



Reduced-order models for uncertainty quantification and parameter estimation in cardiac models

Stefano Pagani[△]

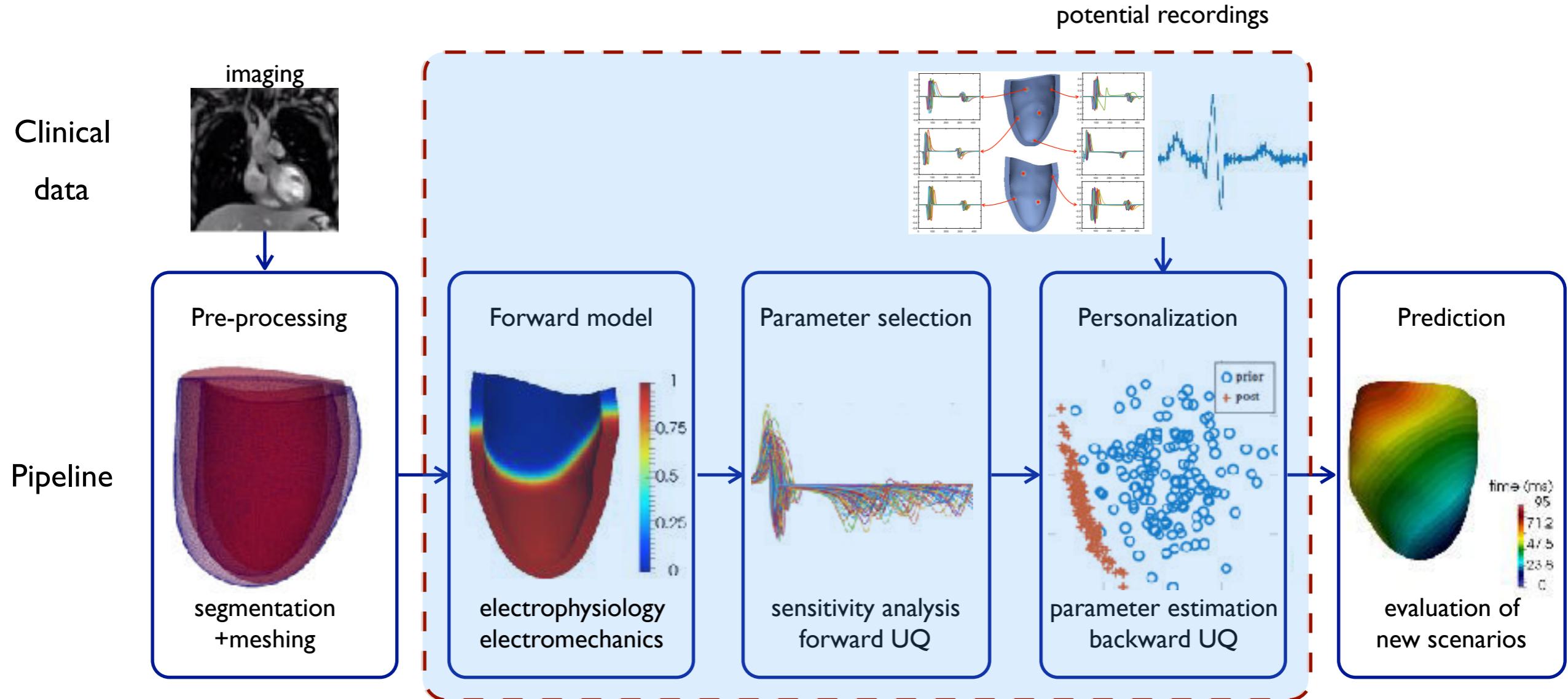
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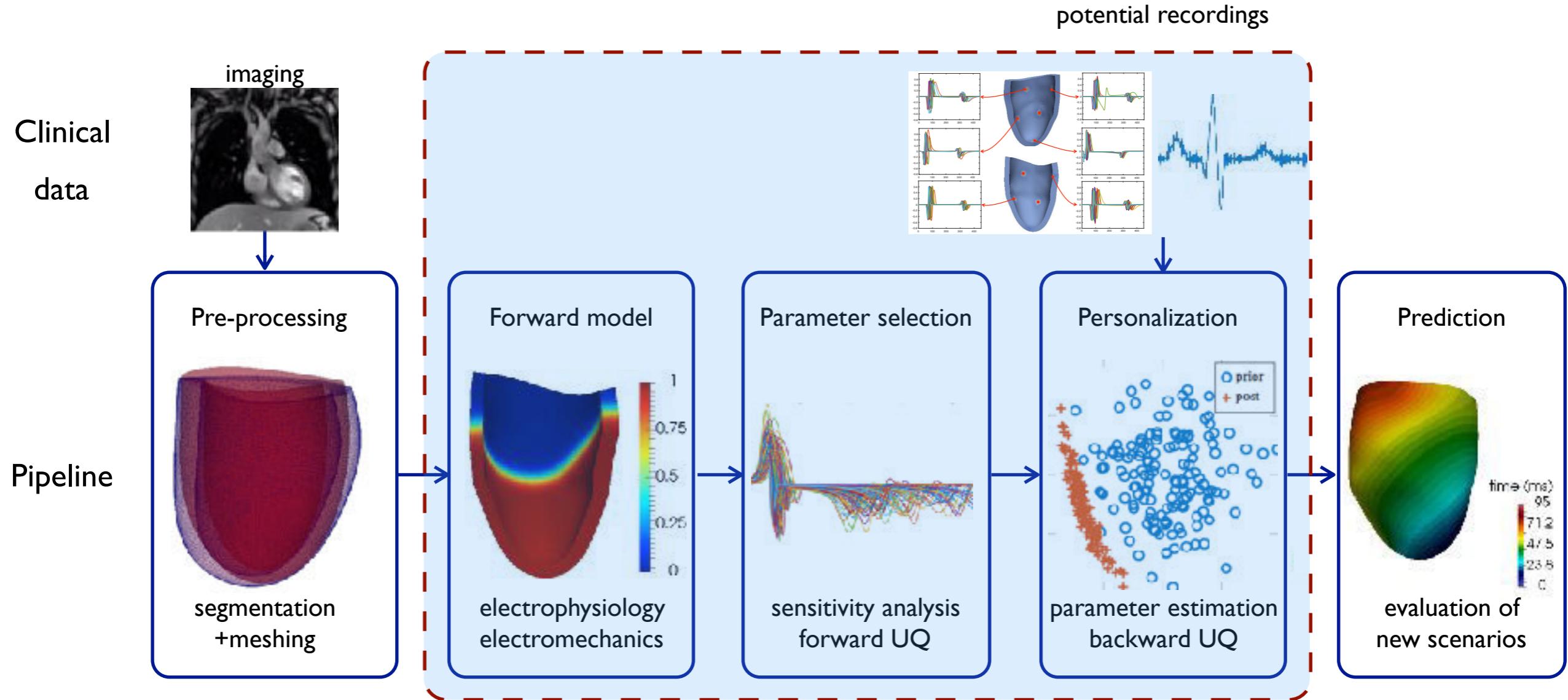
Integrating data within mathematical models



Challenging issues:

- ▶ computational complexity of full-order models (e.g. finite element method);
- ▶ noisy clinical data;
- ▶ uncertainties related to geometry, (partially known) physical coefficients, boundary/ initial conditions.

Integrating data within mathematical models



Many-query problems:

- ▶ parameter selection for reducing the uncertainty space dimension (**sensitivity analysis**);
- ▶ uncertainty propagation on outputs of clinical interest (**forward UQ**);
- ▶ parameter estimation for model personalization (**backward UQ**).

Methods

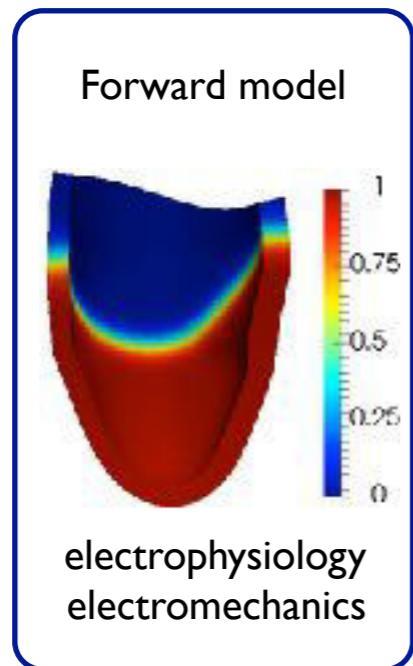
LOCAL Reduced Order Models

local approximation of both nonlinear term and solution

SURROGATE MODELS

kriging and GP-based ROM error surrogate (ROMES)

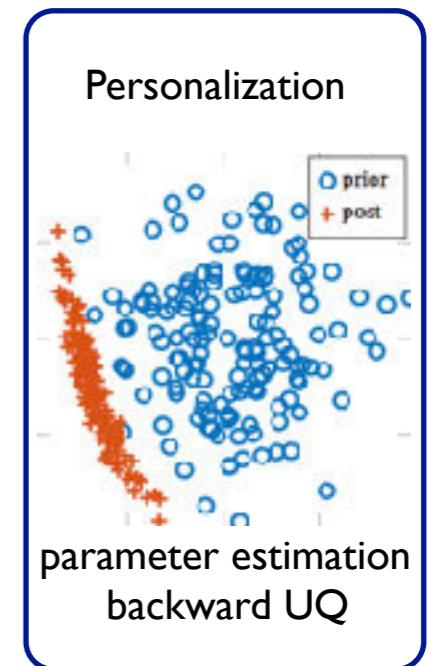
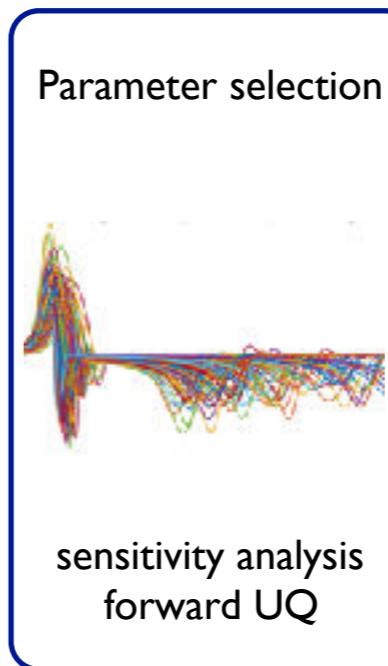
ROMES for time-dependent outputs



Variance-based **sensitivity analysis** for parameter selection

RB-MCMC sampling procedure

Reduced basis Ensemble Kalman filter for sequential state/parameter estimation



- **S. Pagani, A. Manzoni, A. Quarteroni.** "Numerical approximation of parametrized problems in cardiac electrophysiology by a local reduced basis method". *In preparation*, 2017.

- **D. Bonomi.** "Reduced order models for the parametrized cardiac electromechanical problem". PhD Thesis (2017).

- **M. Drohmann and K. Carlberg.** "The ROMES method for statistical modeling of reduced-order-model error". *SIAM/ASA Journal on Uncertainty Quantification*, 3(1):116–145, 2015.

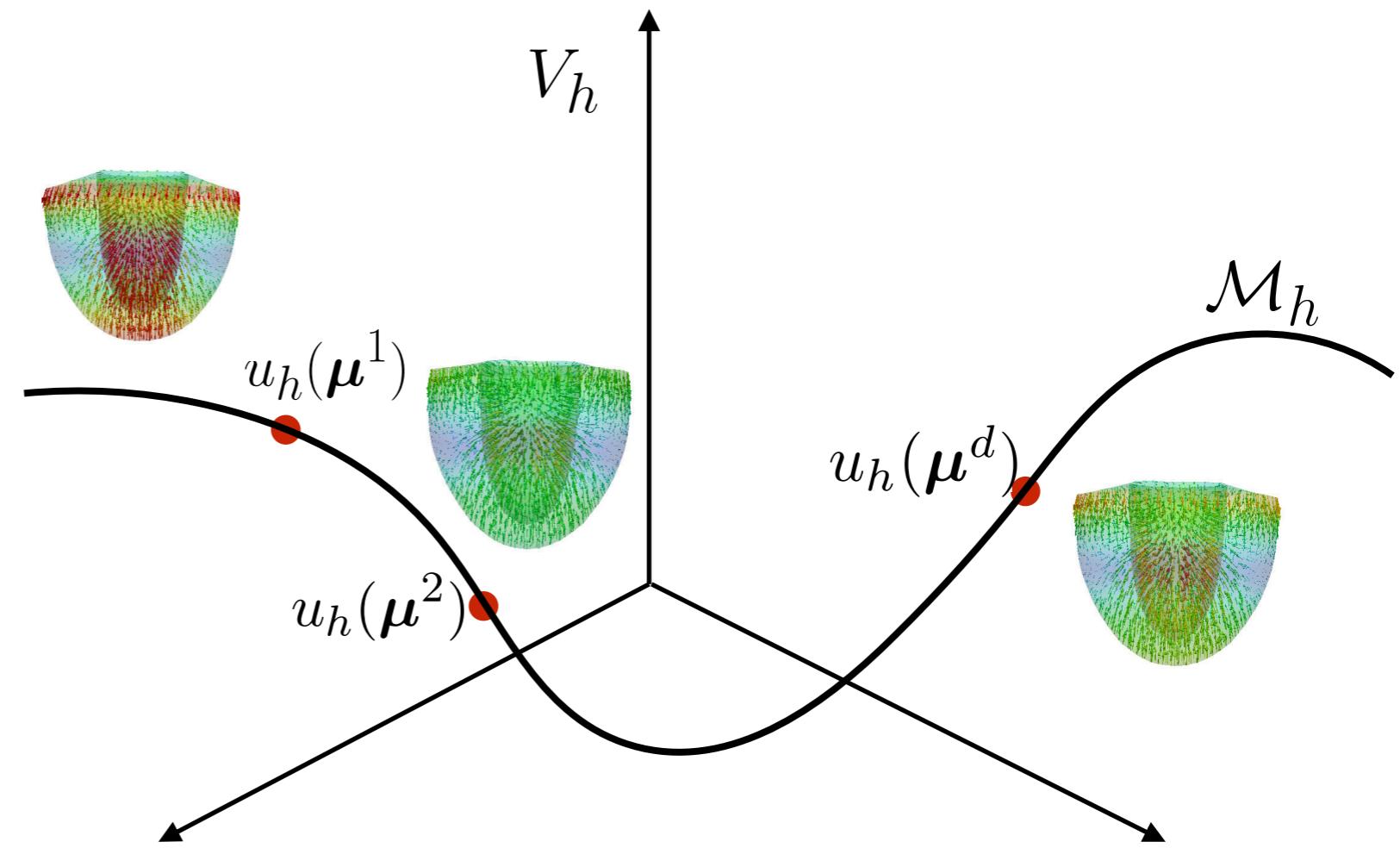
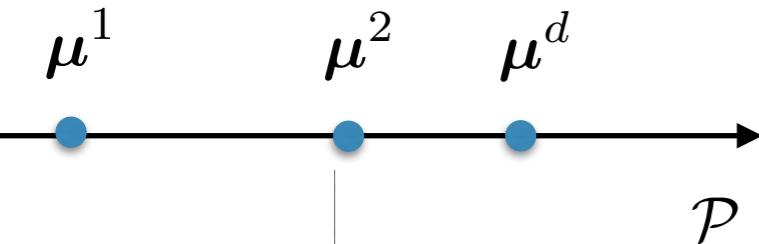
- **S. Pagani.** "Reduced-order models for inverse problems and uncertainty quantification in cardiac electrophysiology". PhD Thesis (2017).

- **S. Pagani, A. Manzoni and A. Quarteroni.** "Efficient state/parameter estimation in nonlinear unsteady PDEs by a reduced basis ensemble Kaman filter". *SIAM/ASA Journal on Uncertainty Quantification*, 5(1):890–921, 2017.

- **A. Manzoni, S. Pagani and T. Lassila.** "Accurate solution of Bayesian inverse uncertainty quantification problems using model and error reduction methods". *SIAM/ASA Journal on Uncertainty Quantification*, 4(1):380–412, 2016.

Reduced basis method in a nutshell

Goal: compute efficiently the solution of a problem when a set of parameters vary



- **parameter-dependent PDEs**
(e.g. cardiac electrophysiology, nonlinear mechanics, coupled electro-mechanics,...)
- (un)steady (non)linear PDEs
- **physical/geometrical parameters**
 - ✓ material coefficients
 - ✓ electrical conductivities
 - ✓ initial/boundary data
 - ✓ geometrical configuration ...

- **Snapshots computed offline**

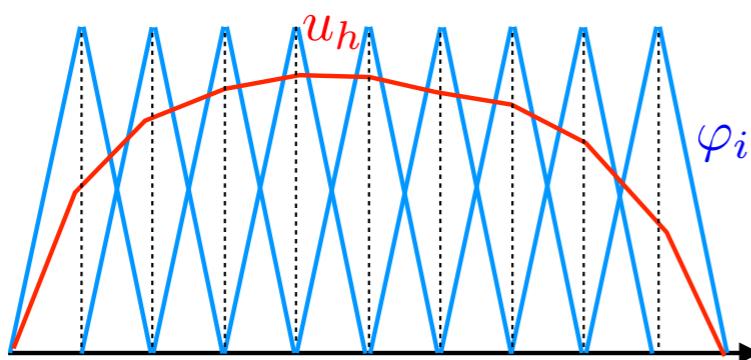
$$\{u_h(\mu^1), \dots, u_h(\mu^n)\}$$

Reduced basis method in a nutshell

- **Idea:** Galerkin approximation on a low dimensional subspace $V_n \subset V_h$ (reduced basis space) of dimension $n \ll N_h = \dim(V_h)$.

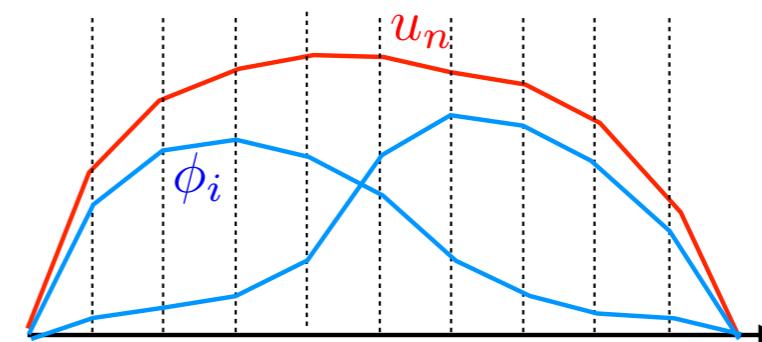
Linear steady case:

Finite Elements method



$$u_h(x; \mu) = \sum_{i=1}^{N_h} u_i^h \varphi_i(x)$$

Reduced Basis method



$$N_h \gg n$$

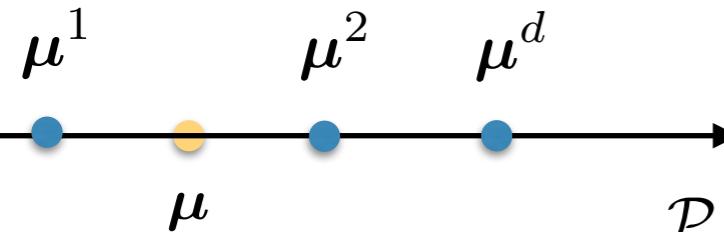
$$u_n(x; \mu) = \sum_{i=1}^n u_i^n \phi_i(x)$$

$$\boxed{\mathbf{A}_h} \quad \boxed{\mathbf{u}_h} = \boxed{\mathbf{f}_h}$$

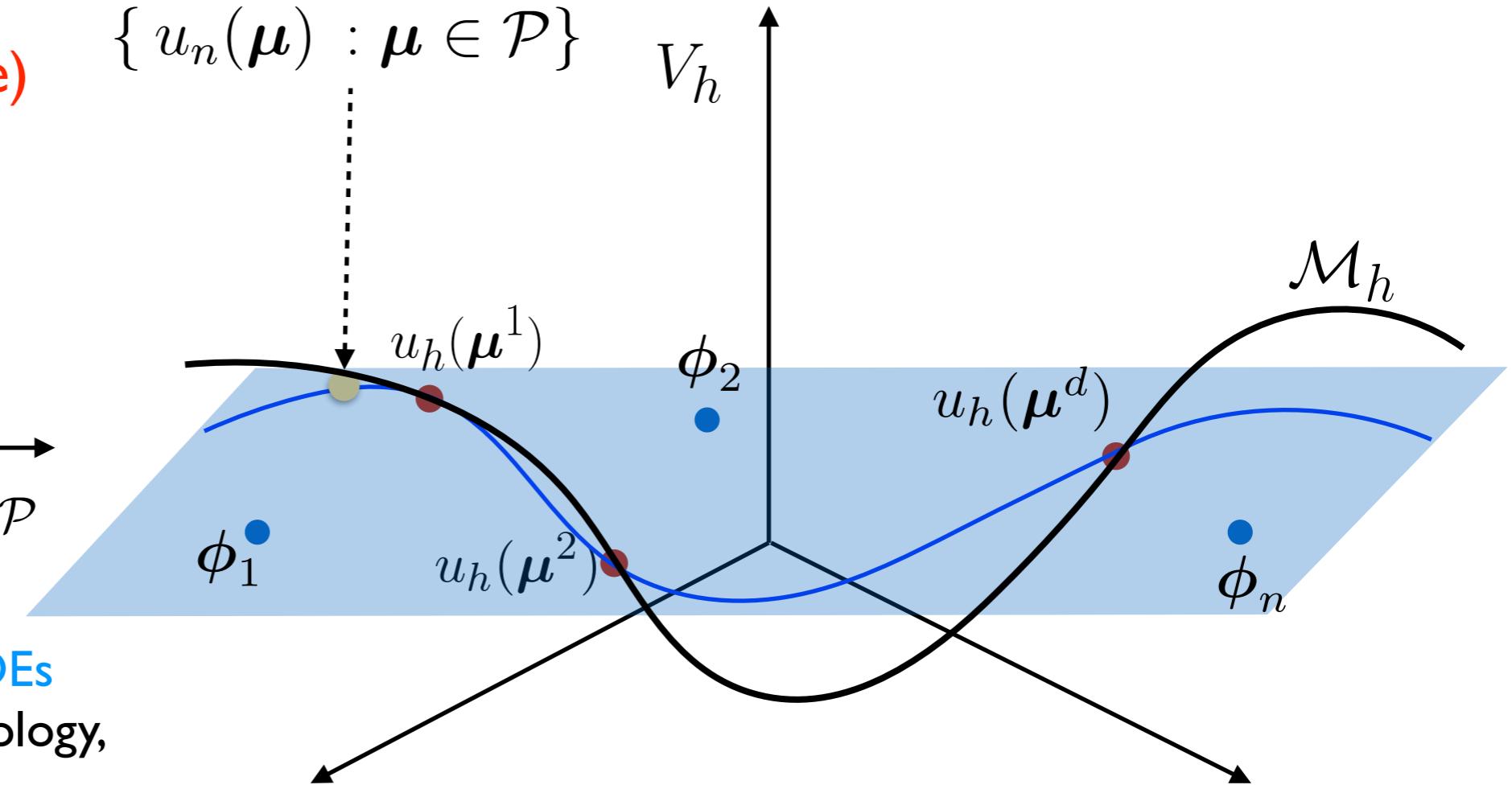
$$\boxed{\mathbf{A}_n} \quad \boxed{\mathbf{u}_n} = \boxed{\mathbf{f}_n}$$

Reduced basis method in a nutshell

RB Approximation
(new parameter value)



$$\{ u_n(\mu) : \mu \in \mathcal{P} \}$$



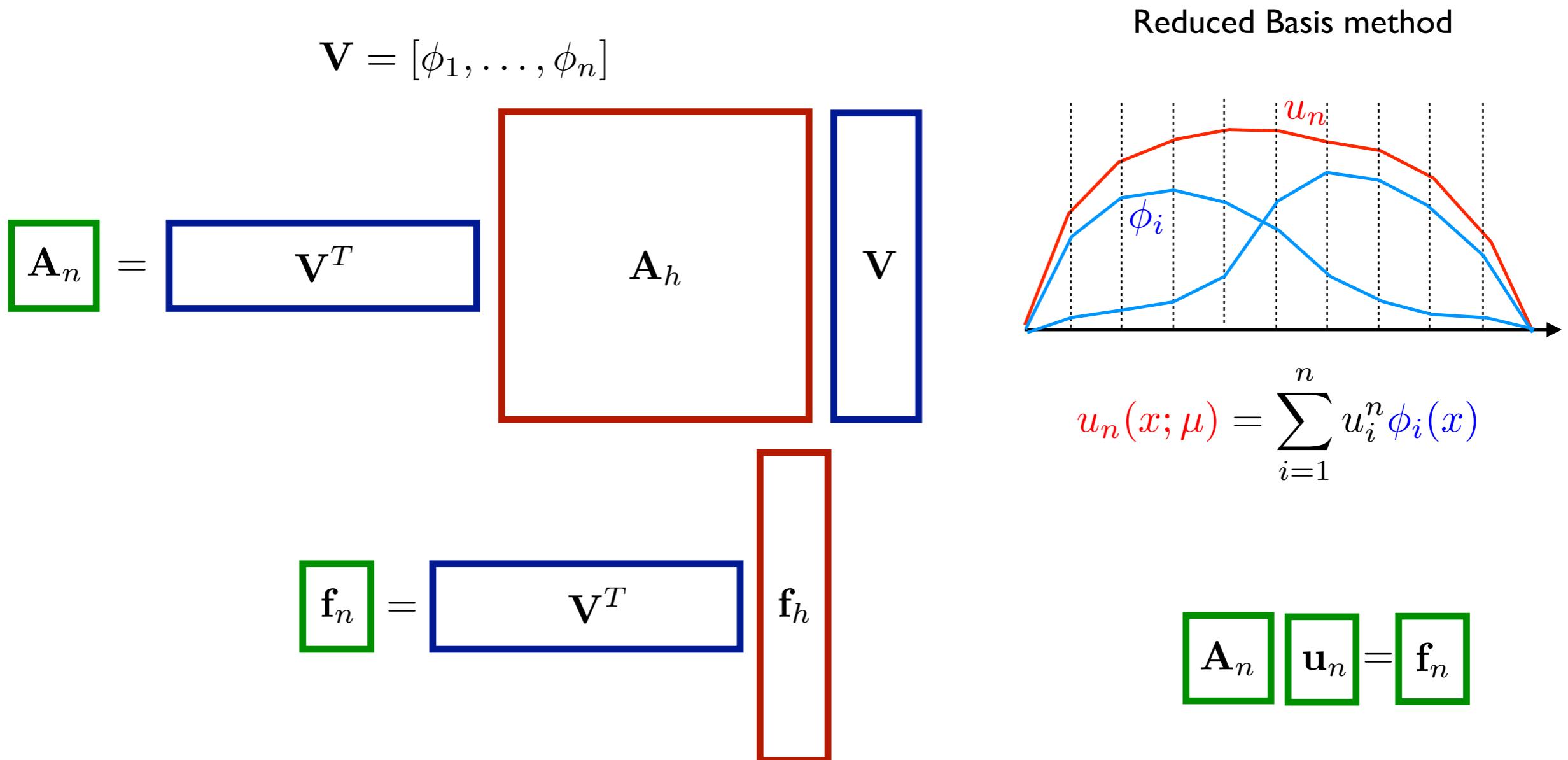
- **parameter-dependent PDEs**
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 - ✓ material coefficients
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 - ✓ initial/boundary data
 - ✓ geometrical configuration ...

- **Snapshots computed offline**
- **RB space:** $V_n = \text{span}\{\phi_1, \dots, \phi_n\}$
- **RB problem** $P_n(\mu)$ solved **online**

$$\boxed{\mathbf{A}_n} \quad \boxed{\mathbf{u}_n} = \boxed{\mathbf{f}_n}$$

Galerkin projection

- ▶ Construction of the subspace: proper orthogonal decomposition (POD) on the set of high-fidelity snapshot $\{u_h(\mu^1), \dots, u_h(\mu^N)\}$
- ▶ ROM: projection of the full-order arrays on the reduced subspace V_n through an orthogonal projection.



Discrete empirical interpolation method

- ▶ To deal efficiently with the nonlinear terms at the reduced order level we employ the discrete empirical interpolation method (DEIM)

$$\mathbf{N}(\mathbf{u}_n; \mu) \approx \underbrace{\mathbf{V}^T \mathbf{U} (\mathbf{P}^T \mathbf{U})^{-1}}_{n \times m_D} \underbrace{\mathbf{N}(\mathbf{P}^T \mathbf{V} \mathbf{u}_n; \mu)}_{m_D \times 1}.$$

Procedure:

- ▶ compute the snapshots matrix of the nonlinear term \mathbf{N} :

$$S_N = [\mathbf{N}(\mathbf{u}_h^{(1)}; \mu_1), \mathbf{N}(\mathbf{u}_h^{(2)}; \mu_1), \dots, \mathbf{N}(\mathbf{u}_h^{(1)}; \mu_2), \mathbf{N}(\mathbf{u}_h^{(2)}; \mu_2) \dots] \in \mathbb{R}^{N_h \times N_s};$$

- ▶ compute the matrix of basis functions $\mathbf{U} = [\phi_1, \dots, \phi_{m_D}]$ by applying the POD technique on S_N ;
- ▶ select m_D degrees of freedom $\{i_1, \dots, i_{m_D}\}$ and construct the index matrix

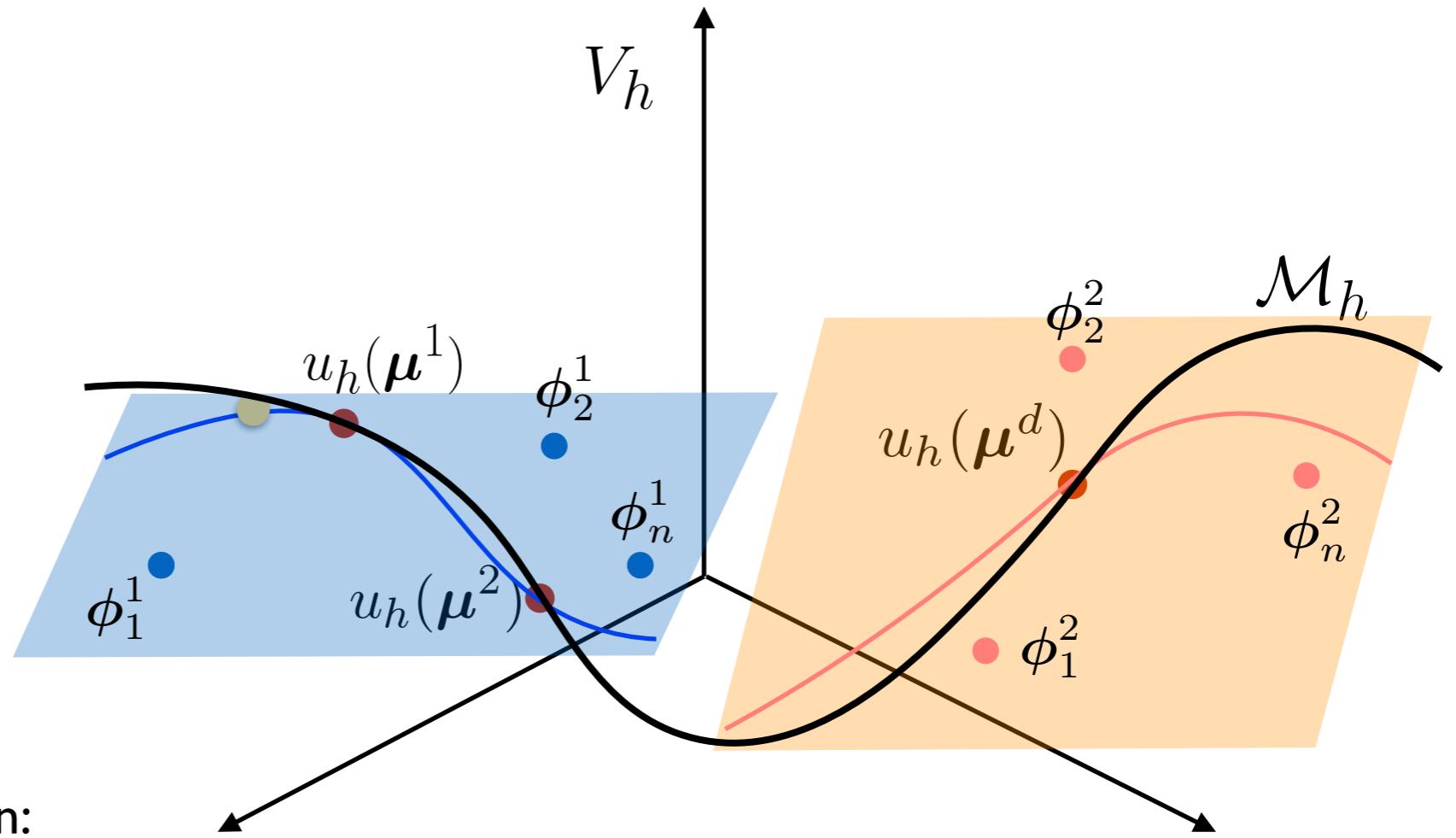
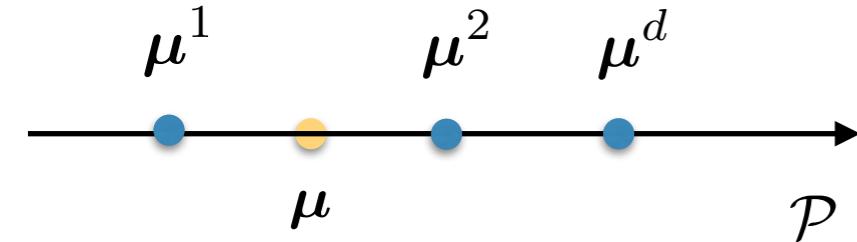
$$\mathbf{P} = [\mathbf{e}_{i_1}, \dots, \mathbf{e}_{i_{m_D}}] \quad (\mathbf{e}_i)_j = \delta_{ij}.$$

Reduced-mesh: we need to assemble the nonlinear operator on the elements related to the degrees of freedom $\{i_1, \dots, i_{m_D}\}$ selected by the DEIM algorithm.

S. Chaturantabut and D. C. Sorensen. “Nonlinear model reduction via discrete empirical interpolation”. *SIAM J. Sci. Comp.*, 32(5):2737–2764, 2010

Local Reduced basis method

- **Warning:** for advection dominant or traveling front problem it is difficult to ensure that $n \ll N_h$.



Tested clustering techniques
for *offline* snapshots subdivision:

- time based
- parameter based
- state based: -projection error based
-k-means

- **Snapshots computed offline**
- **RB space:** $V_n^i = \text{span}\{\phi_1^i, \dots, \phi_{n_i}^i\}$ $i = 1, \dots, N_c$
- **RB problem** $P_n^i(\mu)$ solved **online**

$$\boxed{\mathbf{A}_n} \quad \boxed{\mathbf{u}_n} = \boxed{\mathbf{f}_n}$$

S. Pagani, A. Manzoni, A. Quarteroni. "Numerical approximation of parametrized problems in cardiac electrophysiology by a local reduced basis method". In preparation (2017).

Test case

We consider the Monodomain equation (**tissue** Ω_H level) coupled with the Aliev-Panfilov model (cell level): find $u(x, t)$ and $w(x, t)$ such that

$$\begin{cases} A_m \left(C_m \frac{\partial u}{\partial t} + Ku(u-a)(u-1) + wu \right) - \operatorname{div}(\mathbf{D}(x)\nabla u) = A_m I_{app}(t) & \text{in } \Omega_H, t \in (0, T) \\ \frac{\partial w}{\partial t} = \left(\varepsilon_0 + \frac{c_1 w}{c_2 + u} \right) (-w - Ku(u-a-1)) & \text{in } \Omega_H, t \in (0, T) \\ \nabla u(t) \cdot \mathbf{n} = \nabla w(t) \cdot \mathbf{n} = 0 & \text{on } \partial\Omega_H, t \in (0, T) \\ u(0) = u_0 \quad w(0) = w_0 & \text{in } \Omega_H, t = 0, \end{cases}$$

Under the assumption that the left-ventricle tissue is an axisymmetric anisotropic media the **conductivity tensor** is given by:

$$\mathbf{D}(x) = \sigma_t \mathbf{I} + (\sigma_l - \sigma_t) \mathbf{f}_0(x) \otimes \mathbf{f}_0(x),$$

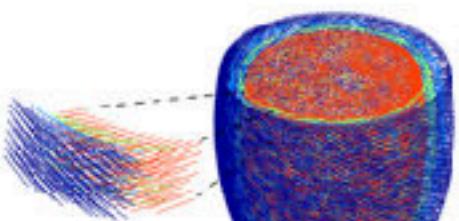
where $\mathbf{f}_0(x)$ is a vector parallel to the fiber direction at any point $x \in \Omega_H$.

Finally \mathbf{f}_0 is rotated with from an angle θ_{epi} on the epicardium to an angle θ_{endo} on the endocardium with the following relationship:

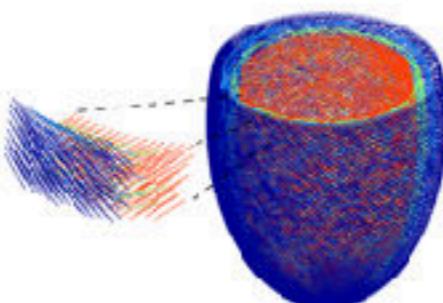
$$\theta = (\theta_{epi} - \theta_{endo}) \frac{r - r_1}{r_2 - r_1} + \theta_{endo}.$$

Influence of the parameters on the solution

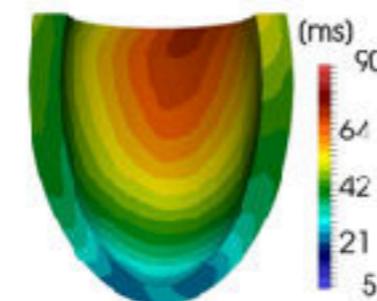
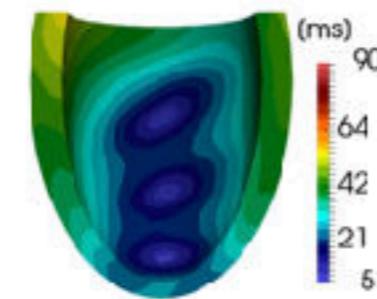
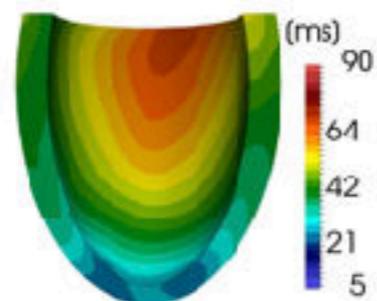
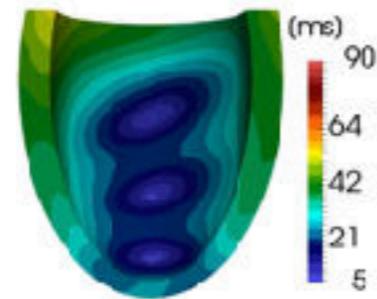
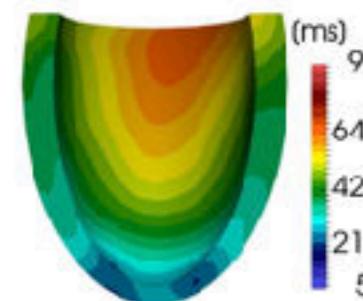
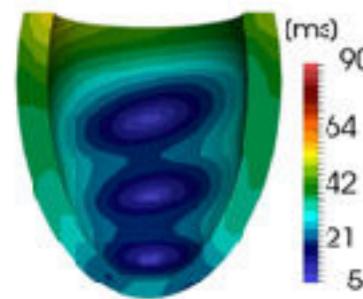
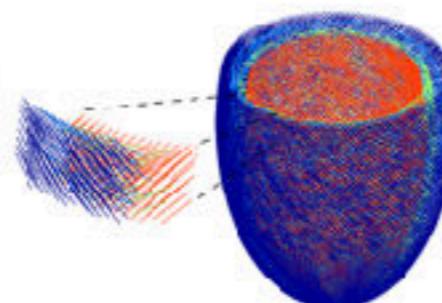
$$\theta_{epi} = 30, \theta_{endo} = -30$$



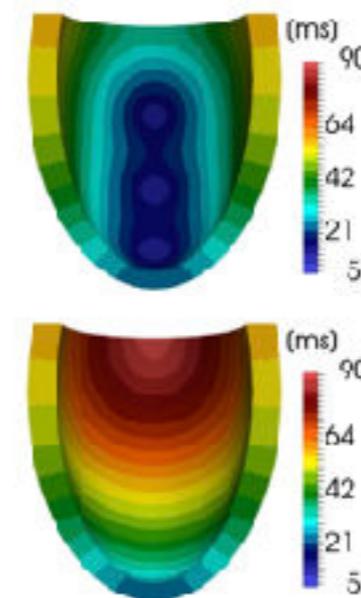
$$\theta_{epi} = 50, \theta_{endo} = -50$$



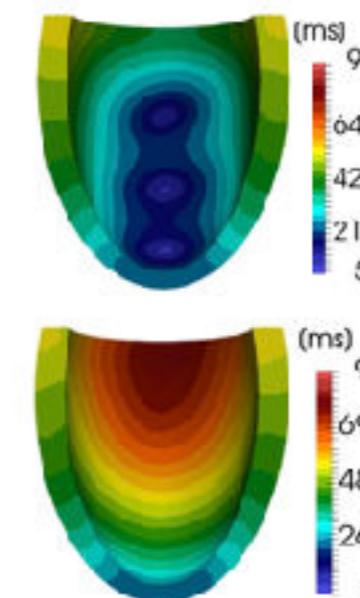
$$\theta_{epi} = 70, \theta_{endo} = -70$$



$$\sigma_l = 0.1, \sigma_t = 0.1$$



$$\sigma_l = 0.175, \sigma_t = 0.055$$



$$\sigma_l = 0.25, \sigma_t = 0.01$$

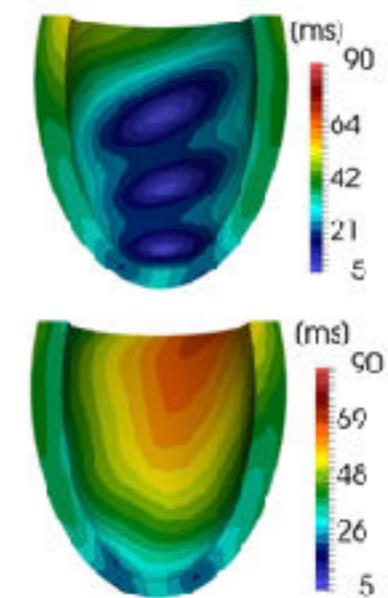
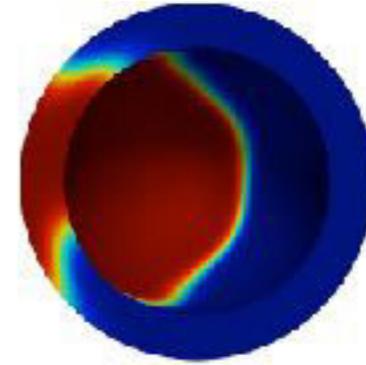
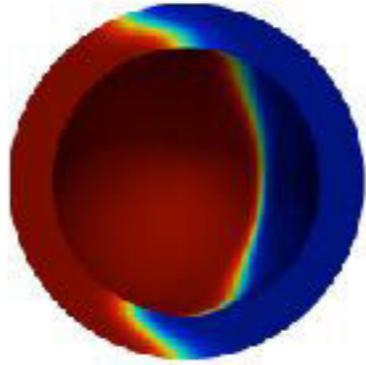
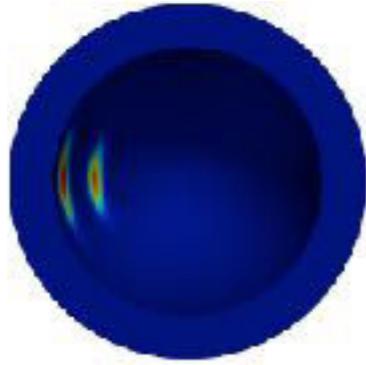


Fig: activation times on varying the epicardial and the endocardial angle of the fibers

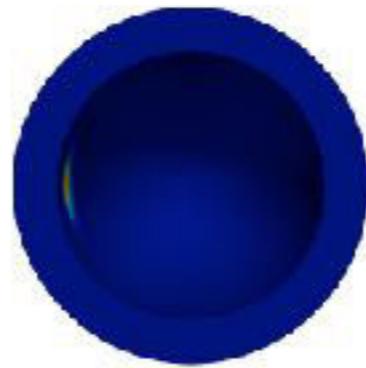
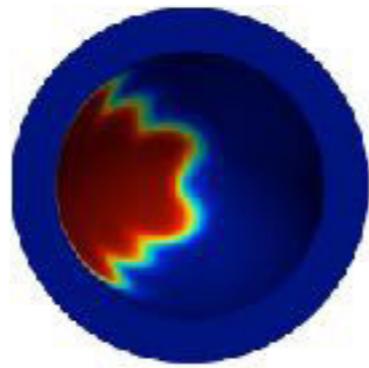
Fig: activation times on varying the longitudinal and the traversal conductivity

Local ROM method

Ingredient: a criterium for the subdivision of the snapshots matrix.



$$\mathbf{S}_u = [\dots, \mathbf{u}_h^{(30)}(\mu_1), \dots, \mathbf{u}_h^{(100)}(\mu_1), \dots, \mathbf{u}_h^{(180)}(\mu_1), \dots, \mathbf{u}_h^{(10)}(\mu_2), \dots, \mathbf{u}_h^{(150)}(\mu_2), \dots].$$



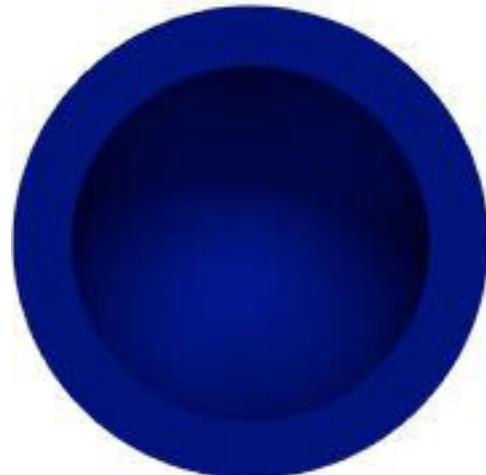
Algorithm:

1. \mathbf{S}_u is partitioned into N_c submatrices \mathbf{S}_u^k , $k = 1, \dots, N_c$;
2. \mathbf{S}_I (matrix of nonlinear term snapshots) is partitioned into N_c submatrices \mathbf{S}_I^k , $k = 1, \dots, N_c$;
3. the localized basis functions are constructed through the POD technique applied to each \mathbf{S}_u^k and \mathbf{S}_I^k , $k = 1, \dots, N_c$;
4. the reduced arrays forming the reduced system are computed by means of the Galerkin projection.

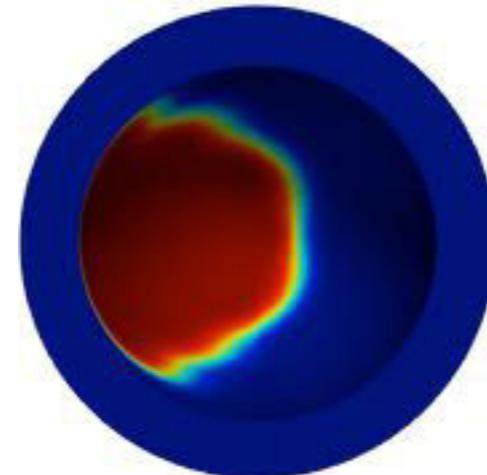
K-means clustering

$$\{\mathbf{S}_u^1, \dots, \mathbf{S}_u^k\} = \arg \min_{\mathbf{S}_u} \sum_{k=1}^{N_c} \sum_{\mathbf{u}_h \in \mathbf{S}_u^k} \|\mathbf{u}_h - \mathbf{c}_h^k\|^2$$

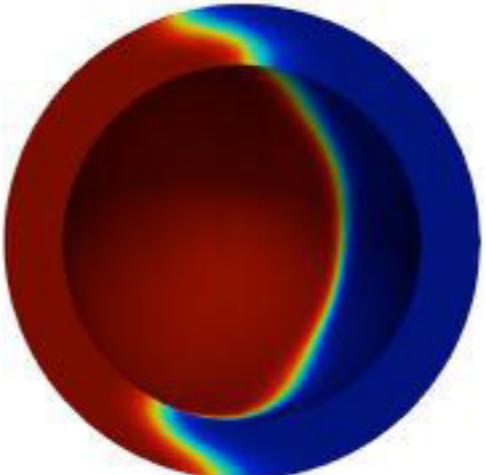
\mathbf{c}_h^1



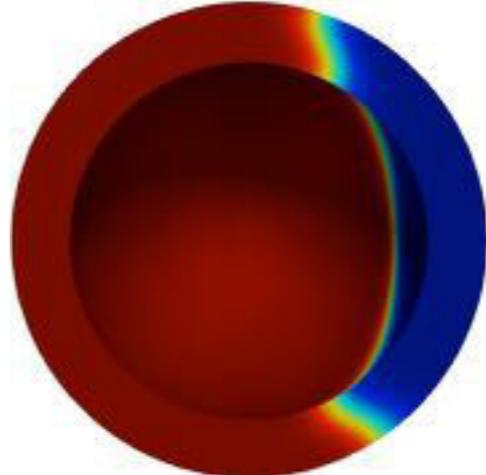
\mathbf{c}_h^2



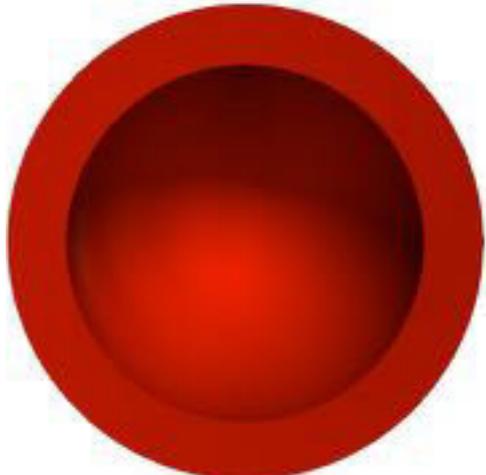
\mathbf{c}_h^3



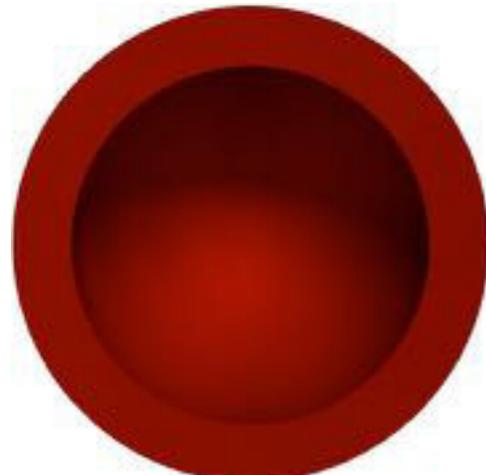
\mathbf{c}_h^4



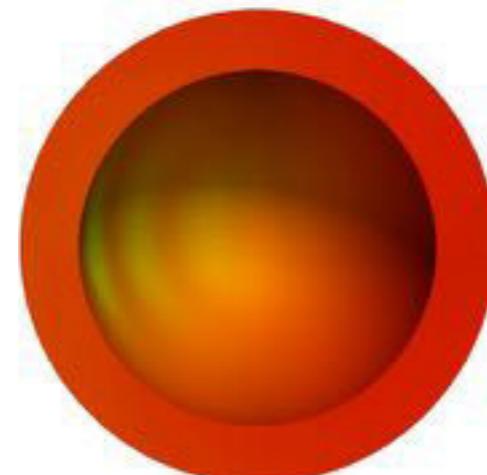
\mathbf{c}_h^5



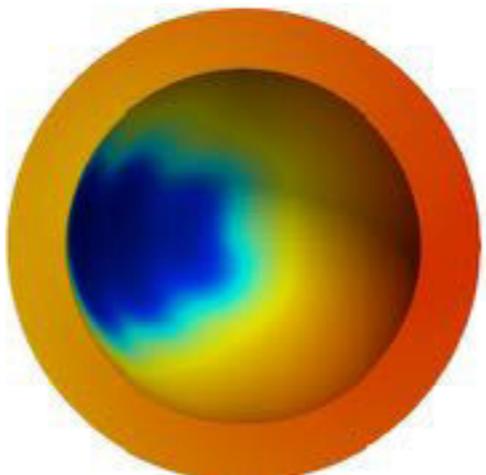
\mathbf{c}_h^6



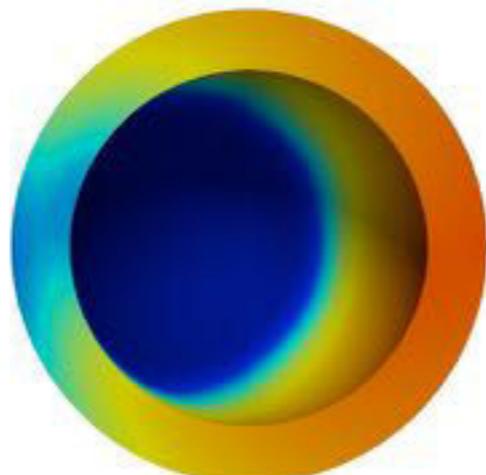
\mathbf{c}_h^7



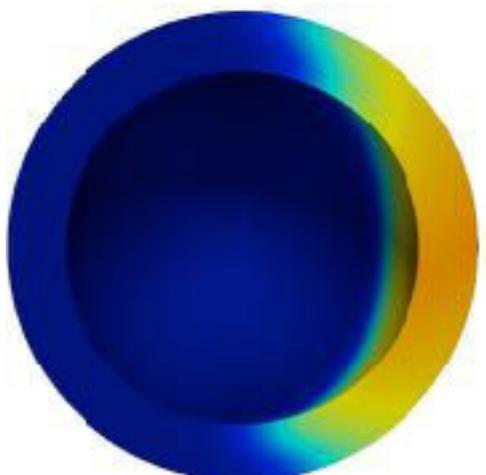
\mathbf{c}_h^8



\mathbf{c}_h^9



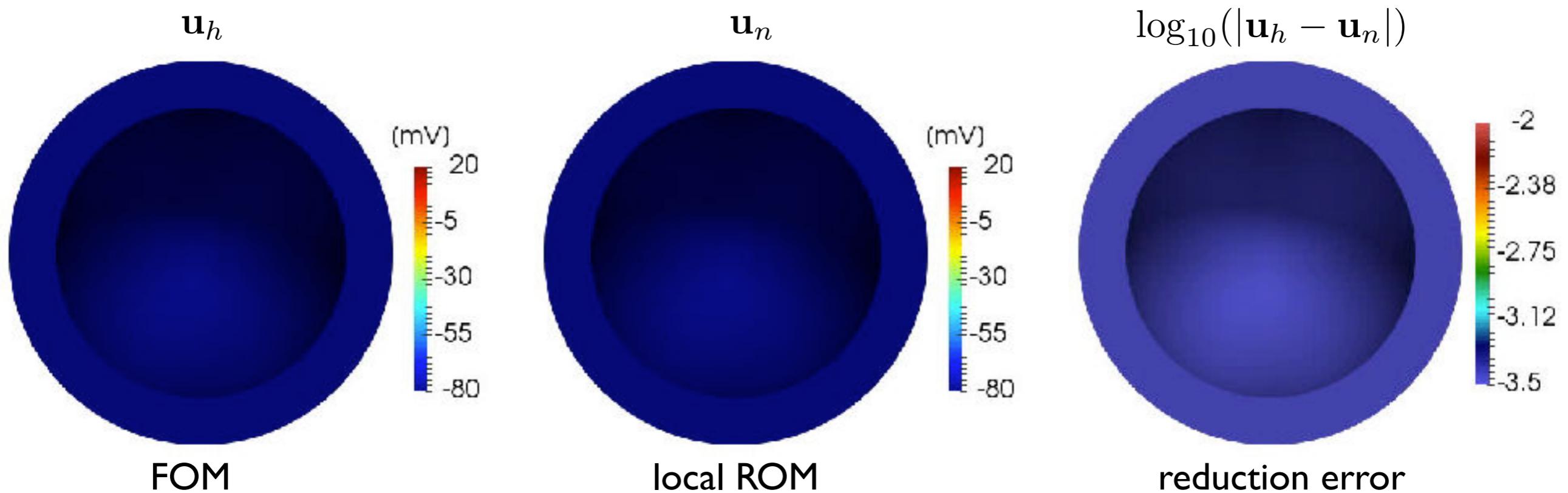
\mathbf{c}_h^{10}



Results

Localized reduced-order model
based on k-means clustering

Parameters μ : - epicardial and endocardial angles
- longitudinal and traversal conductivities



Finite elements DOFs: 31764
Number of Elements: 140271
POD/DEIM ROM speedup: **4.6x**

max # basis functions: 192
min # basis functions: 11
Localized ROM **speedup 25.2x**