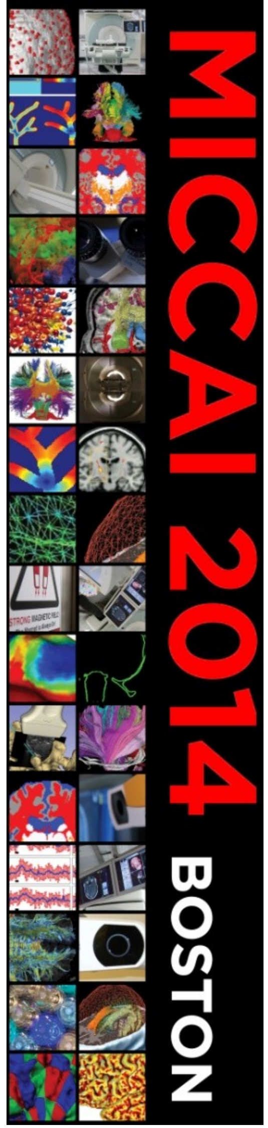
Robust Image-Based Estimation of Cardiac Tissue Parameters and their Uncertainty from Noisy Data

Dominik Neumann[1,2], Tommaso Mansi[1], Bogdan Georgescu[1], Ali Kamen[1]
Elham Kayvanpour[3], Ali Amr[3], Farbod Sedaghat-Hamedani[3], Jan Haas[3],
Hugo Katus[3], Benjamin Meder[3], Joachim Hornegger[2], Dorin Comaniciu[1]

[1] Imaging and Computer Vision, Siemens Corporate Technology
[2] Pattern Recognition Lab, FAU Erlangen-Nürnberg, Germany
[3] University Hospital Heidelberg, Department of Internal Medicine III, Germany



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Heart Failure

Major cause of morbidity & mortality
(McMurray et al., Eur Heart J'12)

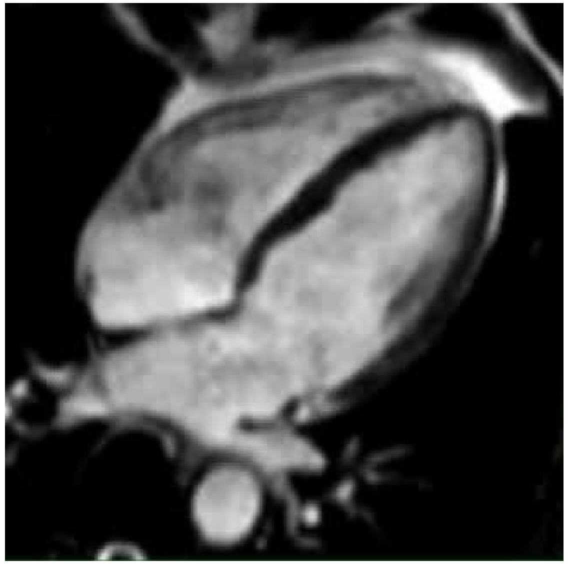
Early diagnosis and treatment difficult

New tools required
- Patient stratification
- Therapy planning

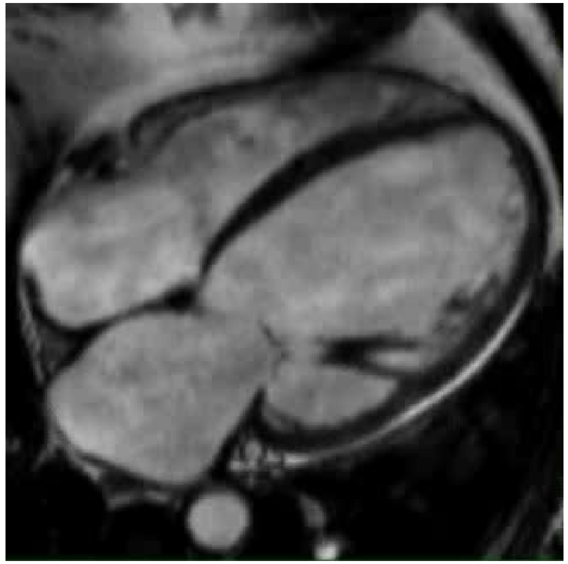
Computational models could help
- Advanced measurements for diagnosis
- Test treatment options in-silicio

Sermesant et al., MedIA'12; Aguado-Sierra et al., Prog Biophys Mol Bio'11; Wang et al., ISBI'12; Seegerer et al., STACOM'14; …

Healthy

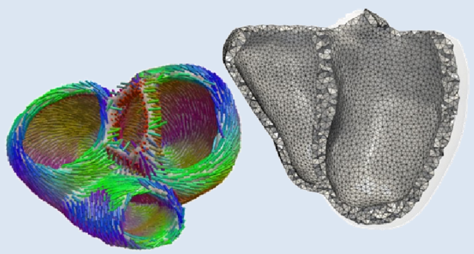


Heart Failure
Dilated Cardiomyopathy



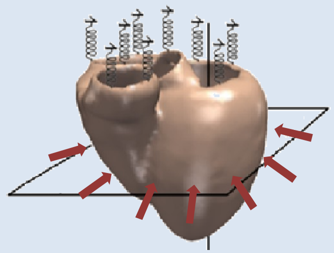
Computational Heart Model

Anatomy

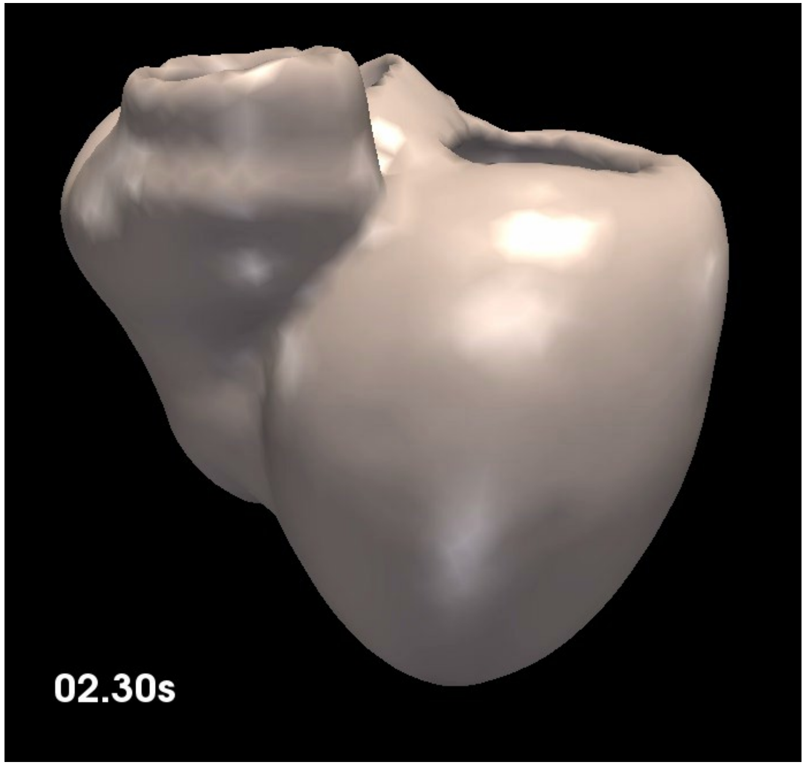


Zheng et al., *TMI'08*
Lu et al., *FIMH'11*
Zhuang et al., *TMI'10*

Hemodynamics

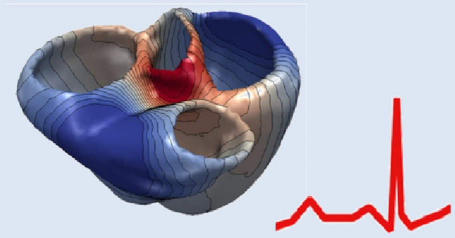


Kerckhoffs et al., *ABE'07*
Arts et al., *Am J Physiol'05*
Westerhof et al., *JAP'71*



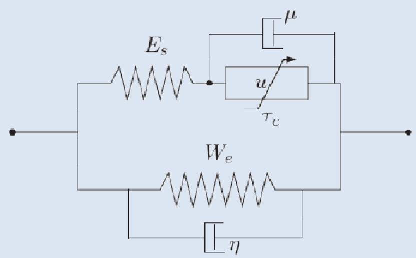
Zettinig et al., *FIMH'13*

Electrophysiology



Zettinig et al., *MedIA'14*
Mitchell & Schaeffer, *BMB'03*
Trayanova et al., *Circ Res'11*

Biomechanics



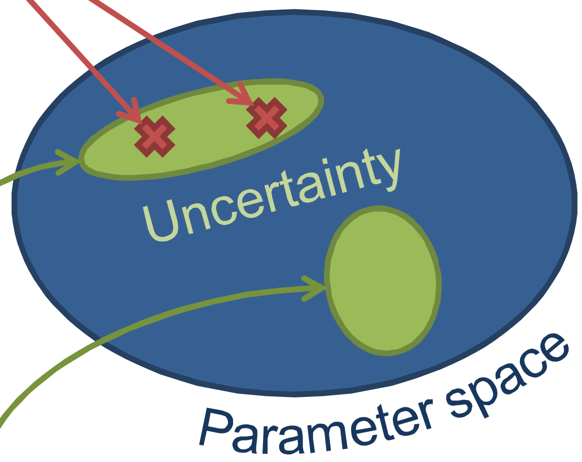
Fung '93
Hunter et al., *Ann Rev Biomed Eng '03*

Model Personalization

Most work: compute “best” set of parameters

Single estimate

Marchesseau et al., MedIA’13; Wong et al., STACOM’13; Chabiniok et al., BMM’12; Lekadir et al., TMI’14; Delingette et al., BME’12; Camara et al., MedIA’14; …



Facts

- Heart: complex
- Data: noisy & sparse
- Models: based on assumptions

Is solution unique?

- “Yes”: How do we know?
- “No”: Clinical value of a single estimate?

Personalization with uncertainty

Probability density

➔ So far only for cardiac electrophysiology

Wallman et al., MedIA’14; Konukoglu et al., PBMB’11

Computational Heart Model
Focus on Biomechanics

Tissue mass *Rayleigh damping* *Other constraints*

$$\mathbf{M}\ddot{\mathbf{u}} + \mathbf{C}\dot{\mathbf{u}} + \mathbf{K}\mathbf{u} = \mathbf{f}_a + \mathbf{f}_p + \mathbf{f}_b$$

Tissue stiffness *Displacement* ***Active force*** *Pressure*

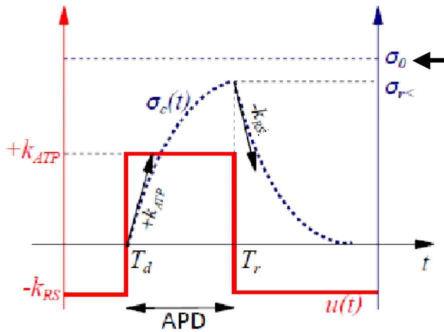
$\boxed{\beta}$ *Holzapfel & Ogden, Phil Trans R Soc A'09*

Sermesant et al.,TMI'06 $\boxed{\sigma_0}$

Scaling factor

$$\Xi = \beta\Psi(\underbrace{I_1, I_{4f}, I_{4s}, I_{8fs}}_{\text{Invariants of deformation tensor}})$$

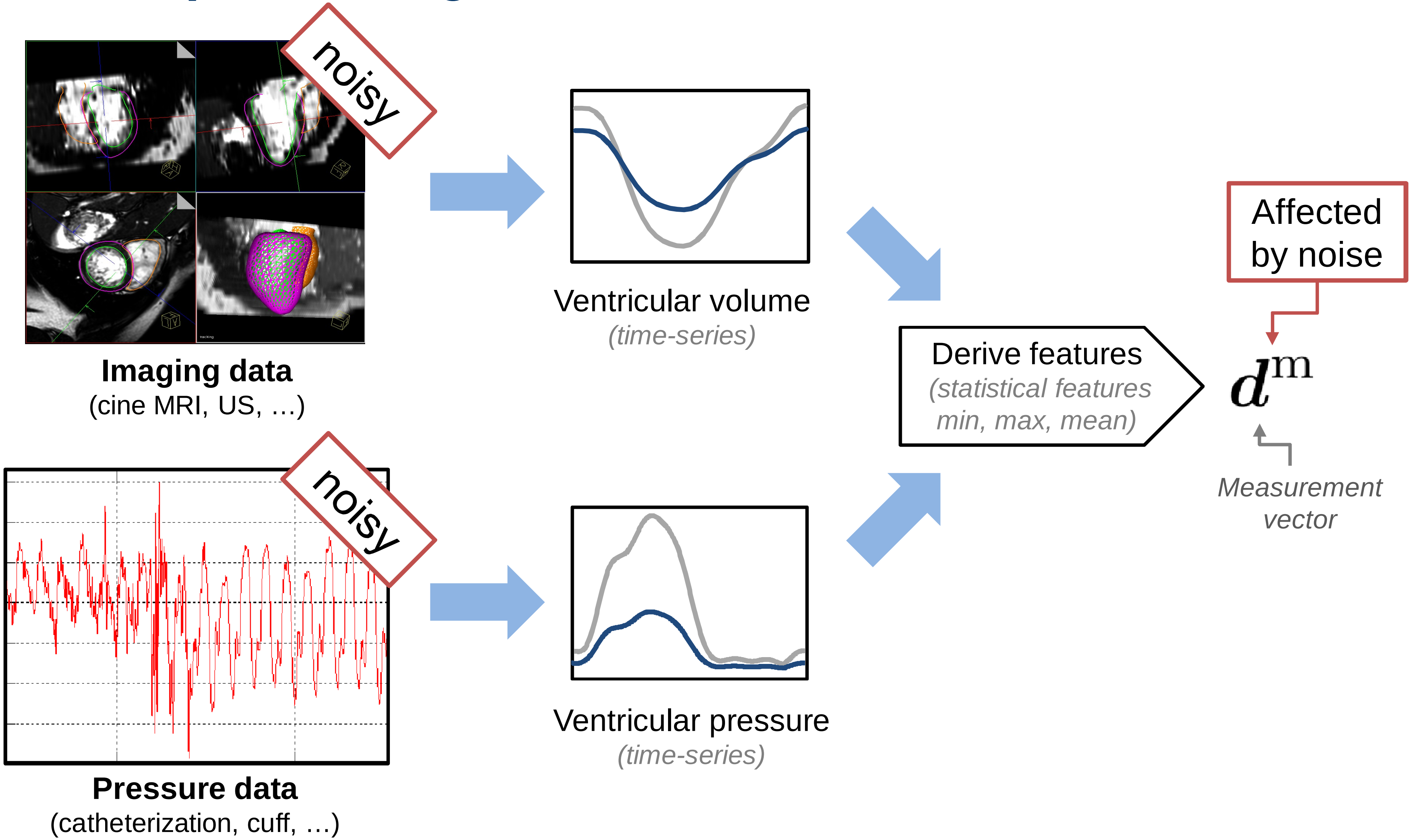
Stress-strain energy



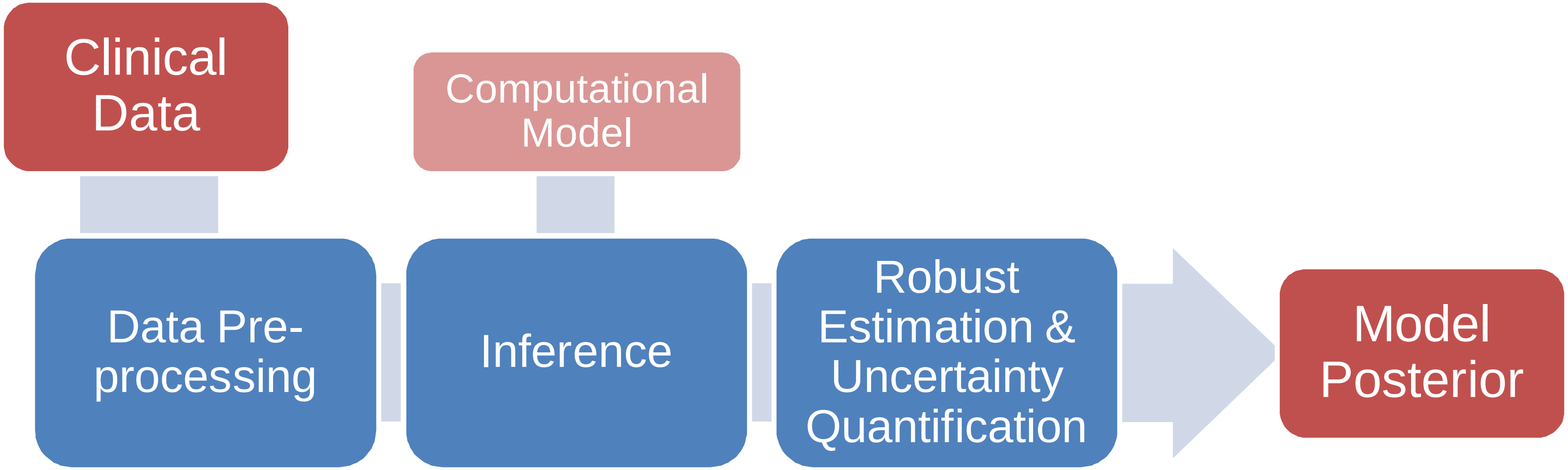
Maximum active force

$\boxed{\theta}$ *Model parameters*

Data Preprocessing



Personalization with Uncertainty



Inference

Statistical Reformulation

$$\underbrace{f}_{\text{Model}}(\boldsymbol{\theta}) = \boldsymbol{d}^{\mathrm{c}}$$

- Random **input** variable $\boldsymbol{\theta}$ *(model parameters)*
- Random **output** variable $\boldsymbol{d}^{\mathrm{c}}$ *(model responses)*

Bayesian Calibration *(compute model posterior)*

Noise level: covariance matrix assuming normal error

$$p(\boldsymbol{\theta}|\boldsymbol{d}^{\mathrm{m}}) \propto \underbrace{p(\boldsymbol{d}^{\mathrm{m}}|\boldsymbol{\theta})}_{\text{Likelihood}} p(\boldsymbol{\theta}) = \exp\left(-1/2\, \varepsilon(\boldsymbol{d}^{\mathrm{c}}, \boldsymbol{d}^{\mathrm{m}})^{\top} \mathrm{S}^{-1} \varepsilon(\boldsymbol{d}^{\mathrm{c}}, \boldsymbol{d}^{\mathrm{m}})\right) p(\boldsymbol{\theta})$$

***Likelihood**: expressed in terms of error ε between responses and measurements*

➔ **Markov Chain Monte Carlo** sampling (MCMC)

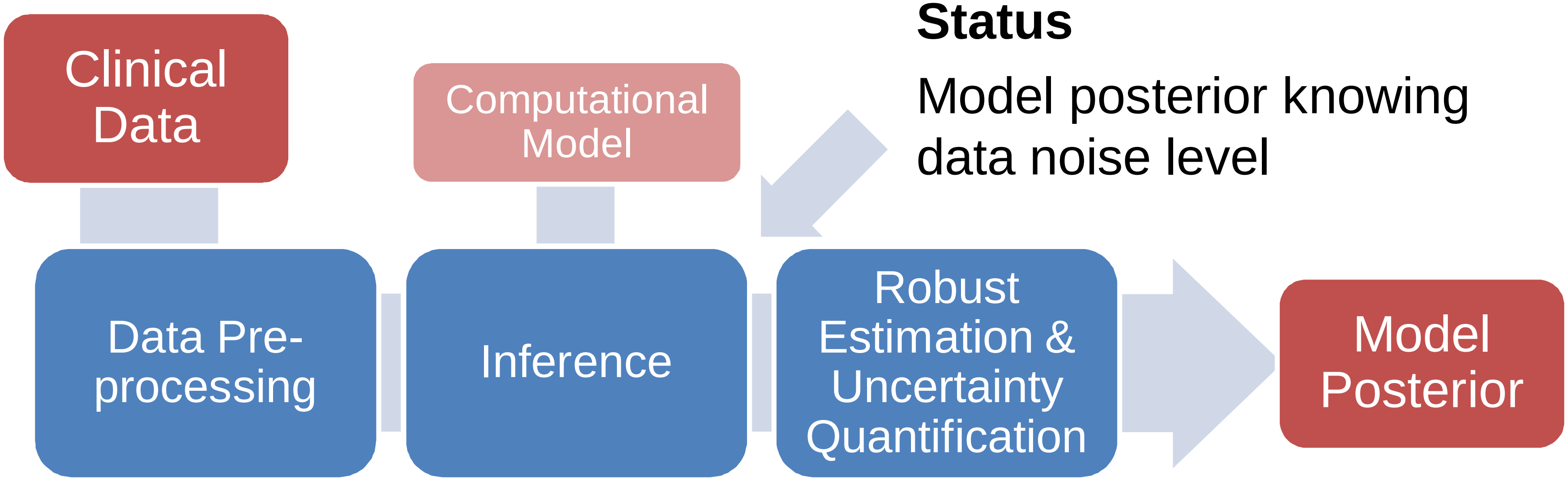
Polynomial Chaos Expansion (PCE) *(Marzouk et al., J Comp Phys'07)*

➔ Fast **surrogate** model to make MCMC tractable

Personalization with Uncertainty

Status

Model posterior knowing data noise level



Data noise not known *(typically)*

- ➔ Compute posteriors for different levels of noise
- ➔ Aggregate into one robust PDF

Step 1

Repeat
with varying S_i

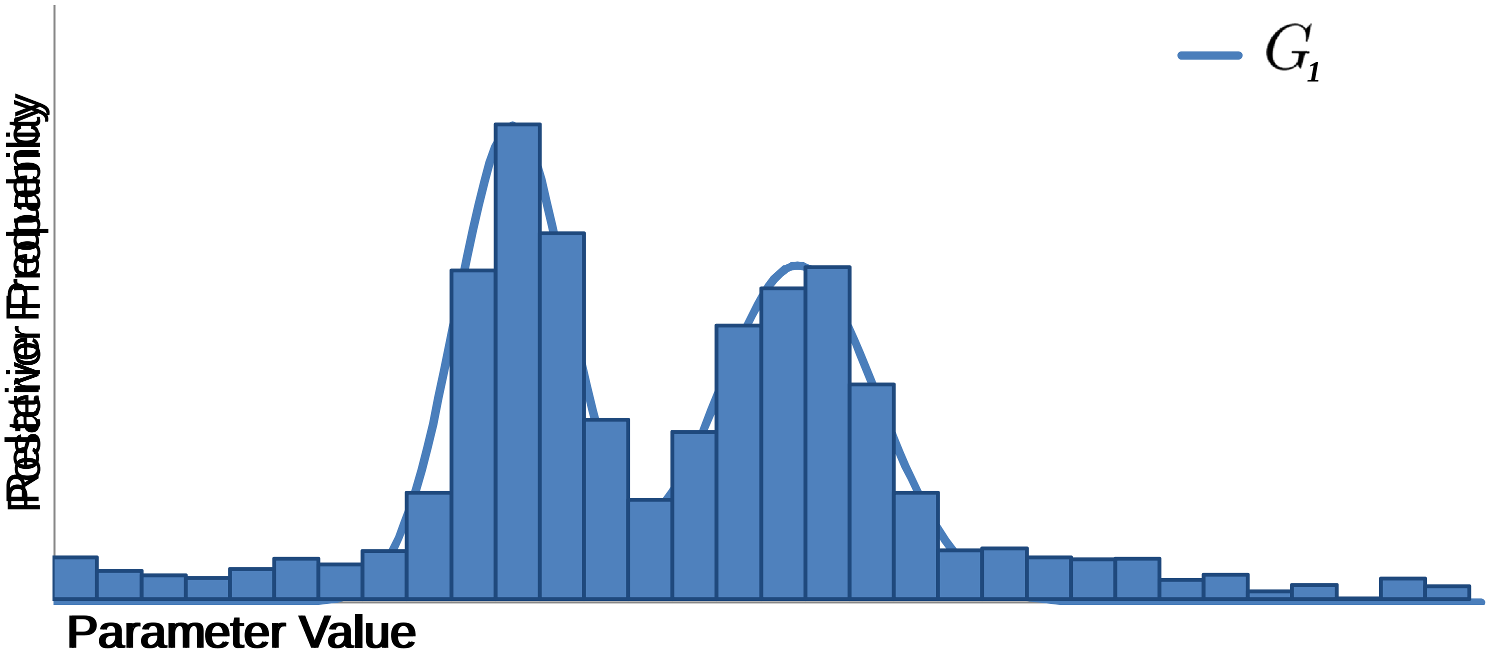
Histogram of MCMC samples

- ➔ Samples generated using noise level S_1
- ➔ Estimate number of modes k_1 using meanshift

$\exp\left(-1/2\,\varepsilon(d^c, d^m)^\top S^{-1} \varepsilon(d^c, d^m)\right)$

Alternative method:
Han et al., *PAMI'08*

- ➔ Fit Gaussian mixture model (GMM) G_1

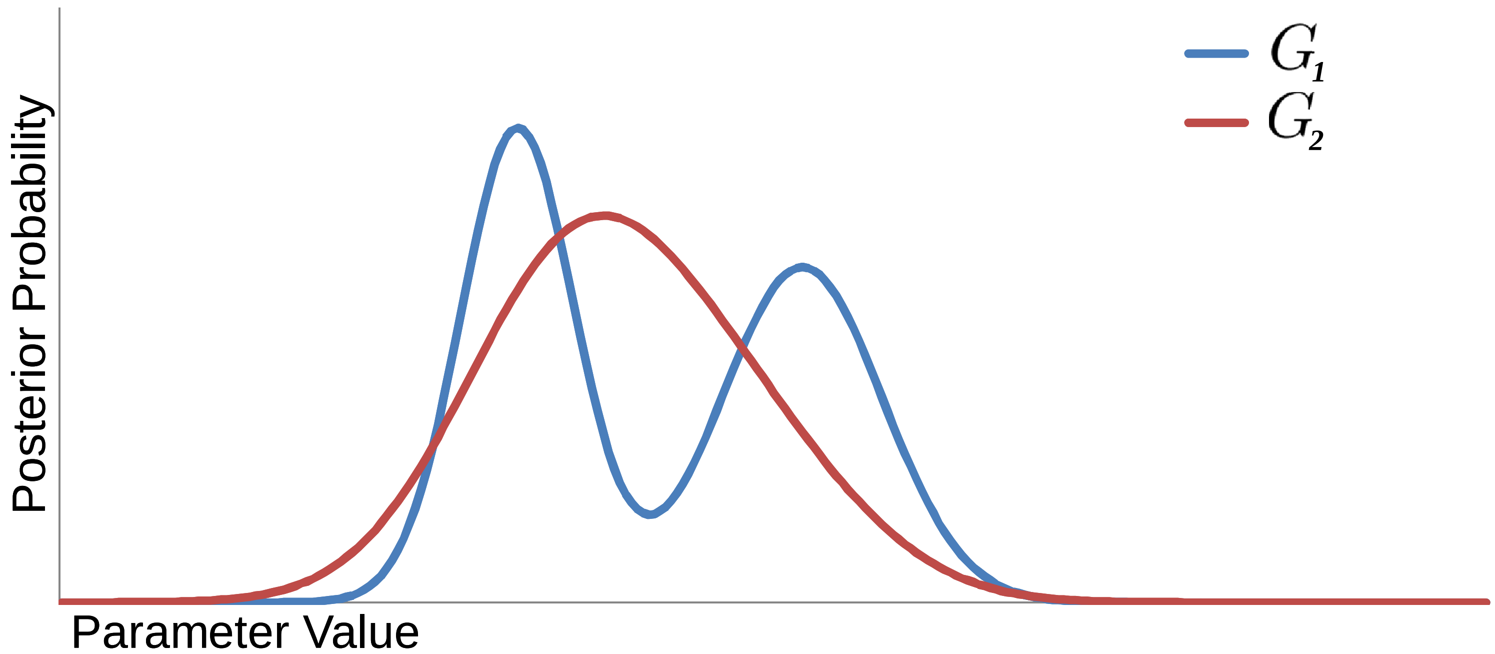


Step 1

Repeat
with varying S_i

Histogram of MCMC samples

- ➔ Samples generated using noise level S_2
- ➔ Estimate number of modes k_2 = 1 using mean-shift
- ➔ Fit Gaussian mixture model (GMM) G_2

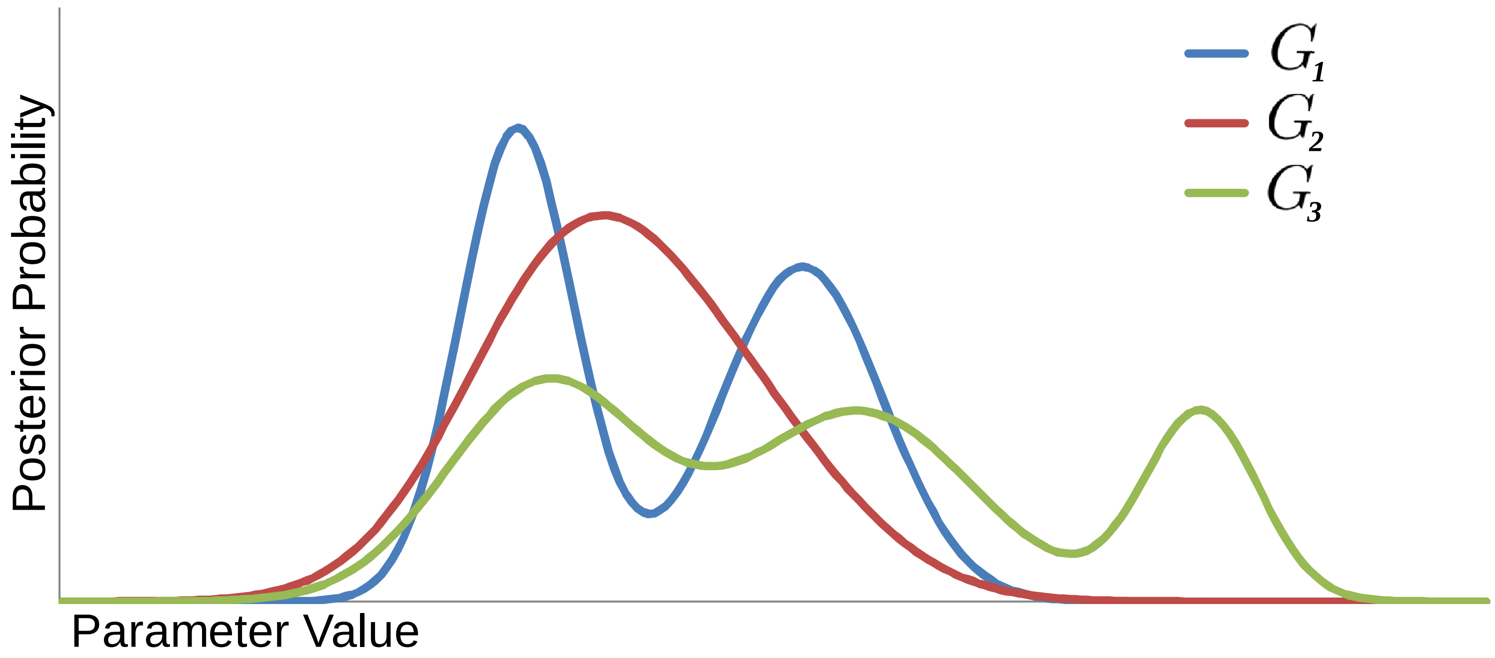


Step 1

Repeat
with varying S_i

Histogram of MCMC samples

- ➔ Samples generated using noise level S_3
- ➔ Estimate number of modes k_3 = 3 using mean-shift
- ➔ Fit Gaussian mixture model (GMM) G_3

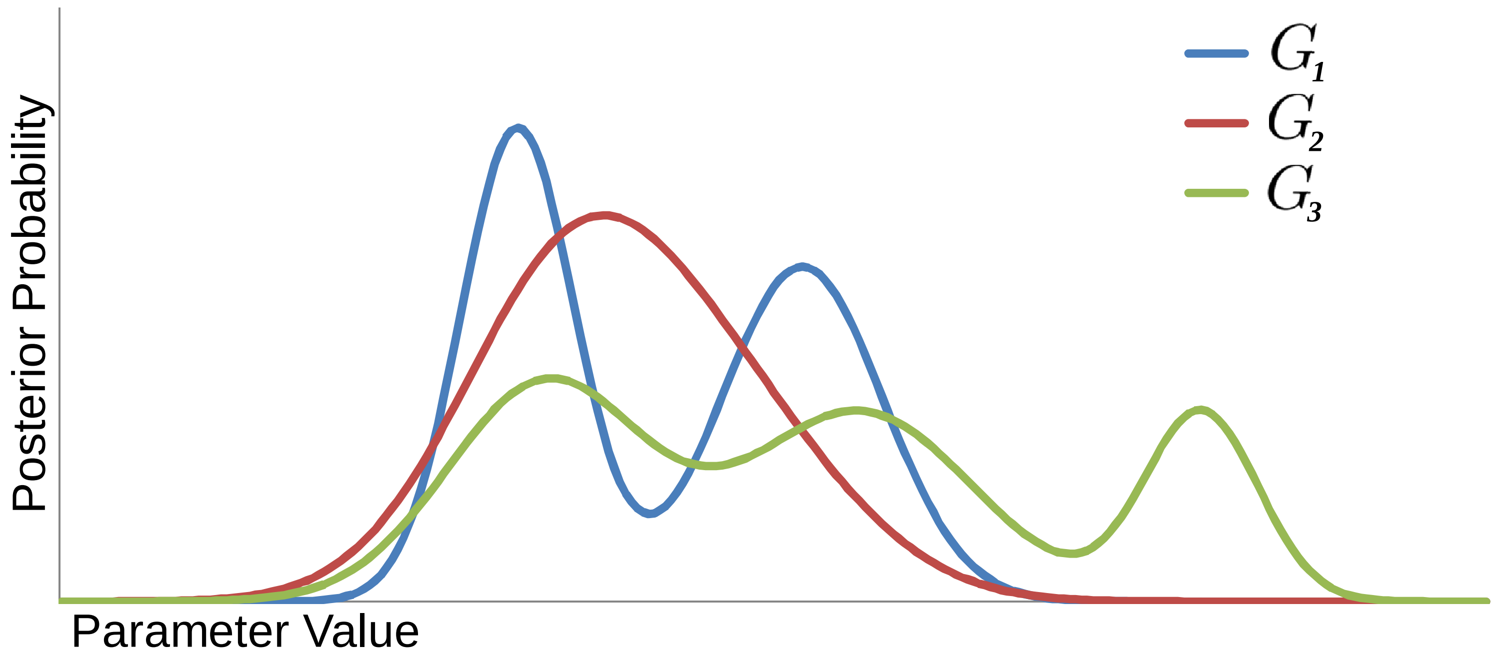


Step 2

Set of intermediate posterior distributions

➔ Aggregate to form a final robust posterior

→ *cluster-based approach*

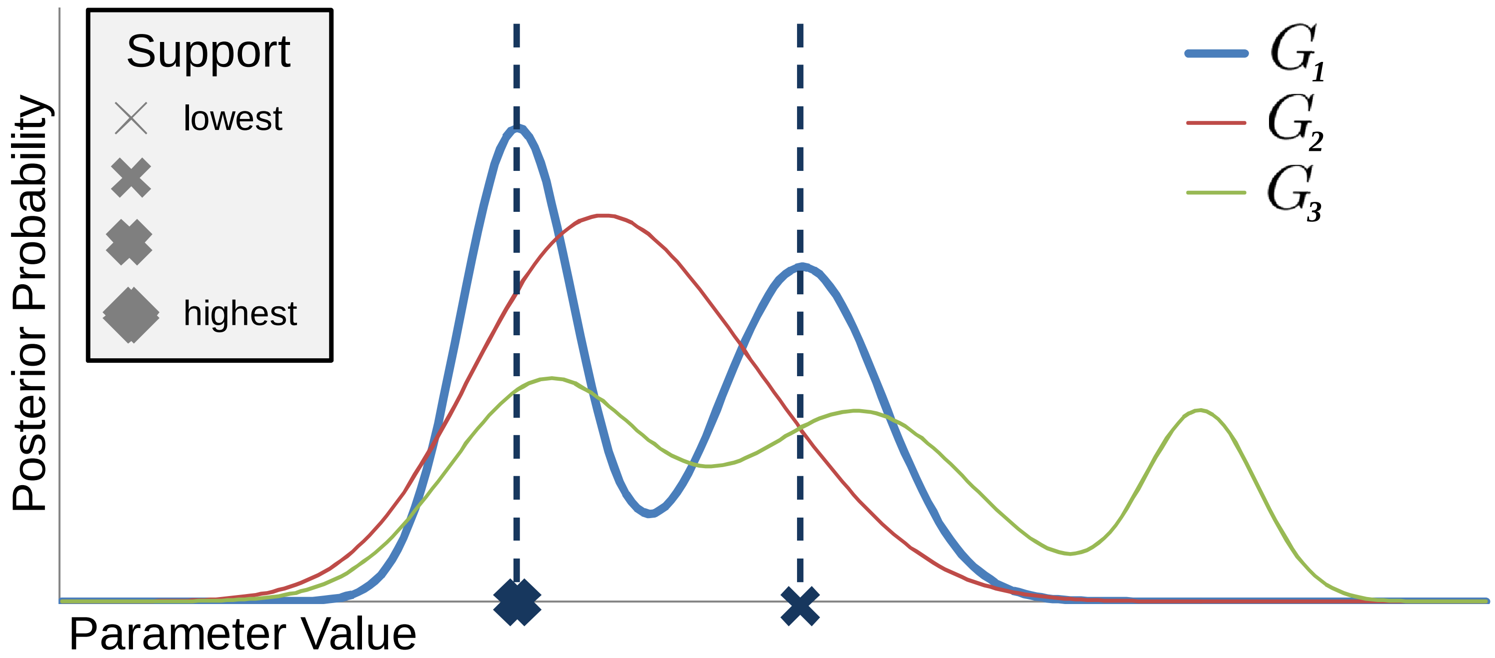


Step 2

Consider one particular G_i

- For each mode $\boldsymbol{\mu}_{ij}$: compute support by other GMMs

$$\omega_{ij} = \sum_{t \neq i} \log G_t(\boldsymbol{\mu}_{ij})$$



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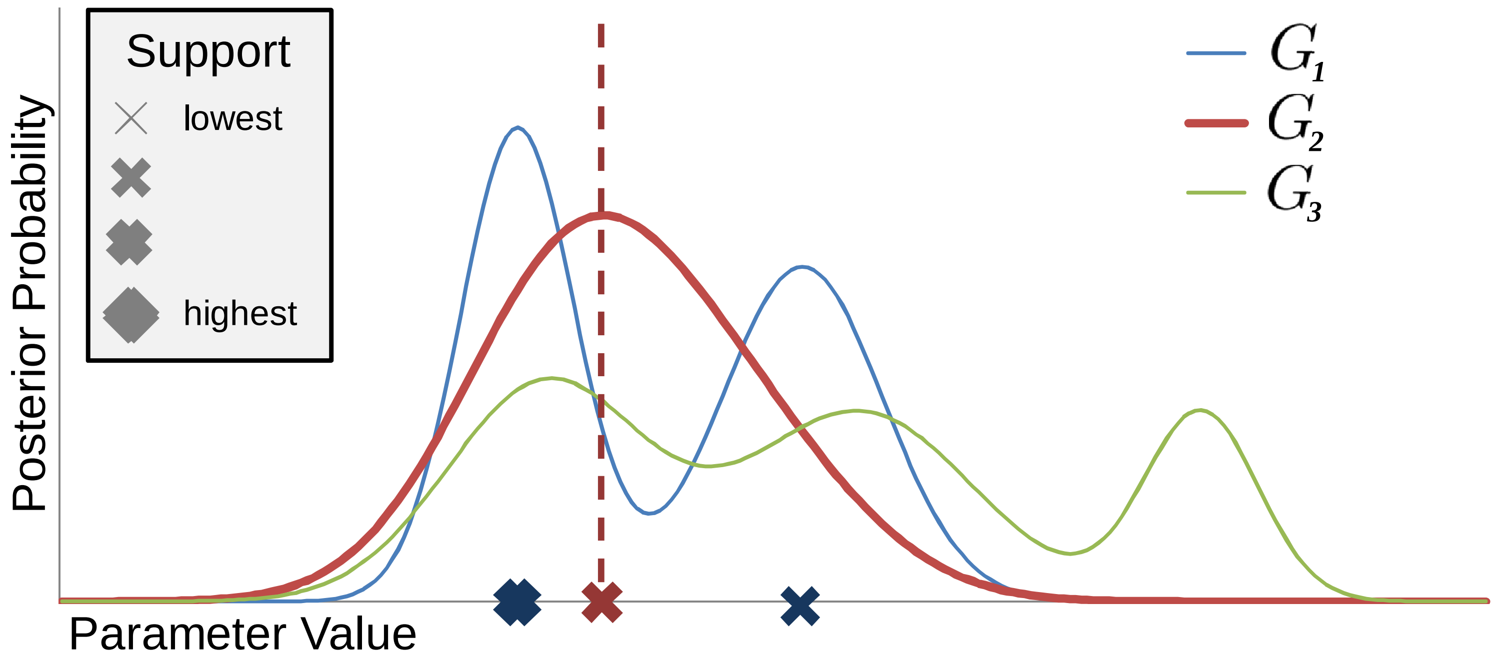

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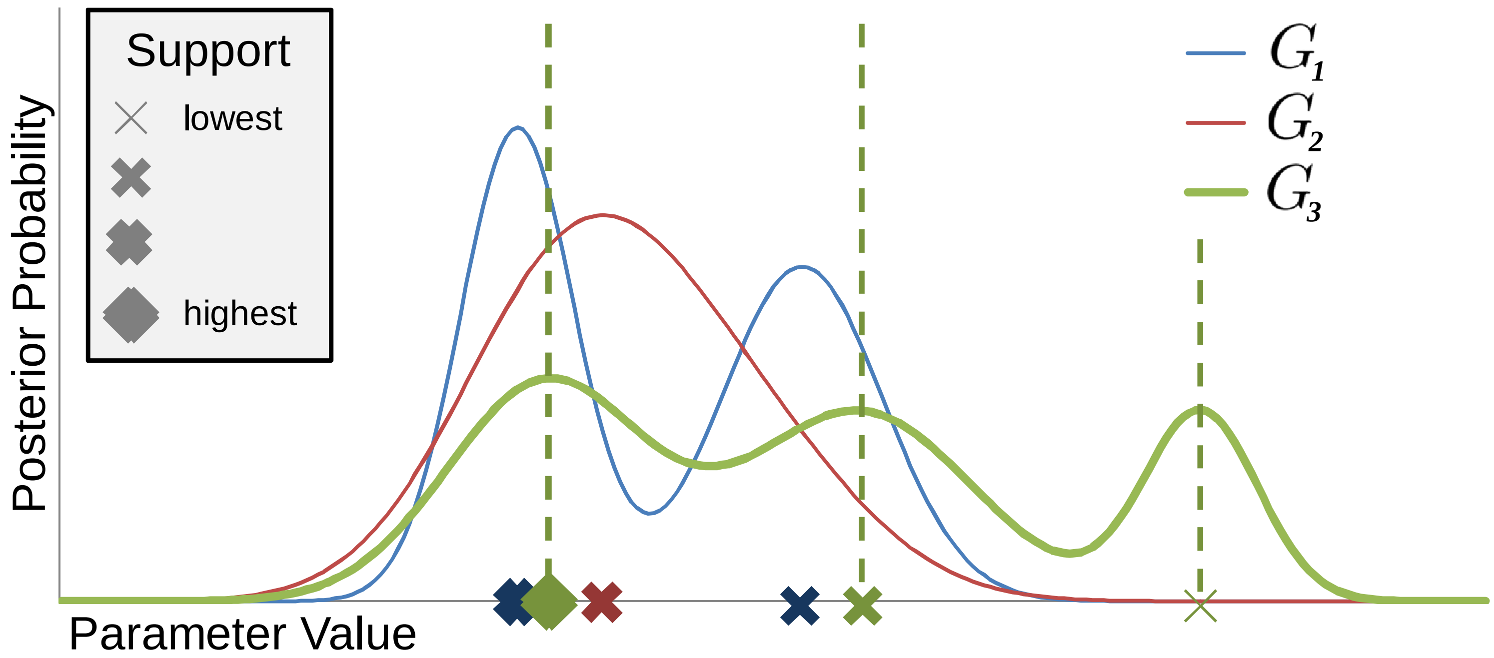
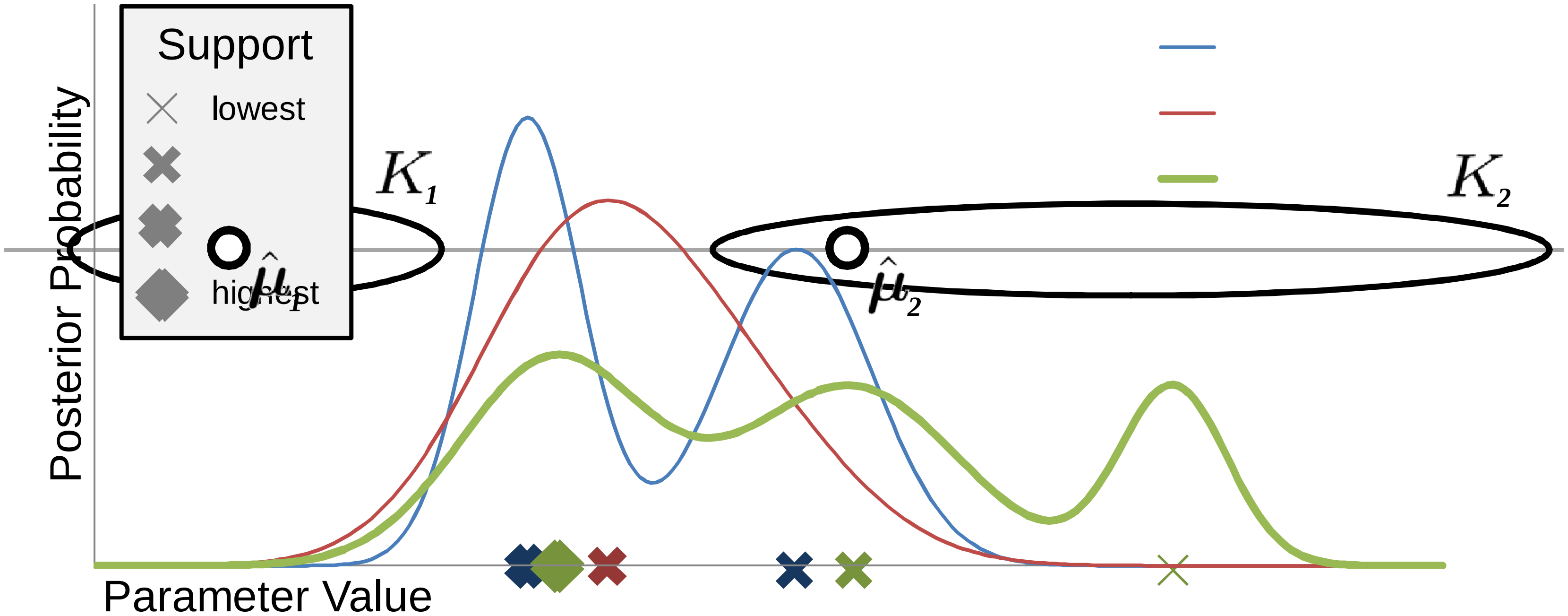


Step 3

Cluster modes into k^* clusters *(determined by voting)*

- Compute barycenter and "combined support" of each cluster

$$\hat{\omega}_l = \sum_{ij \in K_l} \omega_{ij}$$



Step 4

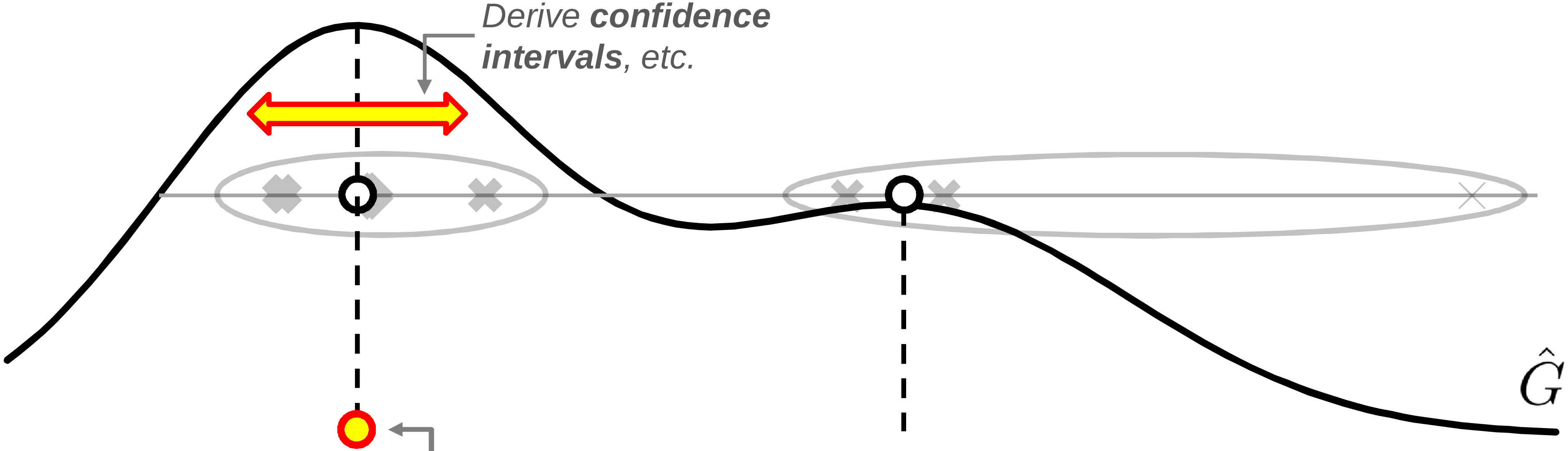
Compute final robust posterior

Cluster barycenter

$$\boxed{\hat{G} = \sum_{l=1}^{k^*} \hat{\omega}_l \mathcal{N}(\hat{\boldsymbol{\mu}}_l, \hat{\Upsilon}_l)}$$

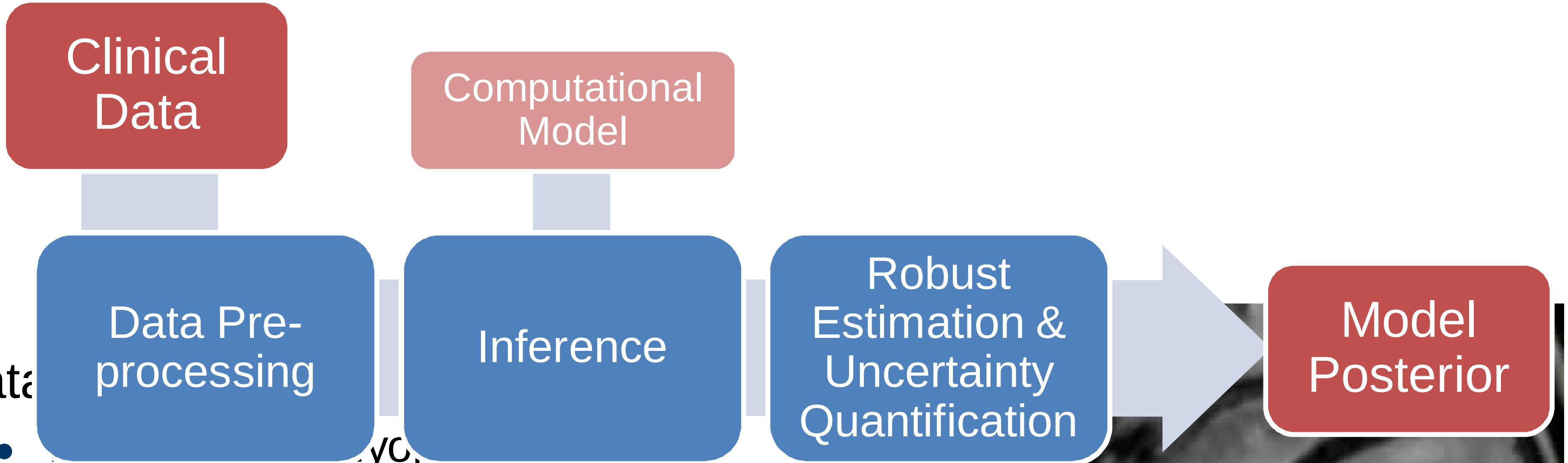
Cluster covariance

Derive ***confidence intervals****, etc.*



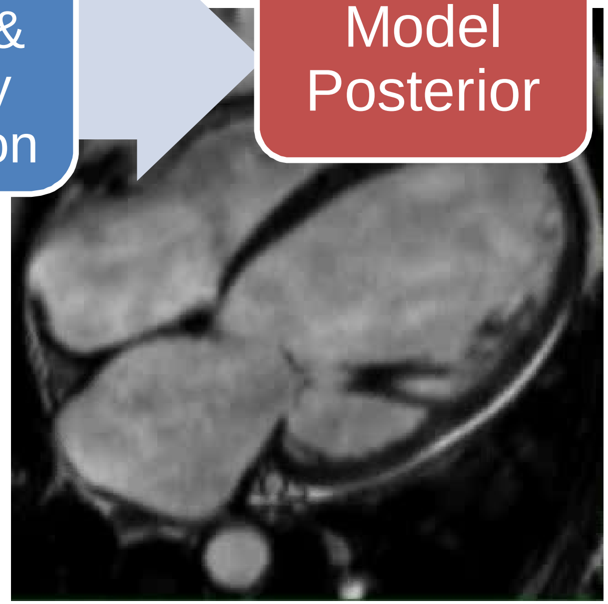
"Primary" estimate*: Barycenter of highest support cluster*

Evaluation



Data

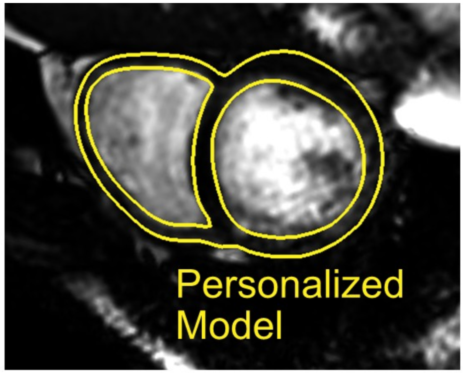
- Large variety in phenotype & disease severity
  - Ejection fraction: 19 – 47 %
  - Stroke volume: 69 – 104 mL

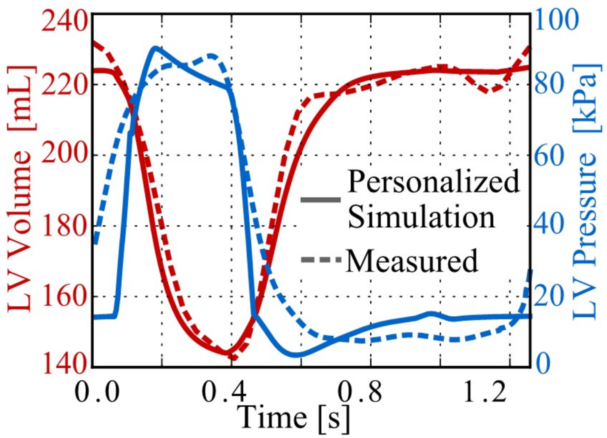


Goodness of Fit to Data

Qualitative fit *(example dataset)*

End-Systolic Fit





Quantitative fit *(8 patients)*

Goodness of Fit	**Proposed**		**Inverse Optimization**	
	EF [%]	**SV** [mL]	**EF** [%]	**SV** [mL]
Mean	**2.3**	8.6	**2.0**	7.6
Std.Dev.	1.3	3.6	0.9	2.6

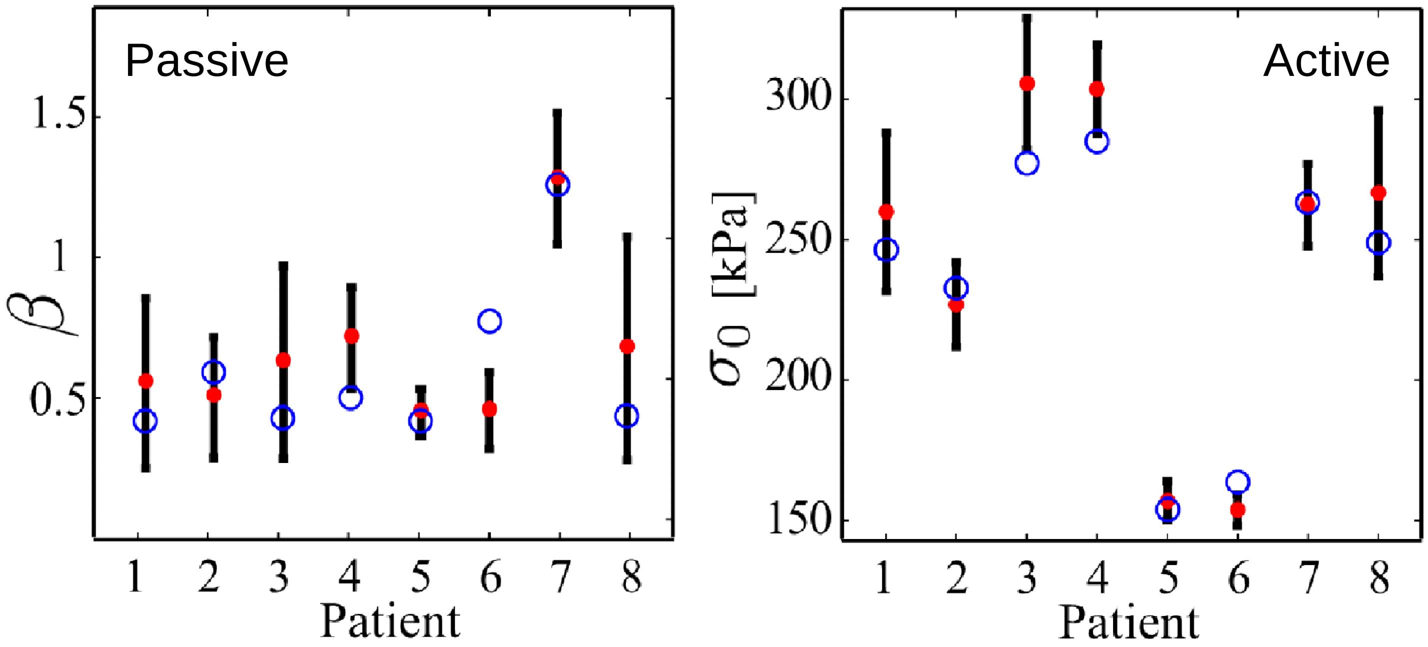
Comparison to state-of-the-art based on BOBYQA *(Powell, 2009)*

$$\arg\min_{\boldsymbol{\theta}} = \|\boldsymbol{d}^{\mathrm{c}} - \boldsymbol{d}^{\mathrm{m}}\|_2^2$$

➔ Results equivalent to deterministic method

Estimated Model Uncertainty

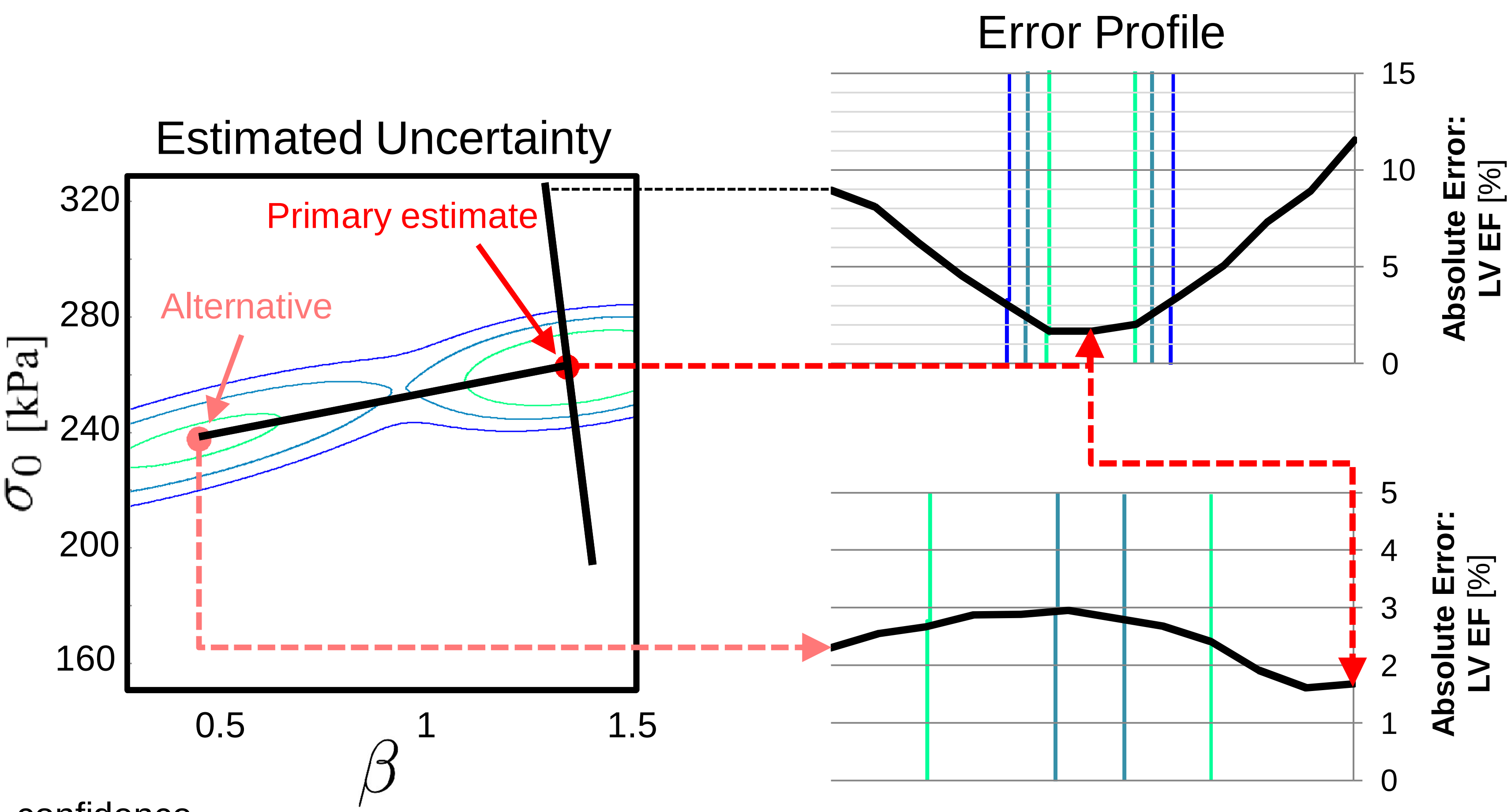
Confidence interval as indicator of uncertainty



- Robust estimates *(proposed solution)*
- Confidence intervals *(95%)*
- Inverse optimization *(single estimate)*

➔ Impact of noise can vary greatly between patients depending on physiology

Empirical Evaluation of Uncertainty



80% confidence
95% confidence
99% confidence

➔ Solution non-uniqueness identified automatically
➔ Promising results towards validation of uncertainty

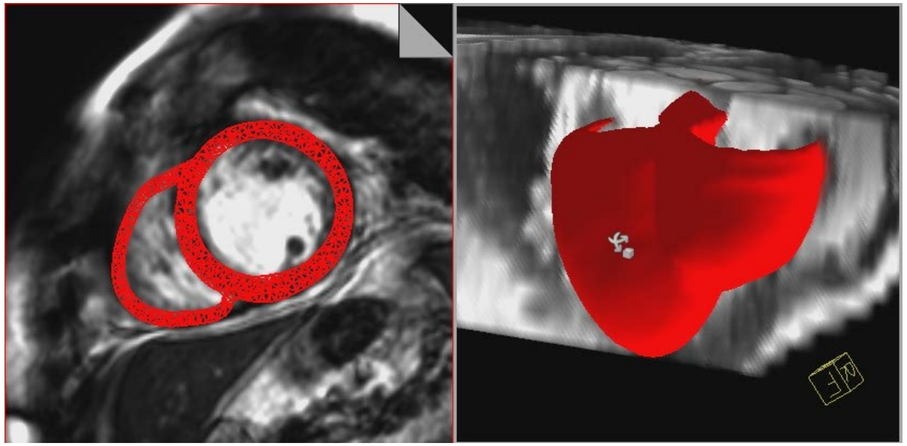
Summary & Conclusion

Model **personalization with uncertainty**

- Bayesian calibration, PCE surrogate
- Robust to unknown level of data noise

Cardiac tissue parameter estimation

- As **effective** as deterministic method
- Solution **non-uniqueness** automatically identified



Perspectives

- Estimate more parameters
- Independent modeling of data and model errors
- Theoretical considerations *(PCE surrogate, GMM aggregation, …)*

Han et al., PAMI'08; Blanchard et al., J Dyn Sys'10; Adams et al., Tech Rep'13; Bozdogan., Psychometrika'87; …

Thank you for your attention.

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