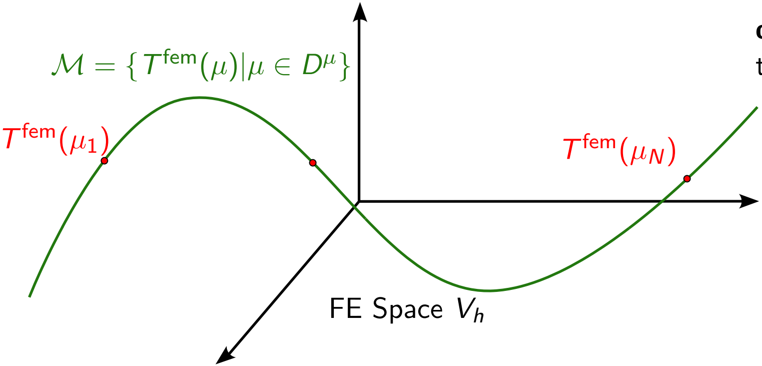
Reduced basis method[a]



- High fidelity model: $\mathcal{M}_{\text{H}}^{\text{fem}} : \mu \mapsto T^{\text{fem}}(\mu)$
- Manifold of solutions: $\mathcal{M} = \{T^{\text{fem}}(\mu), \mu \in D^\mu\}$

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

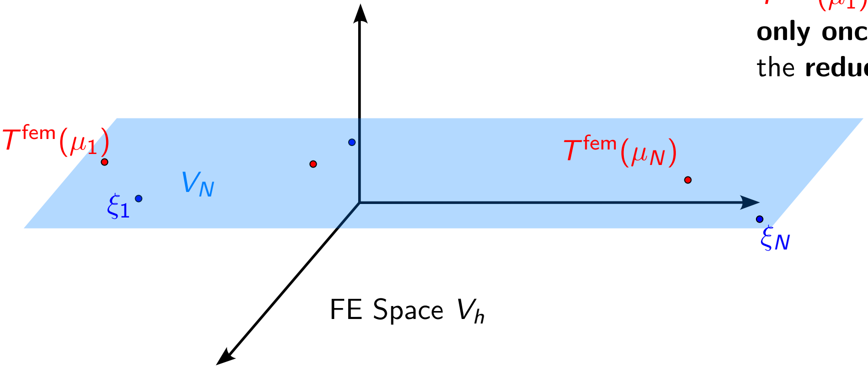
Reduced basis method[a]



- From a set of **snapshots** $T^{\text{fem}}(\mu_1), \cdots, T^{\text{fem}}(\mu_N)$ computed **only once** (*offline stage*), we define the **reduced functional space**:

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

Reduced basis method[a]



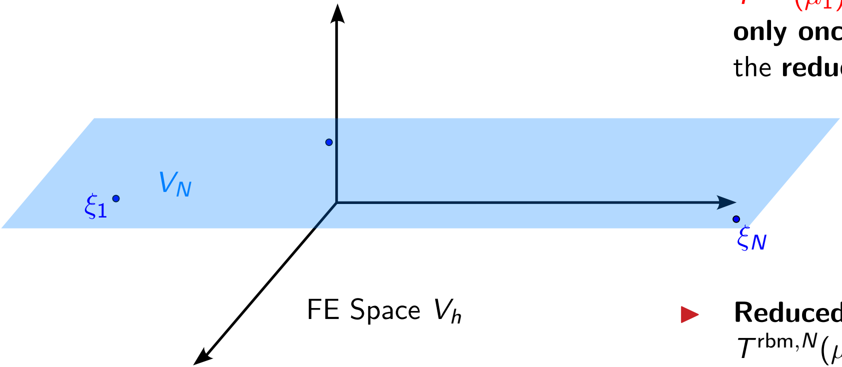
- From a set of **snapshots** $T^{\text{fem}}(\mu_1), \cdots, T^{\text{fem}}(\mu_N)$ computed **only once** (*offline stage*), we define the **reduced functional space**:

$$V_N = \text{span}(\xi_1, \cdots, \xi_N)$$

where $\xi_i = T^{\text{fem}}(\mu_i)$, is orthonormalized.

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

Reduced basis method[a]



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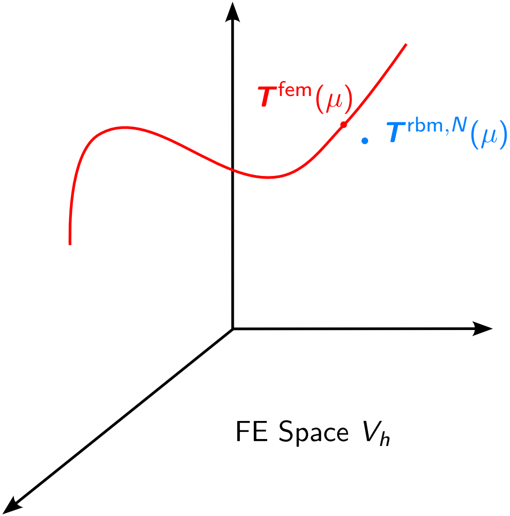
$$V_N = \text{span}(\xi_1, \cdots, \xi_N)$$

where $\xi_i = T^{\text{fem}}(\mu_i)$, is orthonormalized.

- **Reduced solution (*online stage*):** $T^{\text{rbm},N}(\mu)$ solution of the PDE on V_N, **independant** of $\mathcal{N}$.

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

Certified error bound $\Delta_N(\mu)$[a]

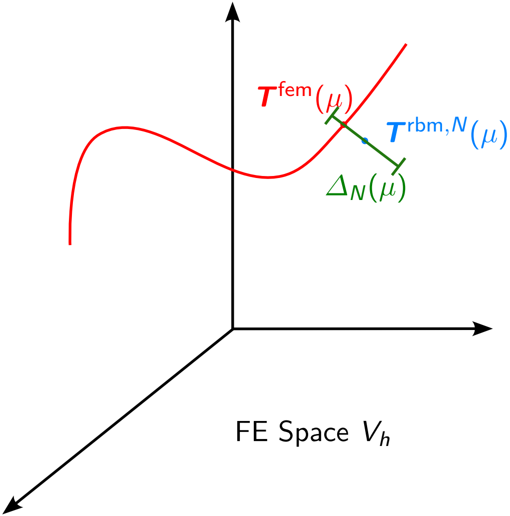


For $\mu \in D^\mu$, we define the error:

$$e(\mu) = T^{\text{fem}}(\mu) - T^{\text{rbm},N}(\mu).$$

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

Certified error bound $\Delta_N(\mu)$[a]



For $\mu \in D^\mu$, we define the error:

$$e(\mu) = T^{\text{fem}}(\mu) - T^{\text{rbm},N}(\mu).$$

We require this error bound to be:

- **Rigorous**: $\|e(\mu)\|_X \leqslant \Delta_N(\mu)$,
- **sharp**: $\dfrac{\Delta_N(\mu)}{\|e(\mu)\|_X} \leqslant \eta_{\max}(\mu)$,
- **efficient**: the computation of $\Delta_N(\mu)$ does not depend on $\mathcal{N}$.

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

Greedy algorithm

Algorithm 1: Greedy algorithm to construct the reduced basis.

Input: $\mu_0 \in D^\mu$, $\Xi_{\text{train}} \subset D^\mu$ and $\varepsilon_{\text{tol}} > 0$
$S \leftarrow [\mu_0]$;
while $\Delta_N^{\max} > \varepsilon_{tol}$ **do**
  $\mu^\star \leftarrow \arg\max_{\mu\in\Xi_{\text{train}}} \Delta_N(\mu)$ (and $\Delta_N^{\max} \leftarrow \max_{\mu\in\Xi_{\text{train}}} \Delta_N(\mu)$);
  $V_{N+1} \leftarrow \left\{\boldsymbol{\xi} = \boldsymbol{T}^{\text{fem}}(\mu^\star)\right\} \cup V_N$;
  Append $\mu^\star$ to S;
  $N \leftarrow N + 1$;
end
Output: Sample S, reduced basis V_N

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.

Results over a sampling $\Xi_{\text{test}} \subset D^{\mu}$ of 100 parameters

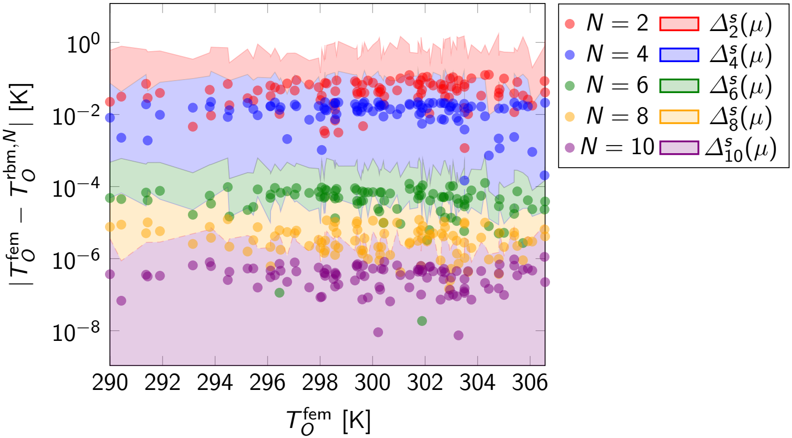


Figure 6: Error on RBM for various reduced basis sizes with error bound $\Delta_N(\mu)$.

Results over a sampling $\Xi_{\text{test}} \subset D^{\mu}$ of 100 parameters

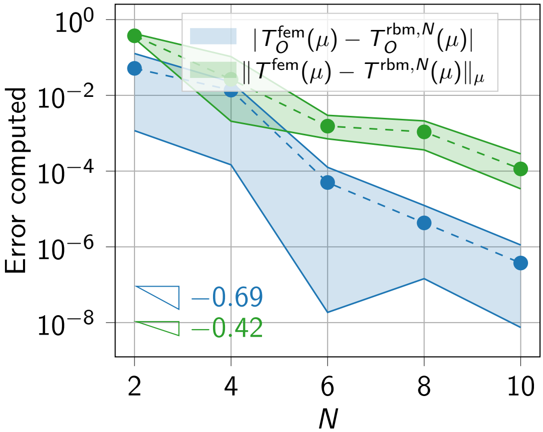


Figure 6: Convergence of the errors on the field and the output on point O.

Sensitivity analysis

Sensitivity analysis

- **Quantifies** the effect of input parameters on the output.
- Two studies were carried:
  1. **Deterministic** sensitivity analysis: all parameters are set to their baseline values, except for one, which varies within the ranges found in the literature,
  2. **Stochastic** sensitivity analysis: all parameters are considered as random variables.

Sobol' indices[a]

- $\mu = (\mu_1, \dots, \mu_n) \in D^\mu$,
- $\mu_i \sim X_i$ where $(X_i)_i$ is a family of **independent** random variables.
- Distributions X_i selected from data available in the literature.
- Output $s_N(\mu) \sim Y = f(X_1, \dots, X_n)$.

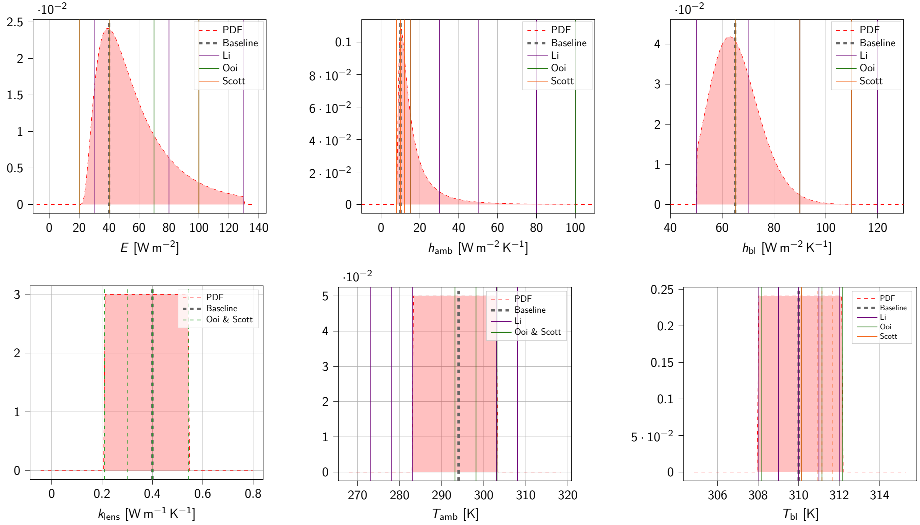
Sobol' indices

- **First-order indices:** $S_j = \dfrac{\mathrm{Var}\left(\mathbb{E}\left[Y|X_j\right]\right)}{\mathrm{Var}(Y)}$ — effect of one parameter on the output
- **Total-order indices:** $S_j^{\mathrm{tot}} = \dfrac{\mathrm{Var}\left(\mathbb{E}\left[Y|X_{(-j)}\right]\right)}{\mathrm{Var}(Y)}$ — interaction of all parameters but one on the output

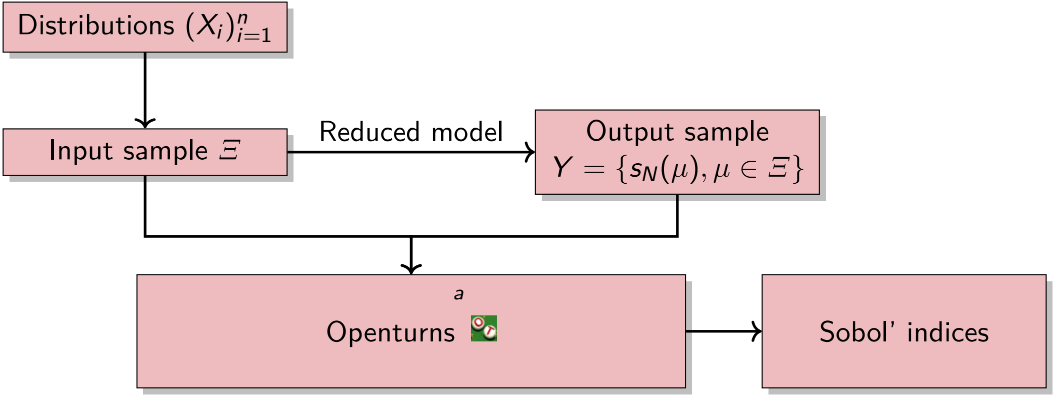
where $X_{(-j)} = (X_1, \dots, X_{j-1}, X_{j+1}, \dots, X_n)$.

[a] Sobol. *Sensitivity Estimates for Nonlinear Mathematical Models.* (1993)

Input parameters distributions



Stochastic sensitivity analysis



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

Stochastic sensitivity analysis

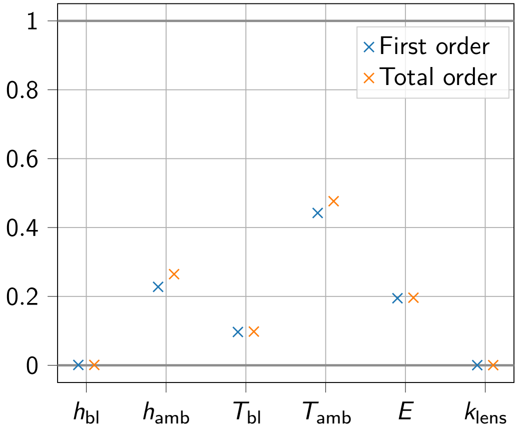
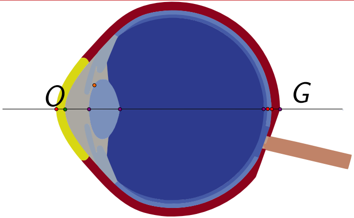


Figure 7: Sobol' indices: temperature at point O.



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}.

Stochastic sensitivity analysis

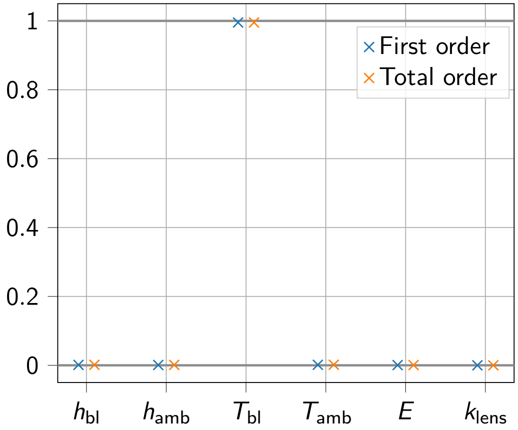
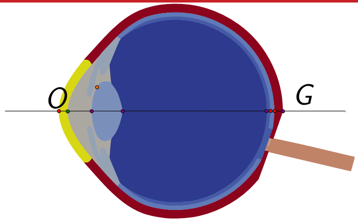


Figure 7: Sobol' indices: temperature at point G.



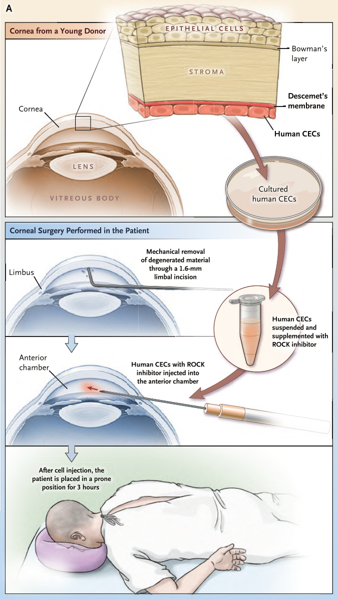
Temperature at the back of the eye:

- only influenced by the blood temperature.

Heat transfer coupled with aqueous humor flow

Motivation: Endothelial cells sedimentation

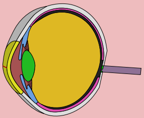
- AH flow plays a significant role in heat distribution, and intraocular pressure[a].
- Focus on the **wall shear stress** of the AH.
- Medical application: **corneal endothelial cell sedimentation** in the cornea[b].



[a] Dvoriashyna *et al.* *Ocular Fluid Dynamics.* (2019)
[b] Kinoshite *et al.* *N Engl J Med.* (2018) (Figure extracted from this reference)

Computational framework of $\mathcal{M}_{\mathrm{HF}}$

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

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

Finite element solver

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

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

Pressure and velocity: impact of the posture

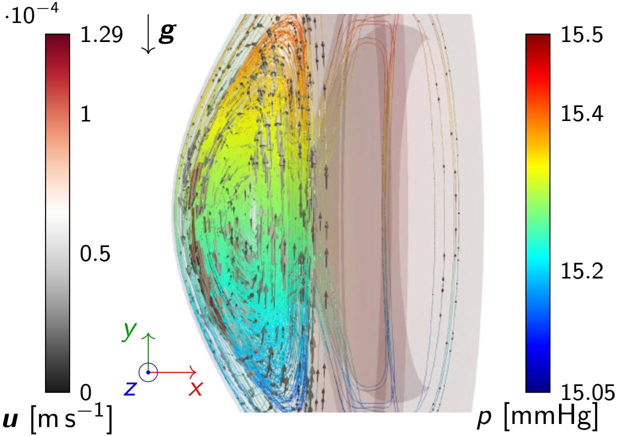


Figure 8: Standing position.

- **Recirculation** of the AH,

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

Pressure and velocity: impact of the posture

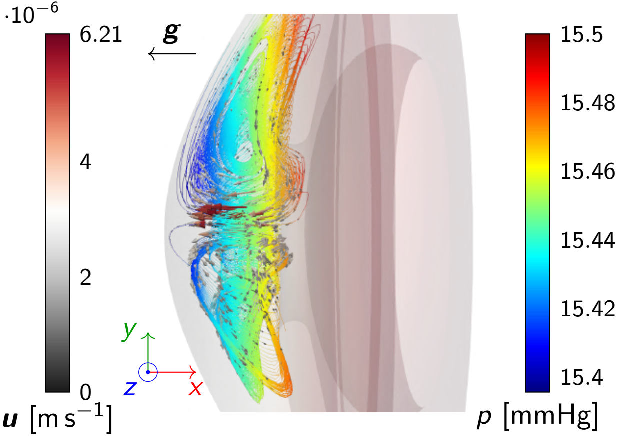


Figure 8: Prone position.

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

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

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

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

Pressure and velocity: impact of the posture

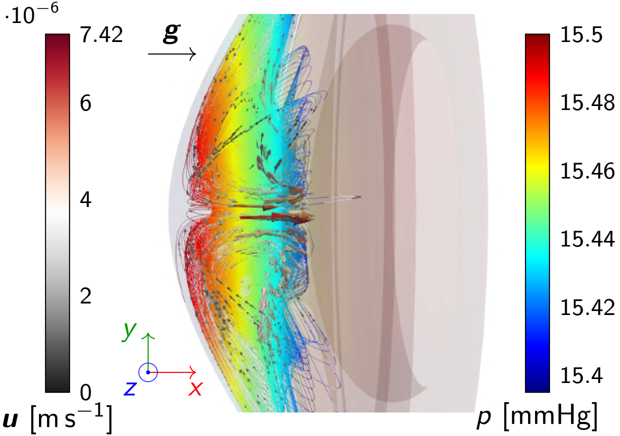
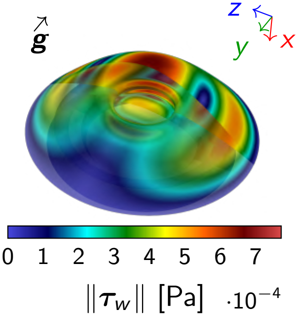


Figure 8: Supine position.

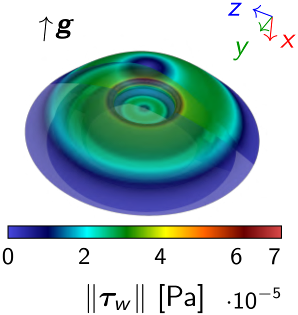
- **Recirculation** of the AH,
- Formation of a **Krukenberg's spindle**, in good agreement with clinical observations and previous studies[abc]
- Fluid dynamics is **strongly influenced by the position of the patient**.

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

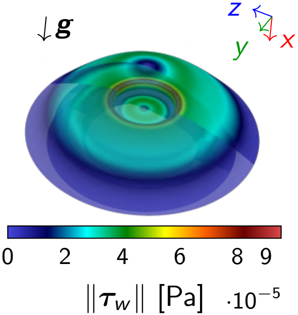
Wall shear stress



(a) Standing.



(b) Prone.



(c) Supine.

Figure 9: Wall shear stress distribution on the corneal endothelium for the three postural orientations.

Wall shear stress

- The WSS distribution is **impacted** by the postural orientation and the ambient temperature.
- **Application:** Control the temperature to enhance the diffusion and the sedimentation of the cells during the treatment.

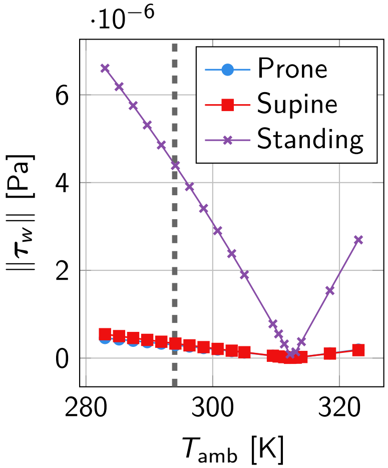


Figure 9: Mean wall shear stress on the corneal surface.

Conclusion and perspectives

- **Heat transport model in the human eye:** FEM simulations, validation against experimental data,
- **Reduced model** with a **certified error bound**,
- **Sensitivity analysis:** computation of Sobol' indices, highlight of the impact of some parameters on the outputs of interest.

- T. Saigre, C. Prud'homme, M. Szopos. Model order reduction and sensitivity analysis for complex heat transfer simulations inside the human eyeball. *Int J Numer Methods Biomed Eng*. (2024)
- T. Saigre, C. Prud'homme, M. Szopos. Associated dataset (publicly available). DOI: `10.5281/ZENODO.13907890` *Zenodo*. (2024)

Conclusion and perspectives

- **Couple heat transfer with AH dynamics:** assess the impact of postural orientation and environmental conditions on the flow and its properties.

- T. Saigre, V. Chabannes, C. Prud'homme, M. Szopos. A coupled fluid-dynamics-heat transfer model for 3D simulations of the aqueous humor flow in the human eye. *CMBE2024 Proceedings*. (2024)
- T. Saigre, C. Prud'homme, M. Szopos, V. Chabannes. Mesh and configuration files to perform coupled heat+fluid simulations on a realistic human eyeball geometry with Feel++, DOI: `10.5281/ZENODO.13886143` *Zenodo*. (2024)

- 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:** modeling the production and drainage of aqueous humor to assess their impact.
- **Clinical perspective:** assess the corneal cell sedimentation after injection.

T. Saigre, V. Chabannes, G. Guidoboni, C. Prud'homme, M. Szopos, SP. Srinivas. Effect of Cooling of the Ocular Surface on Endothelial Cell Sedimentation in Cell Injection Therapy: Insights from Computational Fluid Dynamics. (2025), to appear in IOVS.

- Steps towards a **digital twin** of the eye:
  - incorporate patient-specific data,
  - enhance predictive modeling and personalized medical applications.

Thank you for your attention!

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Linearization of the radiative transfer equation

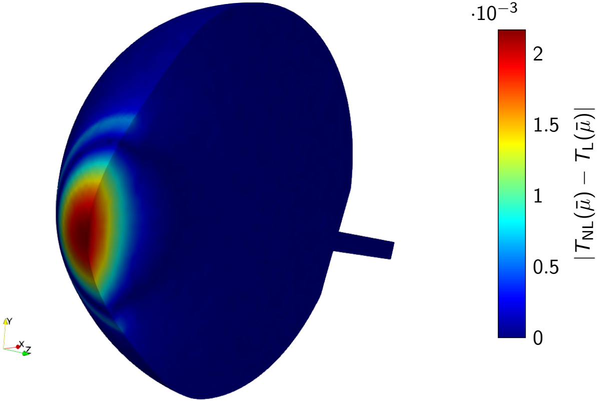


Figure 10: Difference of the temperature between the full model and the linearized model.

Mesh convergence for the high-fidelity model

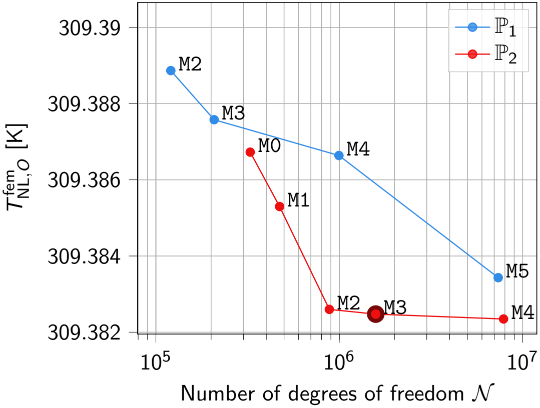
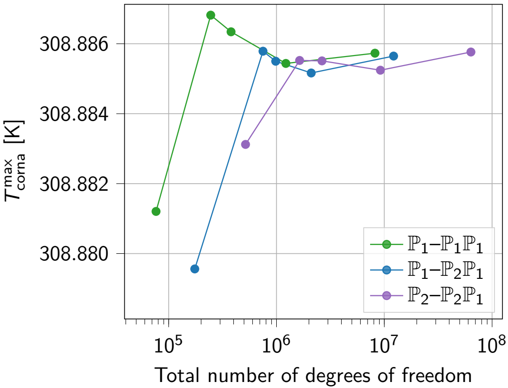
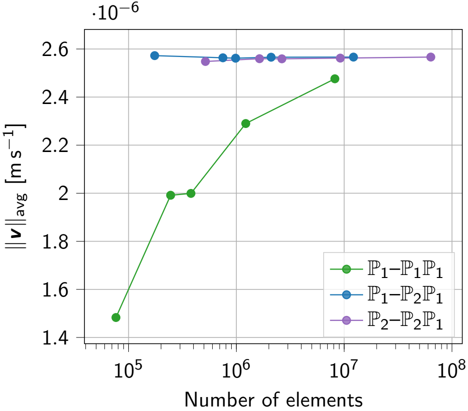


Figure 11: Temperature at the center of the cornea computed with the high-fidelity model $\mathcal{E}_{\text{NL}}(\bar{\mu})$, depending on the level of mesh refinement.

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

Reduced Basis Method

Problem considered

Given $\mu \in D^{\mu}$, evaluate the output of interest

$$s_N(\mu) = \ell(\boldsymbol{T}^{\mathrm{rbm},N}(\mu); \mu)$$

where $\boldsymbol{T}^{\mathrm{rbm},N}(\mu) \in V_N$ is the solution of

$$a(\boldsymbol{T}^{\mathrm{rbm},N}(\mu), v; \mu) = f(v; \mu) \quad \forall v \in V_N$$

- *Snapshots matrix:* $\mathbb{Z}_N = [\xi_1, \cdots, \xi_N] \in \mathbb{R}^{\mathcal{N} \times N}$,

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- *Snapshots matrix:* $\mathbb{Z}_N = [\xi_1, \cdots, \xi_N] \in \mathbb{R}^{\mathcal{N}\times N}$,
- Projection onto V_N: $\underline{\underline{\boldsymbol{A}}}_N(\mu) := \mathbb{Z}_N^T \underline{\underline{\boldsymbol{A}}}(\mu)\mathbb{Z}_N \in \mathbb{R}^{N\times N}$ and $\boldsymbol{f}_N(\mu) := \mathbb{Z}_N^T \boldsymbol{f}(\mu) \in \mathbb{R}^N$,

Reduced basis resolution

Input: $\mu \in D^\mu$,

- Construct $\underline{\underline{\boldsymbol{A}}}_N(\mu)$, $\boldsymbol{f}_N(\mu)$ and $\boldsymbol{L}_{N,k}(\mu)$,
- Solve $\underline{\underline{\boldsymbol{A}}}_N(\mu)\boldsymbol{T}^{\mathrm{rbm},N}(\mu) = \boldsymbol{f}_N(\mu)$,
- Compute outputs $s_{N,k}(\mu) = \boldsymbol{L}_{N,k}(\mu)^T \boldsymbol{T}^{\mathrm{rbm},N}(\mu)$.

Output: Numerical solution $\boldsymbol{T}^{\mathrm{rbm},N}(\mu)$ and outputs $s_{N,k}(\mu)$.

Affine decomposition[a]

- We want to write $\underline{\underline{\boldsymbol{A}}}(\mu) = \sum_{q=1}^{Q_a} \beta_A^q(\mu)\underline{\underline{\boldsymbol{A}}}^q$, and $\boldsymbol{F}(\mu) = \sum_{q=1}^{Q_f} \beta_F^q(\mu)\boldsymbol{F}^q$.
- Compute and store $\underline{\underline{\boldsymbol{A}}}_N^q = \underbrace{\mathbb{Z}_N^T \underline{\underline{\boldsymbol{A}}}^q \mathbb{Z}_N}_{\text{independent of } \mu}$ and $\boldsymbol{F}_N^q = \mathbb{Z}_N^T \boldsymbol{F}^q$.
- Hence, $\underline{\underline{\boldsymbol{A}}}_N(\mu) = \sum_{q=1}^{Q_a} \beta_A^q(\mu)\underline{\underline{\boldsymbol{A}}}_N^q$ and $\boldsymbol{F}_N(\mu) = \sum_{q=1}^{Q_f} \beta_F^q(\mu)\boldsymbol{F}_N^q$.

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

Affine decomposition[a]

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- Compute and store $\underline{\underline{\boldsymbol{A}}}_N^q = \mathbb{Z}_N^T \underline{\underline{\boldsymbol{A}}}^q \mathbb{Z}_N$ and $\boldsymbol{F}_N^q = \mathbb{Z}_N^T \boldsymbol{F}^q$.
- $a(T, v; \mu) = \sum_{q=1}^{4} \beta_A^q(\mu) a^q(T, v)$ with

$$
\begin{aligned}
\beta_A^1(\mu) &= k_{\text{lens}} & a^1(T, v) &= \int_{\Omega_{\text{lens}}} \nabla T \cdot \nabla v \, \mathrm{d}x \\
\beta_A^2(\mu) &= h_{\text{amb}} & a^2(T, v) &= \int_{\Gamma_{\text{amb}}} T v \, \mathrm{d}\sigma \\
\beta_A^3(\mu) &= h_{\text{bl}} & a^3(T, v) &= \int_{\Gamma_{\text{body}}} T v \, \mathrm{d}\sigma \\
\beta_A^4(\mu) &= 1 & a^4(T, v) &= \int_{\Gamma_{\text{amb}}} h_r T v \, \mathrm{d}\sigma + \sum_{i \neq \text{lens}} k_i \int_{\Omega_i} \nabla T \cdot \nabla v \, \mathrm{d}x
\end{aligned}
$$

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

Affine decomposition[a]

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- Compute and store $\underline{\underline{\boldsymbol{A}}}_N^q = \mathbb{Z}_N^T \underline{\underline{\boldsymbol{A}}}^q \mathbb{Z}_N$ and $\boldsymbol{F}_N^q = \mathbb{Z}_N^T \boldsymbol{F}^q$.
- $f(v;\mu) = \sum_{p=1}^{2} \beta_F^p(\mu) f^p(v)$

$$\beta_F^1(\mu) = h_{\text{amb}} T_{\text{amb}} + h_r T_{\text{amb}} - E \qquad f^1(v) = \int_{\Gamma_{\text{amb}}} v \, \mathrm{d}\sigma$$

$$\beta_F^2(\mu) = h_{\text{bl}} T_{\text{bl}} \qquad f^2(v) = \int_{\Gamma_{\text{body}}} v \, \mathrm{d}\sigma$$

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

Offline / Online procedure

Offline:

- Solve N high-fidelity systems depending on $\mathcal{N}$ to form $\mathbb{Z}_N$,
- Form and store $\boldsymbol{F}_N^p(\xi_i)$
- Form and store $\underline{\underline{\boldsymbol{A}}}_N^q(\xi_i)$

Online: independant of $\mathcal{N}$

Given a new parameter $\mu \in D^\mu$,

- Form $\underline{\underline{\boldsymbol{A}}}_N(\mu)$: $O(Q_a N^2)$,
- Form $\boldsymbol{F}_N(\mu)$: $O(Q_f N)$,
- Solve $\underline{\underline{\boldsymbol{A}}}_N(\mu)\boldsymbol{T}^{\mathrm{rbm},N}(\mu) = \boldsymbol{F}_N(\mu)$: $O(N^3)$,
- Compute $s_N(\mu) = \boldsymbol{L}_N(\mu)^T\boldsymbol{T}^{\mathrm{rbm},N}(\mu)$: $O(N)$.

Error bound[a] $\Delta_N(\mu)$

Such an error bound can be constructed efficiently from the *residual* r of the variational problem:

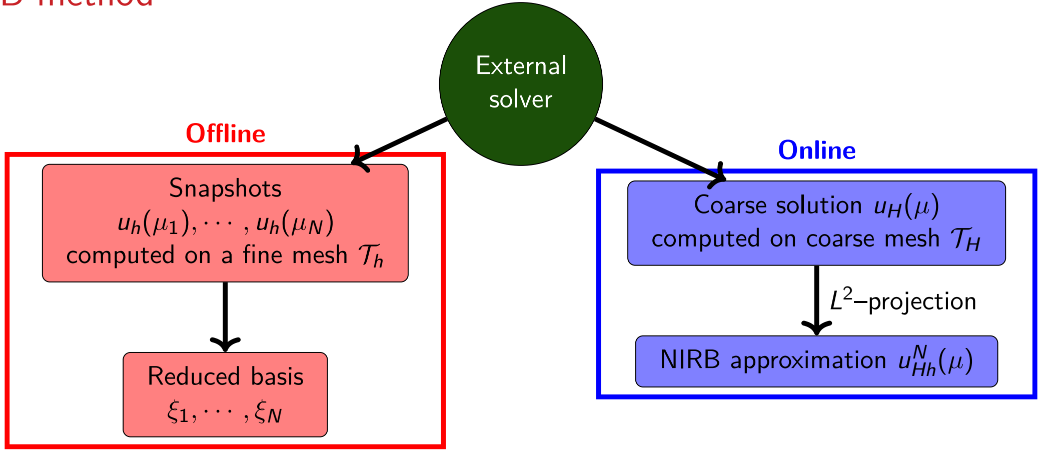
$$r(v,\mu) := \ell(v;\mu) - a(T^{\mathrm{rbm},N}(\mu), v;\mu) \quad \forall v \in V$$

a lower bound $\alpha_{\mathrm{lb}}(\mu)$ of the coercivity constant $\alpha(\mu)$ of $a(\cdot,\cdot;\mu)$, and the affine decomposition of a and f:

$$\Delta_N^s(\mu) := \frac{\|r(\cdot,\mu)\|_{V'}^2}{\alpha_{\mathrm{lb}}(\mu)}$$

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

NIRB method[a]



[a] Chakir & Maday *Comptes Rendus Mathématique*. (2009)

NIRB method[a]

Instead of solving the system $\underline{\underline{\boldsymbol{A}}}^N(\mu)\boldsymbol{U}_h^N(\mu) = \boldsymbol{F}^N(\mu)$ in the online stage and construct the solution by :

$$u_h^N(\mu) = \sum_{i=1}^{N} \boldsymbol{U}_{h,i}^N(\mu)\xi_i$$

Let's denote by $\Pi_N u_h$ the L^2- projection of $\mathbb{FE}$ approximation u_h in the space X_h^N :

$$\Pi_N u_h(\mu) = \sum_{i=1}^{N} \alpha_i^{N,h}(\mu)\xi_i$$

Due to the orhtonormalization of basis function ξ_i, $\alpha_i^{N,h}(\mu)$ are defined by :

$$\alpha_i^{N,h}(\mu) = \langle u_h(\mu), \xi_i \rangle_{L^2}$$

[a] Chakir & Maday *Comptes Rendus Mathématique*. (2009)

- **Coarse** triangulation : $\{\mathcal{T}_H\}_H$ with $H \gg h$,
- new finite element space : X_H such that $\mathcal{N}_H = \dim(X_H) \ll \dim(X_h) = \mathcal{N}_h$,
- the computation of $u_H(\mu) \in X_H$ is less expensive than the one of $u_h(\mu) \in X_h$

The **NIRB method** consists in proposing another alternative of $\alpha_i^{N,h}(\mu)$ defined by :

$$\alpha_i^{N,H}(\mu) = \langle u_H(\mu), \xi_i \rangle_{L^2} ,$$

with $u_H(\mu)$, an approximate solution of the high-fidelity problem in the coarse triangulation.