Multiscale-in-Time Modeling of Myocardial Growth & Disease Progression

FEniCS conference

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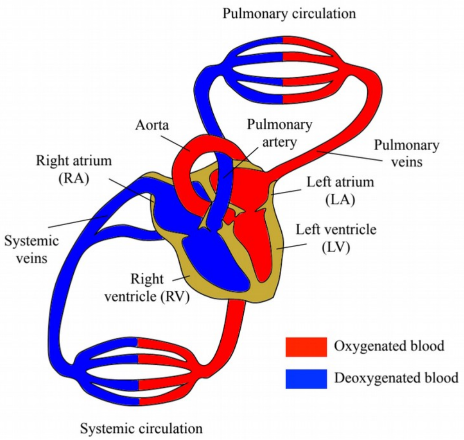
Outline

1.1 Heart Models and the Cardiac Cycle

- **Cardiovascular disease entities** most prevalent in industrialized world [Dimmeler 2011, Luepker 2011]

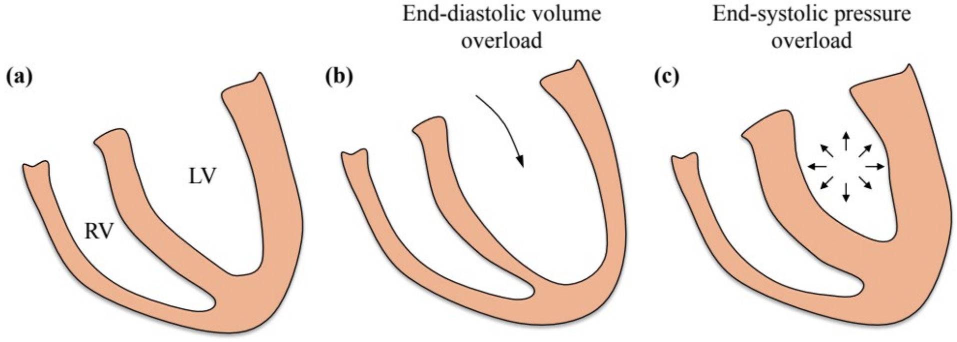


- Diseases of the myocardium (heart muscle) are multifactorial and yet to be fully understood
  - ➢ Altered **mechanical loads**
  - ➢ **Neurohormonal changes**

- Heart may undergo **adaptations in structure and shape** if loading conditions are chronically above a certain physiological level, referred to as **Growth and Remodeling** (G & R) [Rossi et al. 1991]

- **Volume overload** (Fig. (b)):
  - ➢ Heart adapts by **eccentric growth** (systolic heart failure)

- **Pressure overload** (Fig. (c)):
  - ➢ Heart adapts by **concentric growth** (diastolic heart failure)



Healthy heart

Eccentric growth after volume overload

Concentric growth after pressure overload

Outline

2.1 Patient-specific Geometric 3D-0D Heart Model

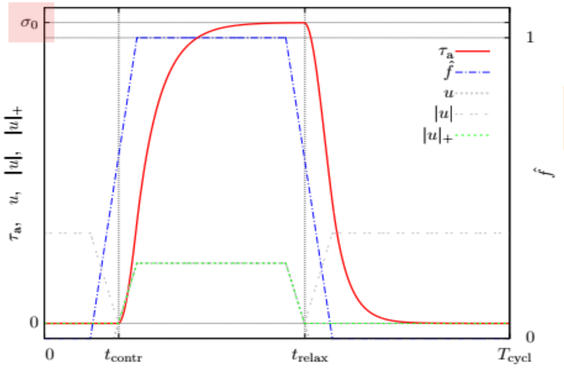
- **Heart muscle:** Nonlinear nearly-incompressible hyperelastic, anisotropic solid [Guccione et al. 1991]

$$\boldsymbol{S} = 2\frac{\partial \Psi}{\partial \boldsymbol{C}} + \tau_{\mathrm{a}}(t)\boldsymbol{f}_0 \otimes \boldsymbol{f}_0 \qquad \Psi = \frac{C_0}{2}e^{Q} + \frac{\kappa}{2}(J-1)^2 \qquad Q = b_f E_{ff}^2 + b_{\mathrm{t}}\left(E_{ss}^2 + E_{nn}^2 + 2E_{sn}^2\right) + b_{fs}\left(2E_{fs}^2 + 2E_{fn}^2\right)$$

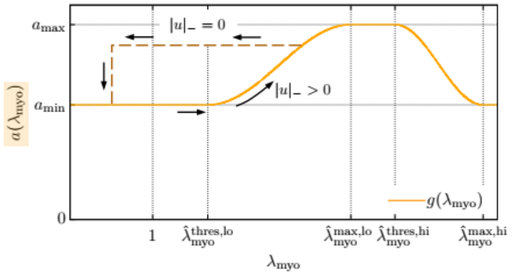
- **Contraction:** Time- and fiber stretch-dependent active stress law [Bestel et al. 2001]

$$\dot{\tau}_{\mathrm{a}} = -|u|\tau_{\mathrm{a}} + a\,\sigma_0|u|_+ \qquad \dot{a}(\lambda_{\mathrm{myo}}) = \dot{g}(\lambda_{\mathrm{myo}})\,\mathbb{I}_{|u|_->0}$$

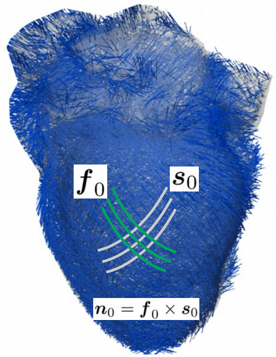
$$u = \hat{f}(t)\cdot\alpha_{\max} + (1-\hat{f}(t))\cdot\alpha_{\min}$$



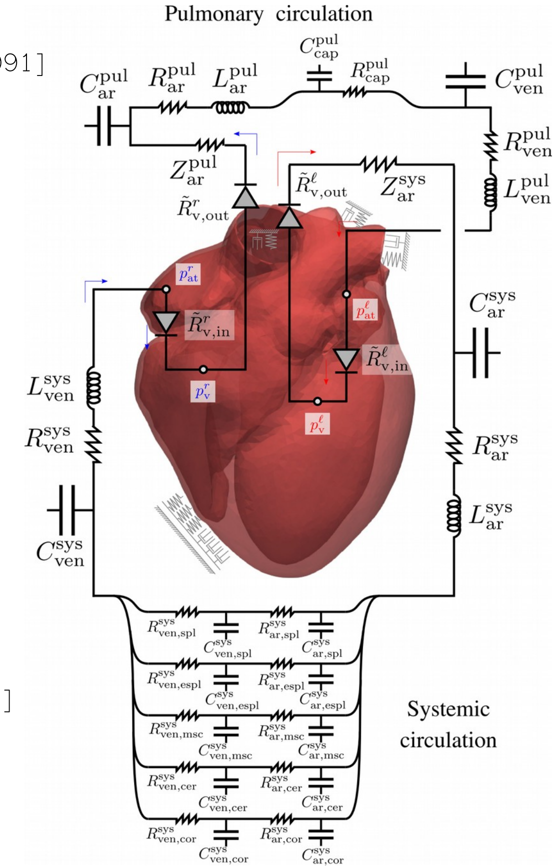
Frank-Starling mechanism [Solaro 2007]



$$\lambda_{\mathrm{myo}} = \sqrt{\boldsymbol{f}_0 \cdot \boldsymbol{C}\boldsymbol{f}_0}$$



Rule-based fiber directions
Transmural variation (-60°, 60°)
[Doste et al. 2019, Bayer et al. 2012]



Free heart STL geometry from https://www.icmm.ru/tomogram-to-fem

- **Circulatory system** is modeled with a lumped-parameter 0D flow model (compliances, resistances inertances) [Hirschvogel et al. 2017, Trenhago et al. 2016, Ursino and Magosso 2000a,b]

2.2 Continuum Mechanical Modeling of G&R

- G&R computed in a **kinematic growth framework** with multiplicative split of deformation gradient into elastic and inelastic (growth) part [Lee et al. 1969, Rodriguez et al. 1994]

$$\boldsymbol{F} = \boldsymbol{F}^{\mathrm{e}}\boldsymbol{F}^{\mathrm{g}}$$

- Growth deformation gradient is function of growth stretch ϑ and possibly of preferred directions $\boldsymbol{f}_0$:

$$\boldsymbol{F}^{\mathrm{g}} = f(\vartheta, \boldsymbol{f}_0, ...)$$

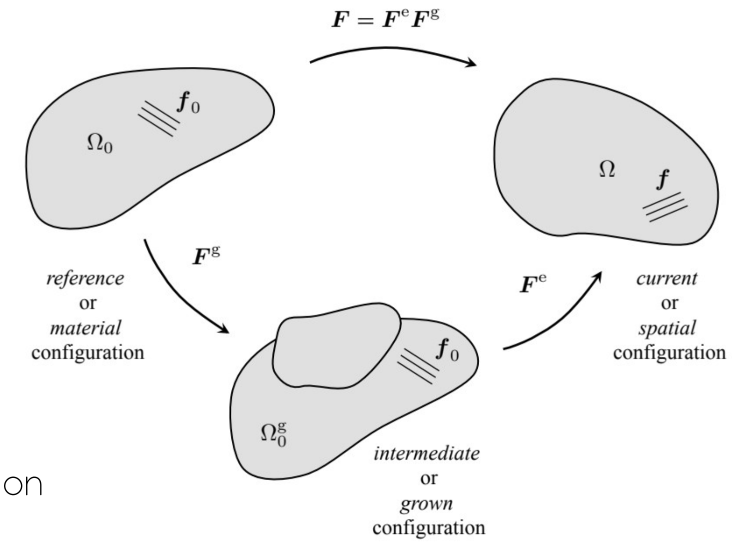
- Growth stretch usually is governed by an evolution equation and can depend on mechanical or other stimuli:

$$\dot{\vartheta} = f(\vartheta, \boldsymbol{C}, \boldsymbol{S}, \boldsymbol{f}_0, ...)$$

- **Remodeling** is taken into account by additively decomposing the stress response into a part governing the reference and one describing the remodeled material (similar to [Thon et al. 2018]):

$$\boldsymbol{S} = \phi(\vartheta)\boldsymbol{S}_{(\mathrm{remod})} + (1-\phi(\vartheta))\boldsymbol{S}_{(\mathrm{base})}$$

$\phi(\vartheta)$: Fraction of grown material



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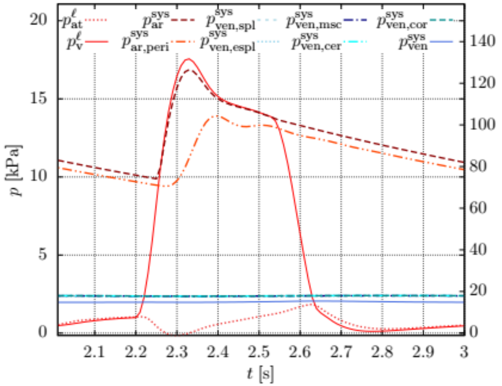
3.1 3D-0D Coupled Elastodynamics

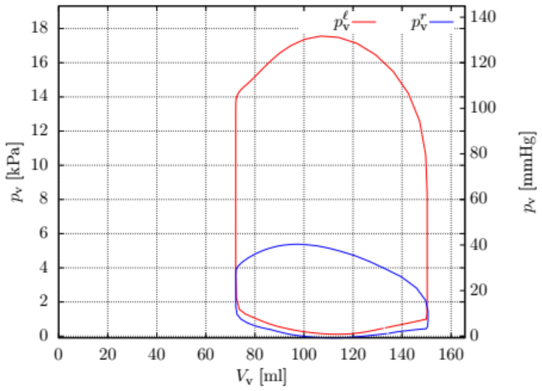
- **Nonlinear elastodynamics** using Generalized-alpha time integration [Chung and Hulbert 1993]
- Strongly coupled 3D-0D monolithic solution of **solid mechanics** and **lumped flow models** [Hirschvogel et al. 2017]
- Use of direct solver (SuperLU) or block-pre-conditioned GMRES [Elman et al. 2008]

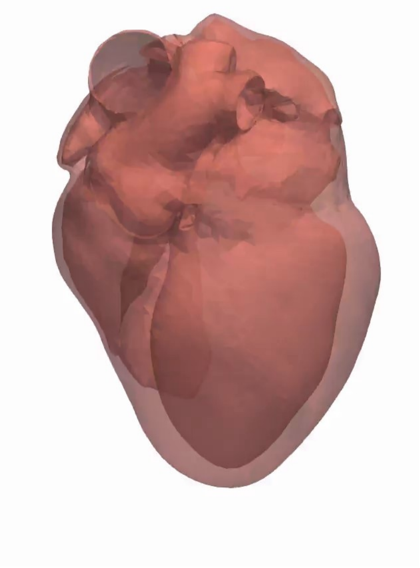
$$\begin{bmatrix} \mathbf{K}^{uu} & \mathbf{K}^{us} \\ \mathbf{K}^{su} & \mathbf{K}^{ss} \end{bmatrix}_{n+1}^{i} \begin{bmatrix} \Delta\mathbf{d} \\ \Delta\mathbf{s} \end{bmatrix}_{n+1}^{i+1} = - \begin{bmatrix} \mathbf{r}^{u} \\ \mathbf{r}^{s} \end{bmatrix}_{n+1}^{i}$$

- ~90'000 linear displacement-based tetrahedral elements, ~60'000 unknowns

  ➢ Example healthy heart cycle simulation:







Open-source Python FEniCS-based solver for cardiac mechanics
https://github.com/marchirschvogel/ambit

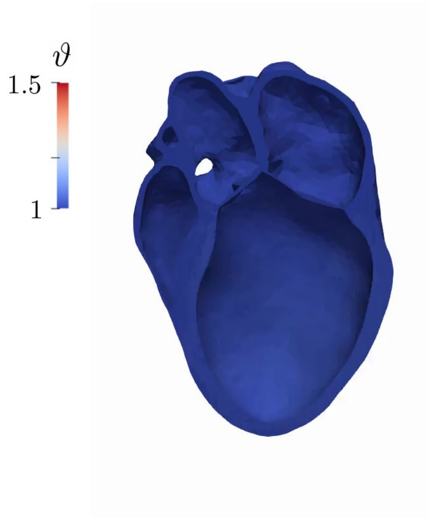
3.2 Inelastic Deformation-Dependent Growth & Remodeling

- Fiber stretch-driven **anisotropic growth** in fiber direction

$$\boldsymbol{F}^{\mathrm{g}} = \boldsymbol{1} + (\vartheta - 1)\boldsymbol{f}_0 \otimes \boldsymbol{f}_0 \qquad \dot{\vartheta} = k(\vartheta)\left(\lambda_{\mathrm{myo}}^{\mathrm{e}} - \hat{\lambda}_{\mathrm{myo}}^{\mathrm{crit}}\right)$$

$$k(\vartheta) = \begin{cases} \frac{1}{\tau}\left(\frac{\vartheta_{\max}-\vartheta}{\vartheta_{\max}-\vartheta_{\min}}\right)^{\gamma}, & \lambda_{\mathrm{myo}}^{\mathrm{e}} \geq \hat{\lambda}_{\mathrm{myo}}^{\mathrm{crit}}, \\ \frac{1}{\tau_{\mathrm{rev}}}\left(\frac{\vartheta-\vartheta_{\min}}{\vartheta_{\max}-\vartheta_{\min}}\right)^{\gamma_{\mathrm{rev}}}, & \lambda_{\mathrm{myo}}^{\mathrm{e}} < \hat{\lambda}_{\mathrm{myo}}^{\mathrm{crit}}, \end{cases}$$

$$\lambda_{\mathrm{myo}}^{\mathrm{e}} = \frac{1}{\vartheta}\lambda_{\mathrm{myo}} = \frac{1}{\vartheta}\sqrt{\boldsymbol{f}_0 \cdot \boldsymbol{C}\boldsymbol{f}_0}$$



- Stress in inner virtual work depending on deformation and internal variable ϑ, which is deformation-dependent itself in a nonlinear way (needs local Newton to solve)

$$\delta\mathcal{W}_{\mathrm{int}} = \int\limits_{\Omega_0} \boldsymbol{S}(\boldsymbol{C}(\boldsymbol{u}), \vartheta(\boldsymbol{C}(\boldsymbol{u}))) : \frac{1}{2}\delta\boldsymbol{C}\,\mathrm{d}V$$

- Full material tangent operator reads: $\mathbb{C} = 2\frac{\partial \boldsymbol{S}}{\partial \boldsymbol{C}} + 2\left(\frac{\partial \boldsymbol{S}}{\partial \boldsymbol{F}^{\mathrm{g}}} : \frac{\partial \boldsymbol{F}^{\mathrm{g}}}{\partial \vartheta}\right) \otimes \frac{\partial \vartheta}{\partial \boldsymbol{C}}$

  ➢ FEniCS UFL can only take care of first term, since no analytic expression $\vartheta(\boldsymbol{C}) = \ldots$ possible

  ➢ Express virtual work linearization directly as form without using "derivative" and add second term manually to $\mathbb{C}$

$$D_{\Delta\boldsymbol{u}}\delta\mathcal{W}_{\mathrm{int}} = \int\limits_{\Omega_0} \left(\mathrm{Grad}\delta\boldsymbol{u} : \mathrm{Grad}\Delta\boldsymbol{u}\,\boldsymbol{S} + \boldsymbol{F}^{\mathrm{T}}\mathrm{Grad}\delta\boldsymbol{u} : \mathbb{C} : \boldsymbol{F}^{\mathrm{T}}\mathrm{Grad}\Delta\boldsymbol{u}\right)\mathrm{d}V$$

$$\frac{\partial \boldsymbol{S}}{\partial \boldsymbol{F}^{\mathrm{g}}} = -\left(\boldsymbol{F}^{\mathrm{g}^{-1}} \overline{\otimes} \boldsymbol{S} + \boldsymbol{S} \underline{\otimes} \boldsymbol{F}^{\mathrm{g}^{-1}}\right) - \left(\boldsymbol{F}^{\mathrm{g}^{-1}} \overline{\otimes} \boldsymbol{F}^{\mathrm{g}^{-1}}\right) : \frac{1}{2}\check{\mathbb{C}}^{\mathrm{e}} : \left(\boldsymbol{F}^{\mathrm{g}^{-\mathrm{T}}} \overline{\otimes} \boldsymbol{C}^{\mathrm{e}} + \boldsymbol{C}^{\mathrm{e}} \underline{\otimes} \boldsymbol{F}^{\mathrm{g}^{-\mathrm{T}}}\right)$$

Elastic part of $2\frac{\partial \boldsymbol{S}}{\partial \boldsymbol{C}}$

  ➢ Depending on growth law, can render excessive FFC-X compilation times! (between 5 and 30 minutes!)

3.3 Multiscale-in-Time Analysis: Volume Overload and Eccentric Growth in the Heart

- Homeostatic healthy heart beat computation
- Acute disease state (e.g. mitral valve regurgitation) computation, evaluation of **end-diastolic volume overload**
- **Set state "large time scale":**

$$\boldsymbol{u}^{(\mathcal{L})} \leftarrow \boldsymbol{u}(t_{\mathrm{ed}})^{(\mathcal{S})} \qquad \hat{p}_c^{i,(\mathcal{L})} \leftarrow p_c^{i,(\mathcal{S})}(t_{\mathrm{ed}}) \qquad \hat{\tau}_{\mathrm{a}}^{(\mathcal{L})} \leftarrow \tau_{\mathrm{a}}(t_{\mathrm{ed}})^{(\mathcal{S})}$$

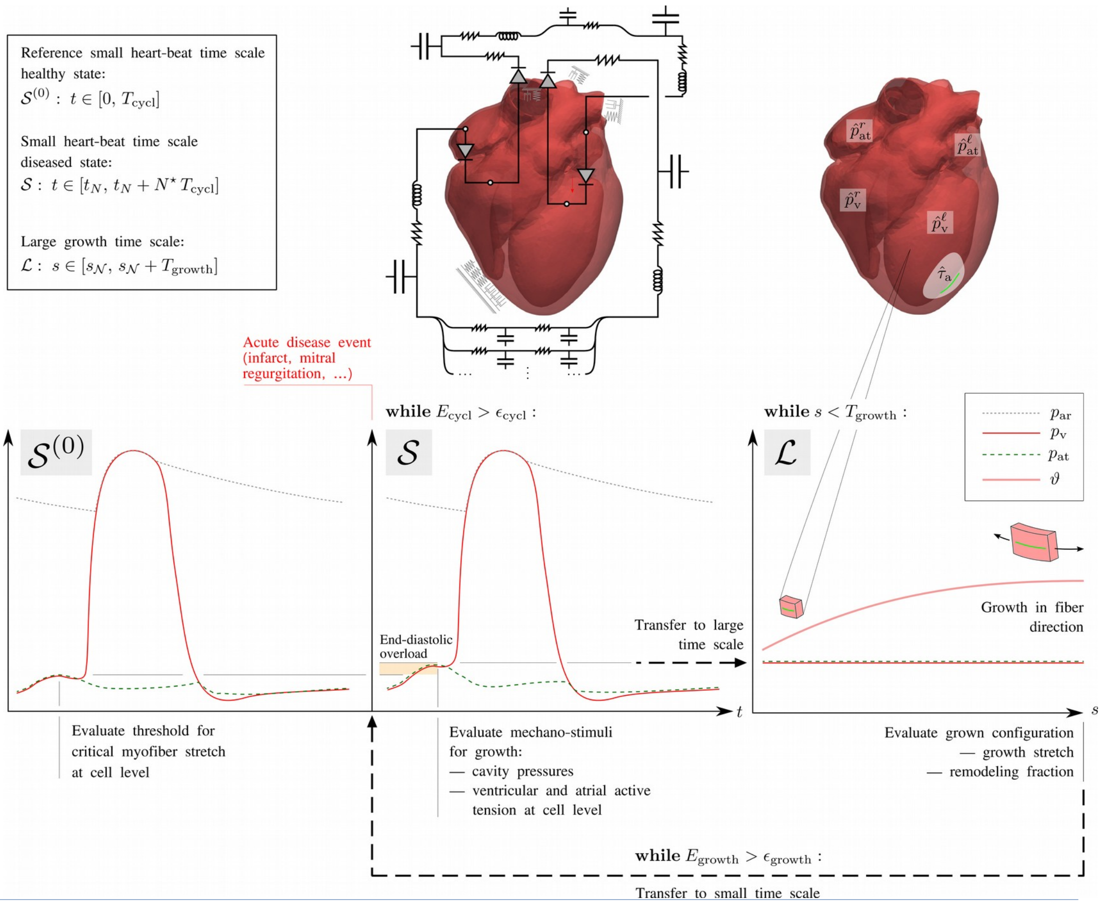
➢ Quasi-static growth computation

- **Set state "small time scale":**

$$\hat{\vartheta}^{(\mathcal{S})} \leftarrow \vartheta^{(\mathcal{L})} \qquad \boldsymbol{u}^{(\mathcal{S})} \leftarrow \boldsymbol{u}^{(\mathcal{L})} - \boldsymbol{u}(t_{\mathrm{ed}})^{(\mathcal{S})}$$

➢ Compute new homeostatic heat beat state

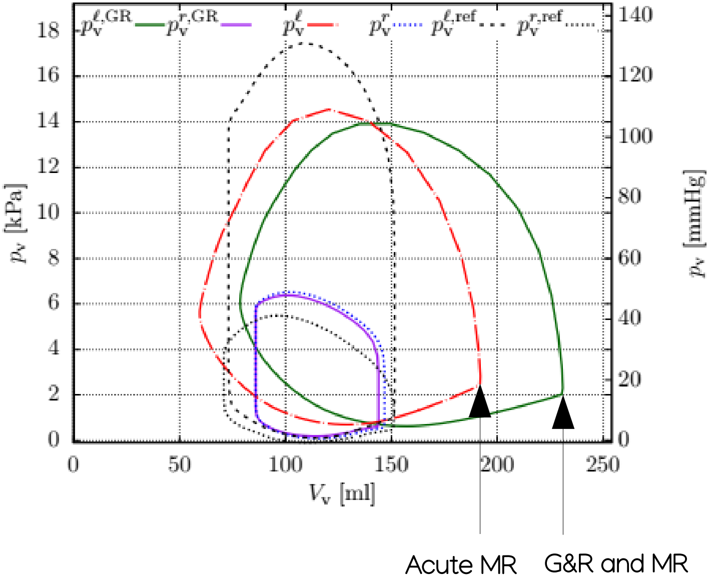
- Mutually revisit small and large scale until growth falls below a certain tolerance

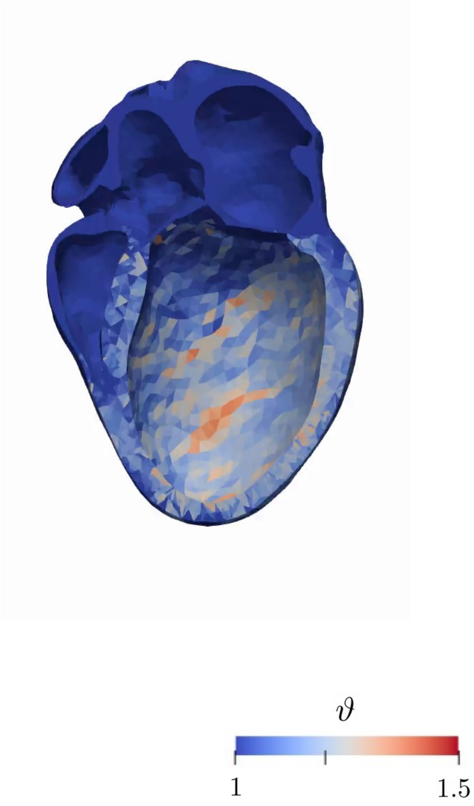


Outline

4.1 Eccentric Growth in the Heart: Results for Mitral Regurgitation (MR)

- G&R after mitral valve regurgitation
  - ➢ Loss of isovolumetric contraction phases
  - ➢ **Right-shift** of pressure-volume relationship
  - ➢ LV wall thinning
  - **“Heart failure with reduced ejection fraction”**





- **Remodeling**: Assumption that only active material is reduced with growth (cardio-myocytes are elongated, degradation and disruption of fibrillar collagen, impaired contractility [Aurigemma et al. 2006]):

$$\boldsymbol{S}_{(\mathrm{remod})} = 2\frac{\partial \Psi}{\partial \boldsymbol{C}}$$

Outline

5 Summary & Outlook

- Multiphysics and multiscale approach to cardiac growth and remodeling using FeniCS-X
  - 3D-0D coupled nonlinear **elastodynamics** and **reduced-dimensional flow**
  - **Inelastic deformation-dependent growth** solved at integration point level
- Physiological results and growth patterns, but …
  - Need of fine-tuning to match experimental data
- Need for **higher-order spatial approximation** to avoid spurious effects of low-order finite elements, but …
  - Missing Quadrature function spaces in FEniCS-X! For linear elements with one integration point (CG1), growth material is specified as discontinuous DG0 function pace
  - No quadratic convergence for growth material living on DG1 space for higher-order mesh (CG2)
- Need for strategies of reducing FFC-X compiler times for complex constitutive UFL expressions

Thank you for your attention!

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