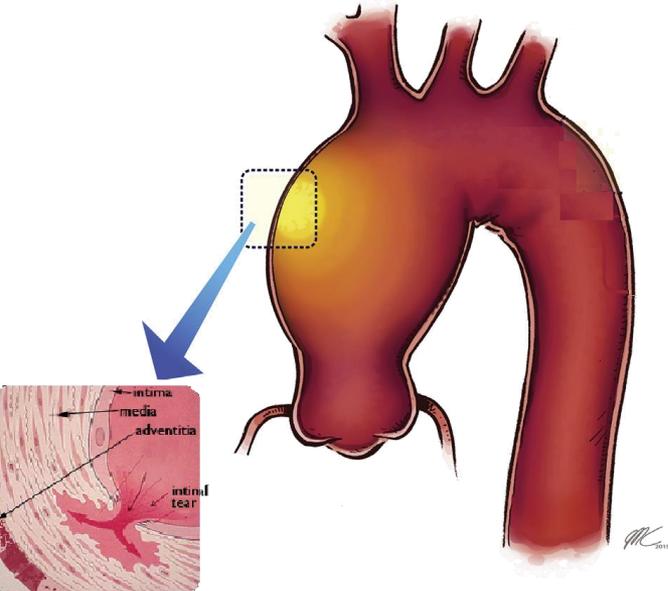
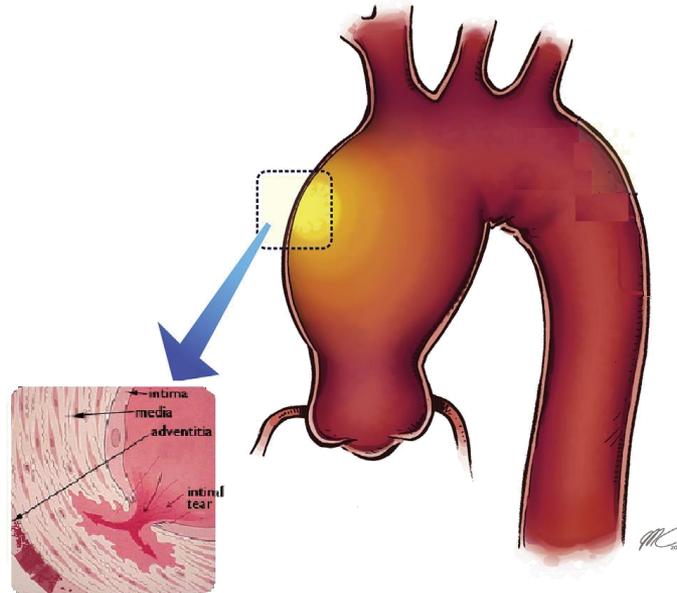
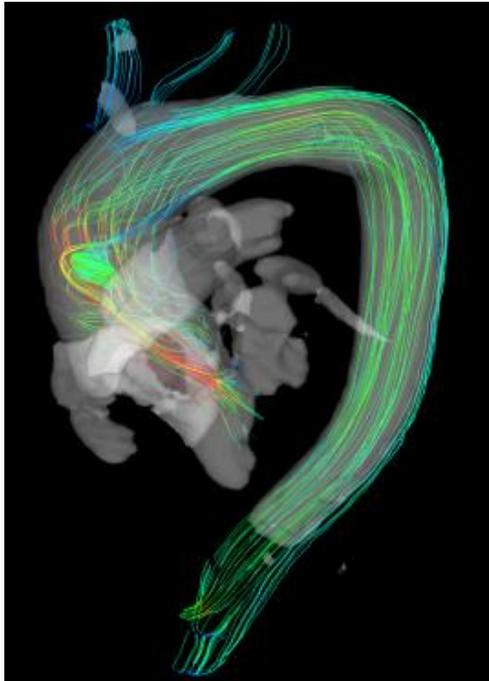


Prevention and treatment of aortic aneurysms using computational biomechanics combined with cell mechanobiology

Prof Stéphane AVRIL



Aneurysms and Dissections of the aorta



== Devastating complications!

OUTLINE

- PART I: Industrial applications of continuum mechanics models in cardiovascular medicine
- PART II: Coupling continuum mechanics models and biology to predict aortic aneurysm progression
- PART III: Towards continuum mechanics of tensional homeostasis down to the subcellular level



OUTLINE

- ❑ **PART I: Industrial applications of continuum mechanics models in cardiovascular medicine**
- ❑ PART II: Coupling continuum mechanics models and biology to predict aortic aneurysm progression
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Continuum mechanics can predict health!!

It even enables decisions everyday in healthcare combined with ROM and AI



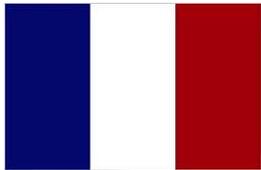
2014: FDA allows marketing of HeartFlow vFFR-CT tool for optimal treatment of coronary stenosis

Gaus S, *et al*, JCCT 2013, 7(5):279-88.



2019: FEops HEARTguide in silico tool for planning transcatheter aortic valve implantation is CE-marked

El Faquir N, *et al* Int J Cardiovasc Img 2019



2014: Sim&Cure

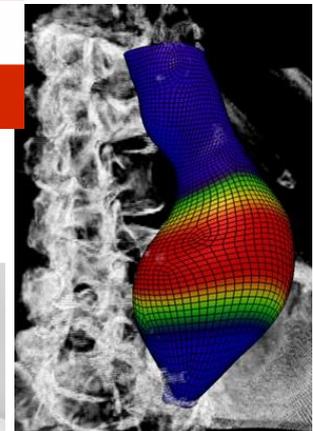


2017: Predisurge

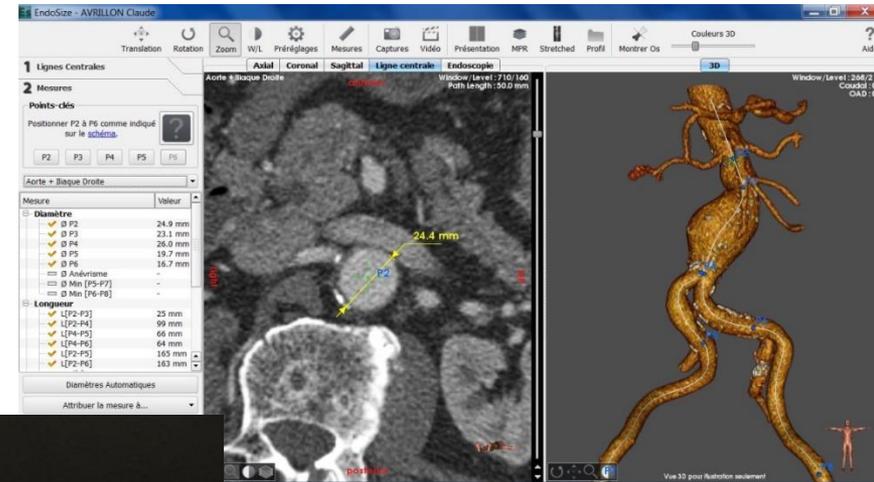
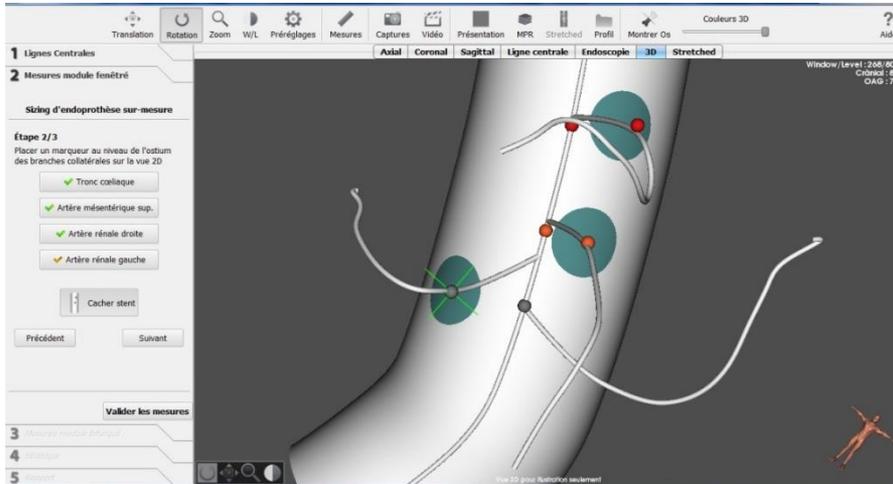
Derycke, *et al* Circulation Img 2021



Vascops



Planification / sizing of fenestrated stent grafts in EVAR procedures



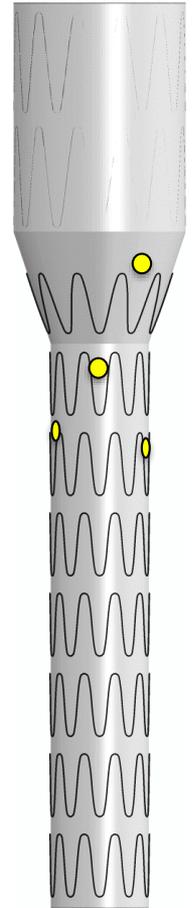
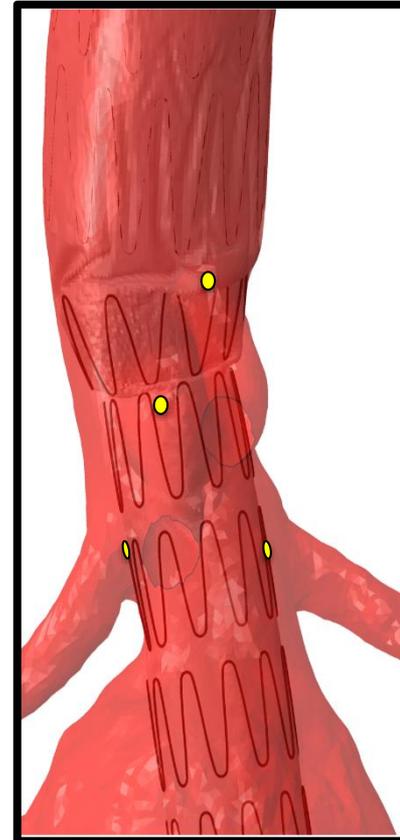
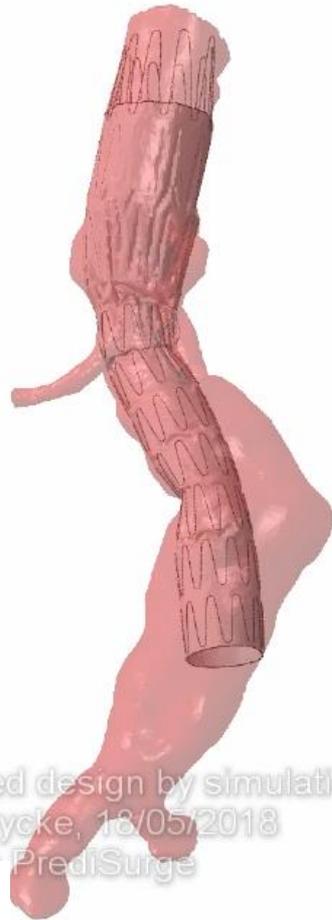
PrediSurge



Clinically validated for FEVAR Zenith® Cook Medical



ALBERT CHENEVIER - JOFFRE-DUPLYTREN
EMILE ROUX - GEORGES CLEMENCEAU



Cook fenestrated design by simulation
Lucie Derycke, 18/05/2018
www.PrediSurge



OPEN QUESTIONS I AM INTERESTED IN

- ❑ Understand and explain the role of mechanics in the progression of cardiovascular diseases
- ❑ Simulate the progression of cardiovascular diseases using patient-specific computational models
- ❑ Develop predictive models of mechano-regulation by vascular cells in arteries



OUTLINE

- PART I: Industrial applications of continuum mechanics models in cardiovascular medicine
- **PART II: Coupling continuum mechanics models and biology to predict aortic aneurysm progression**
- PART III: Towards continuum mechanics of tensional homeostasis down to the subcellular level

From Complexity Comes Simplicity

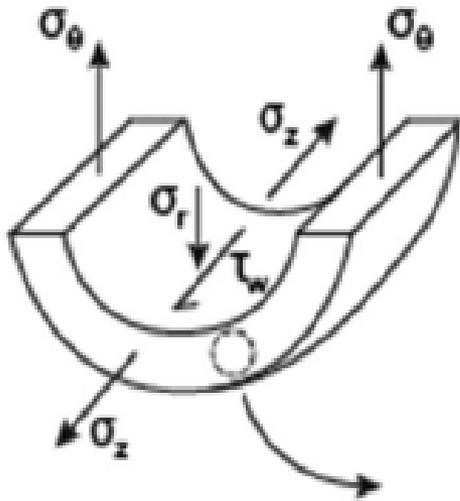
- Nonlinear Material Properties and Large Strain
- Anisotropy (circumferential muscle, axial collagen)
- Residual Stresses
- Smooth Muscle Activation
- Heterogeneity (functionally graded)

→ MECHANOREGULATION

Early Stress Analyses (~1979)

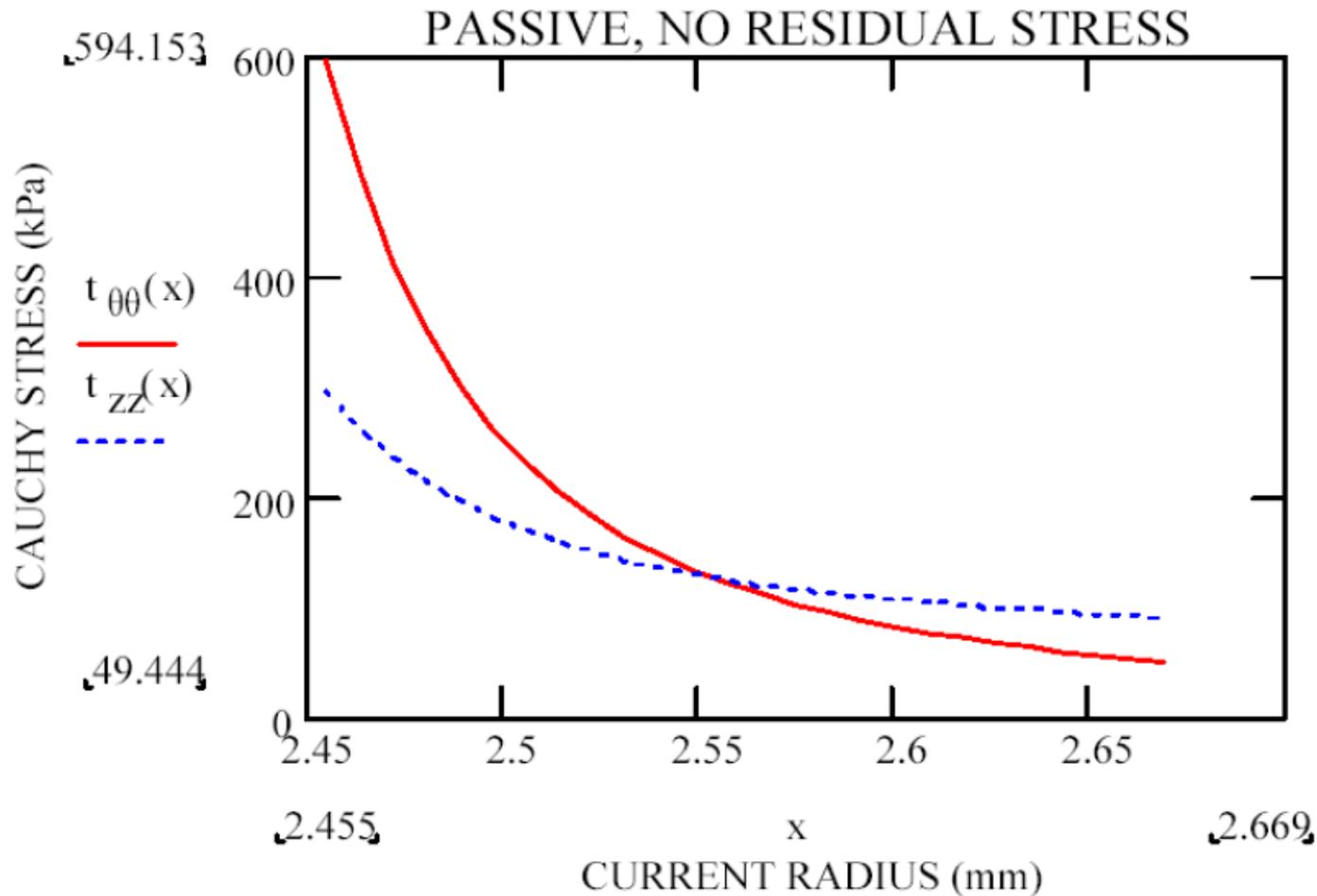
$$\mathbf{t} = -p\mathbf{I} + \frac{1}{2}ce^{\rho} \mathbf{F} \cdot \frac{\partial Q}{\partial \mathbf{E}} \cdot \mathbf{F}^T$$

$$\text{div } \mathbf{t} = 0$$



$$\mathbf{F} = \text{diag} \left[\frac{\partial r}{\partial R}, \frac{r}{R}, \lambda \Lambda \right]$$

Early Stress Analyses (~1979)

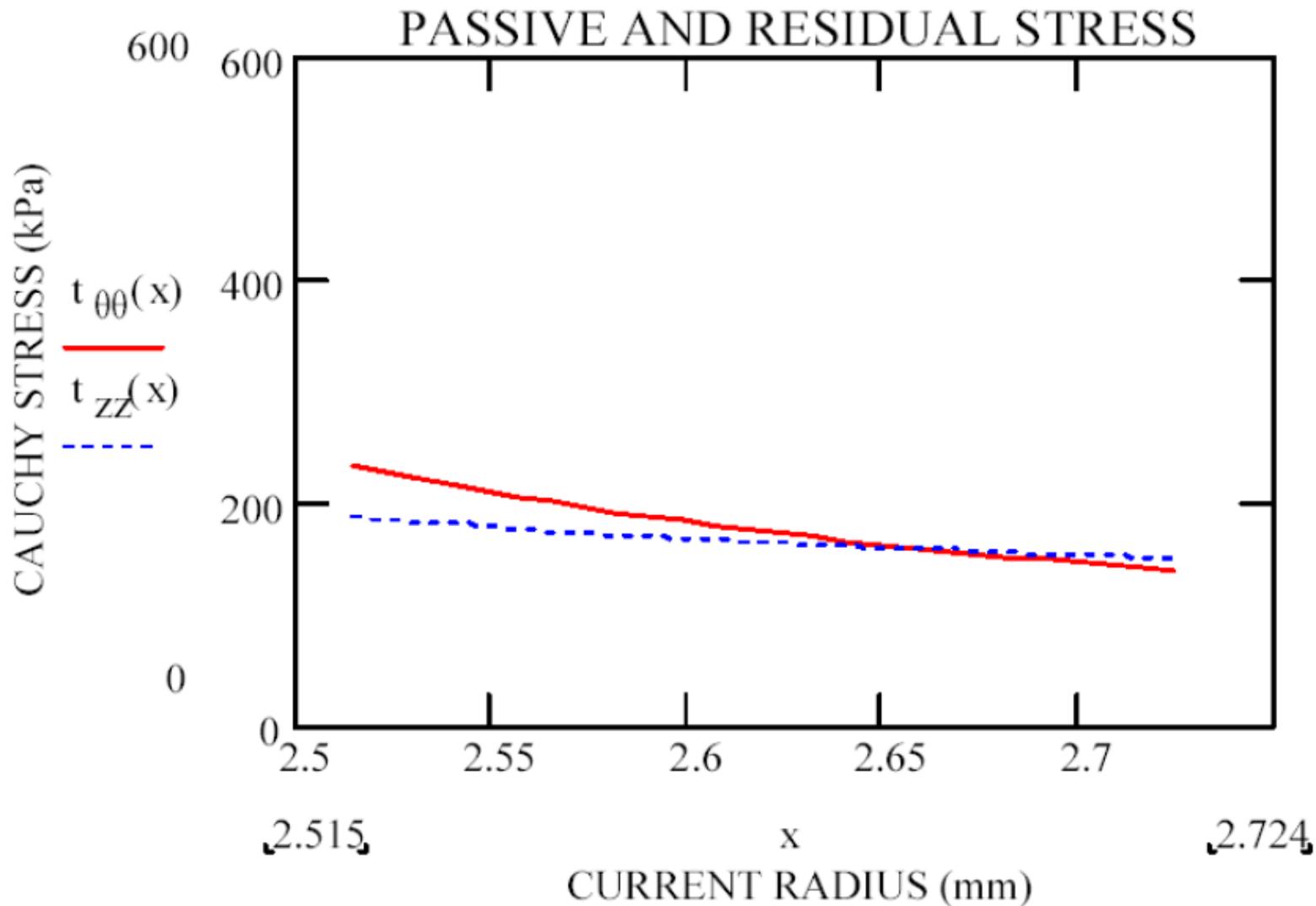


Importance of Residual Stress (~1986)

$$\mathbf{t} = -p\mathbf{I} + \frac{1}{2}ce^{\rho}\mathbf{F} \cdot \frac{\partial Q}{\partial \mathbf{E}} \cdot \mathbf{F}^T \quad \text{div } \mathbf{t} = 0$$

$$\mathbf{F} = \text{diag} \left[\frac{\partial r}{\partial R}, \frac{r}{R}, \dots, \lambda \Lambda \right]$$

Importance of Residual Stress (~1986)

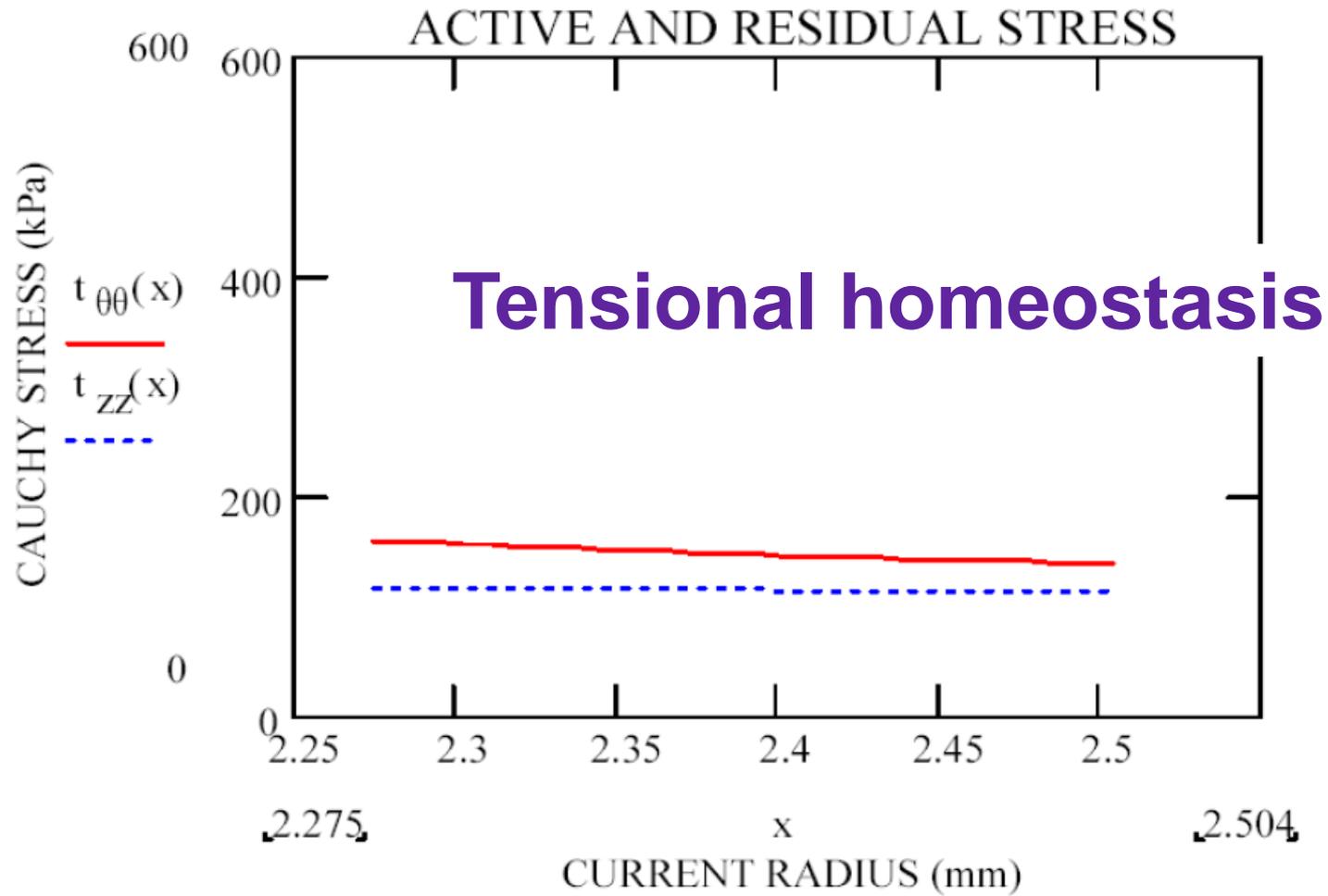


Importance of Smooth Muscle (~1999)

$$\mathbf{t} = -p\mathbf{I} + \frac{1}{2}ce^{\rho}\mathbf{F} \cdot \frac{\partial Q}{\partial \mathbf{E}} \cdot \mathbf{F}^T \quad \text{div } \mathbf{t} = 0$$

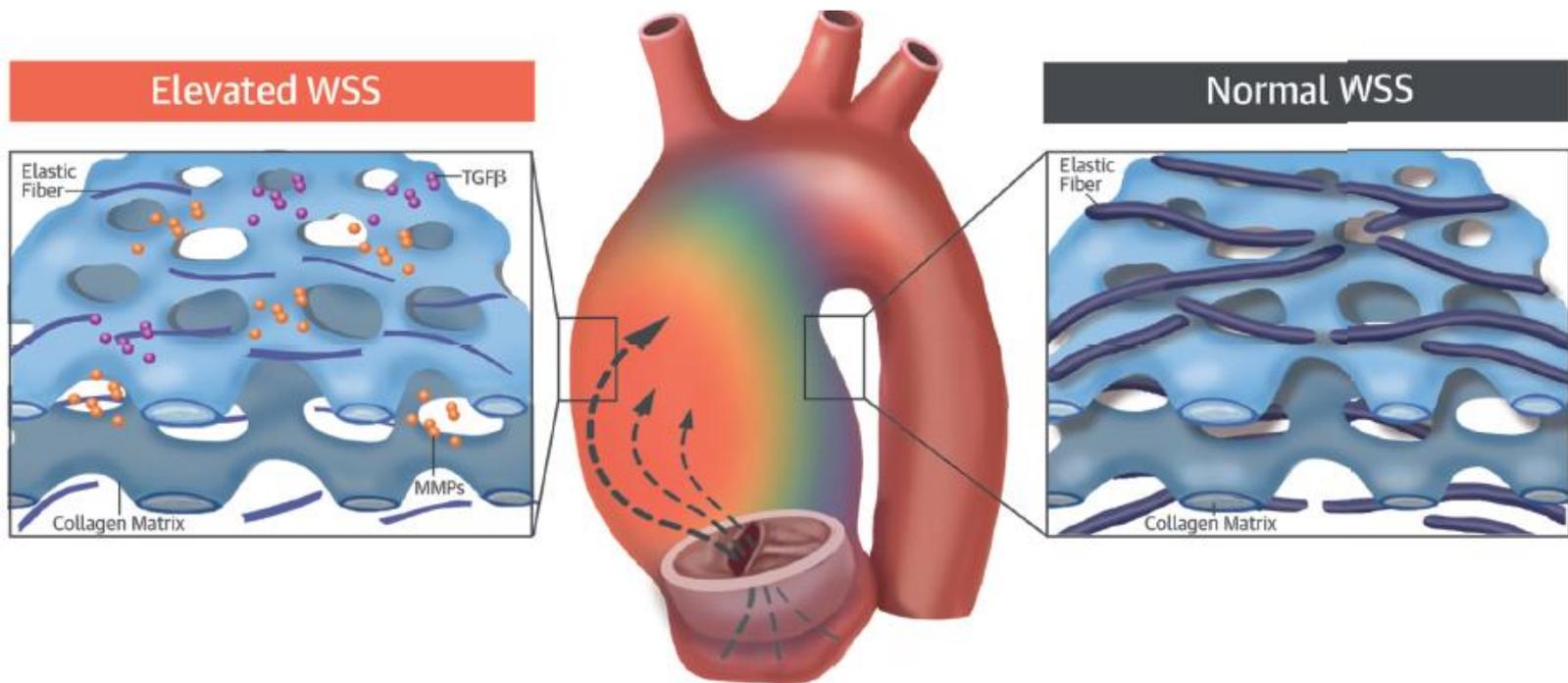
$$\mathbf{F} = \text{diag} \left[\frac{\partial r}{\partial R}, \frac{r\pi}{R\Theta_o}, \lambda\Lambda \right]$$

Importance of Smooth Muscle (~1999)



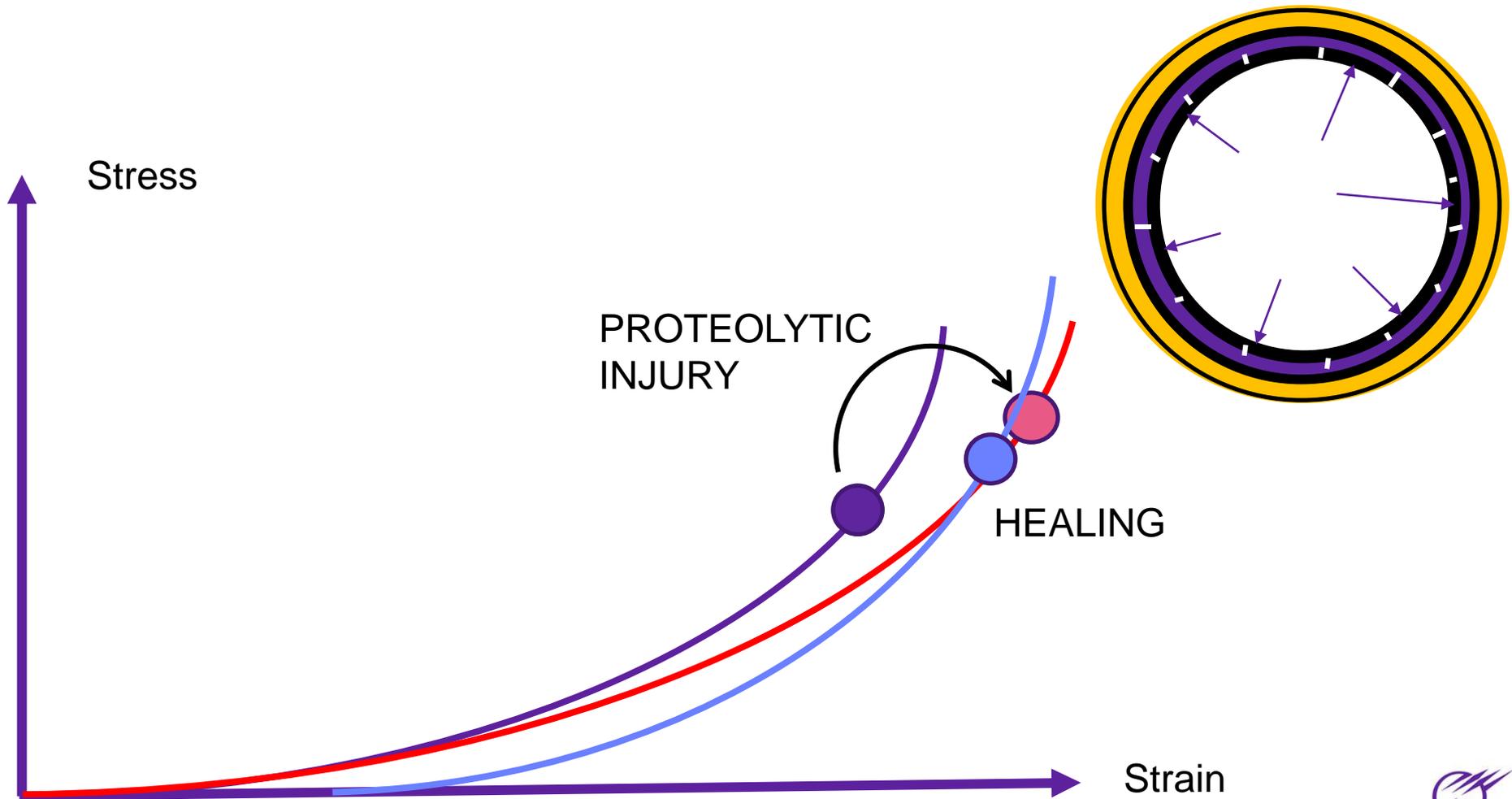
Tensional homeostasis in ATAA?

ATAAs are triggered by local proteolytic injury, which induce adaptation in the ascending thoracic aorta

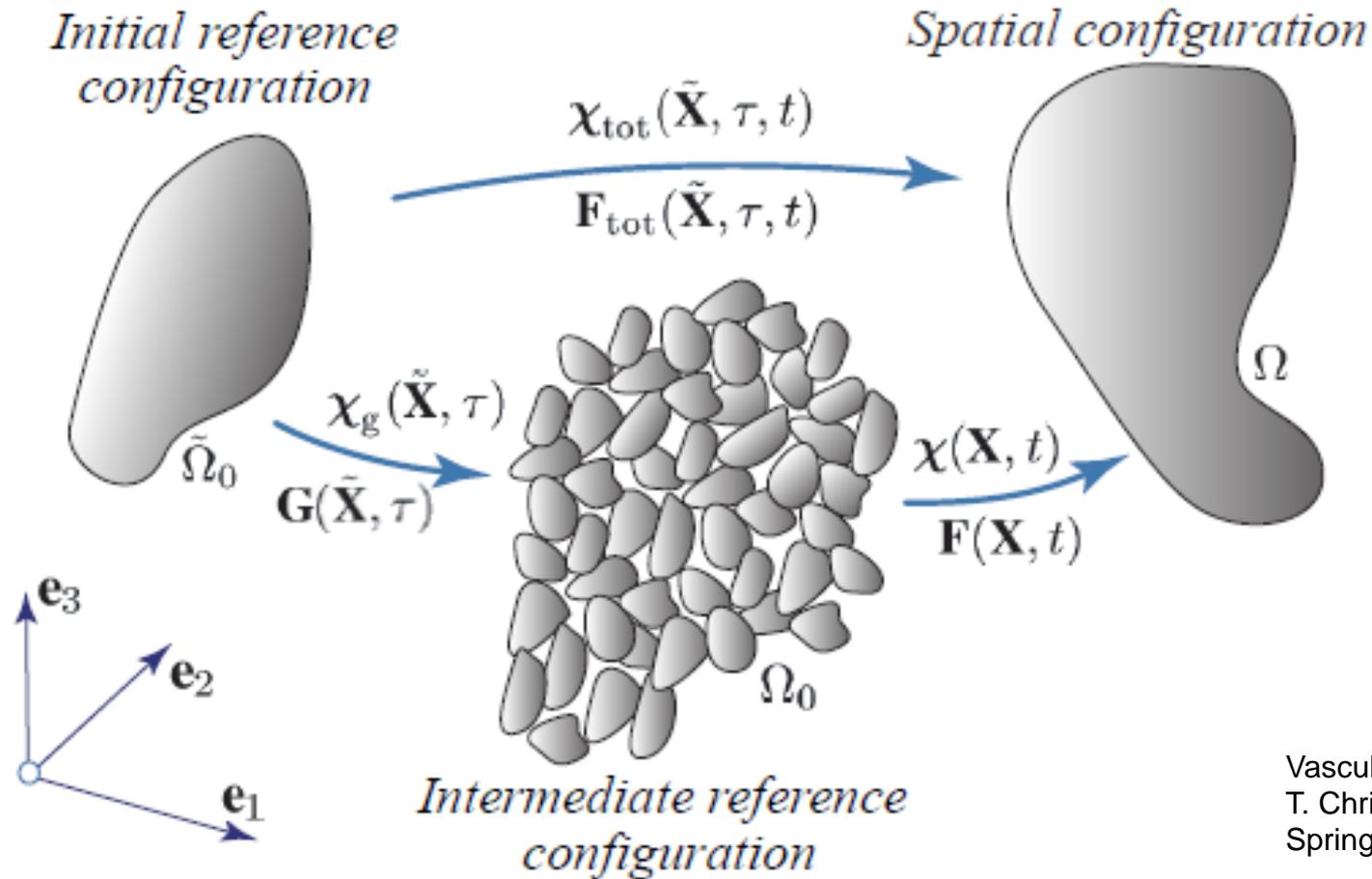


Guzzardi et al, JACC (2014), Condemi et al, IEEE TBME (2019)

Proteolytic injury and tissue adaptation

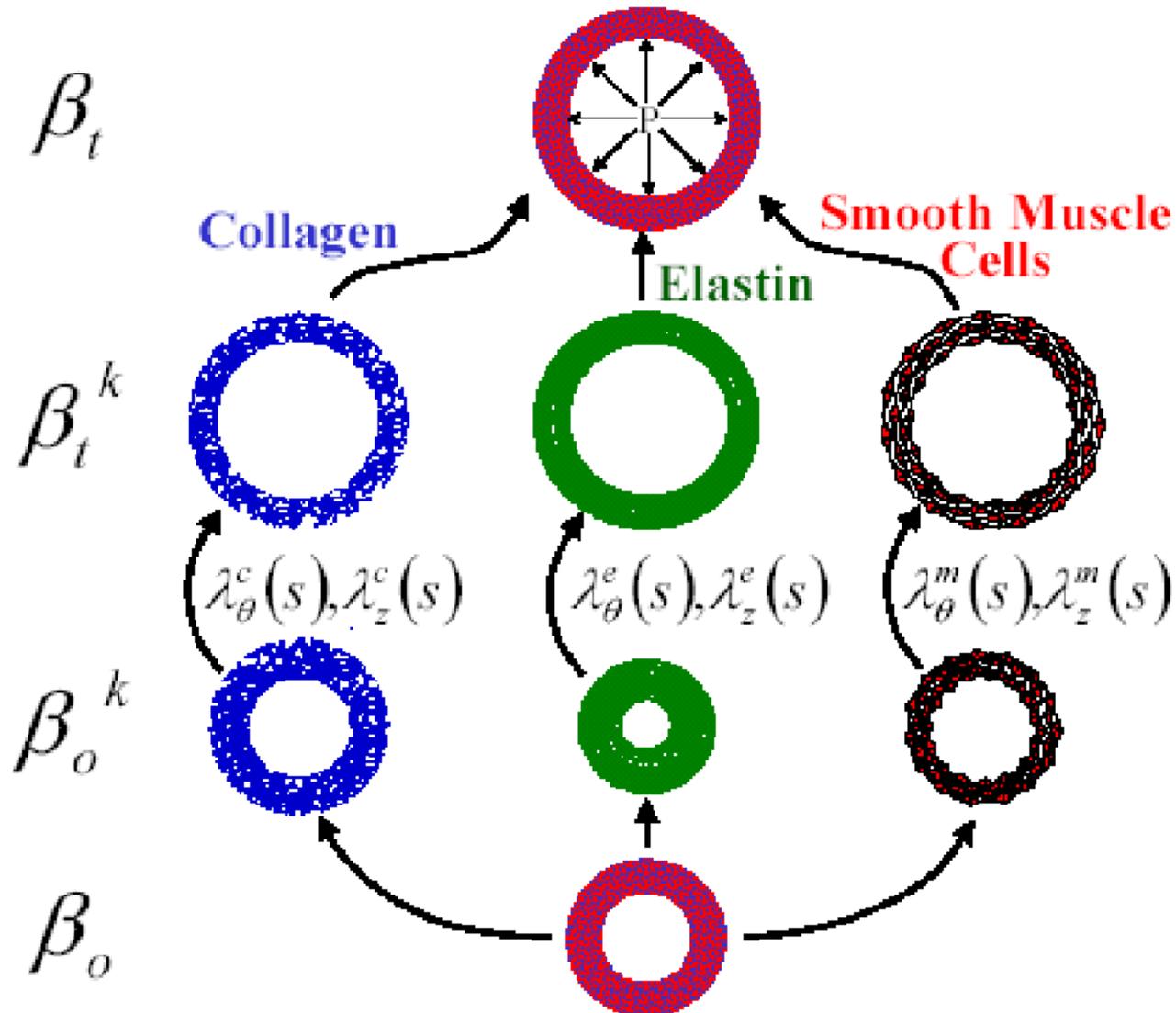


Kinematics-based growth description



Vascular Biomechanics
T. Christian Gasser
Springer

Constrained mixture models



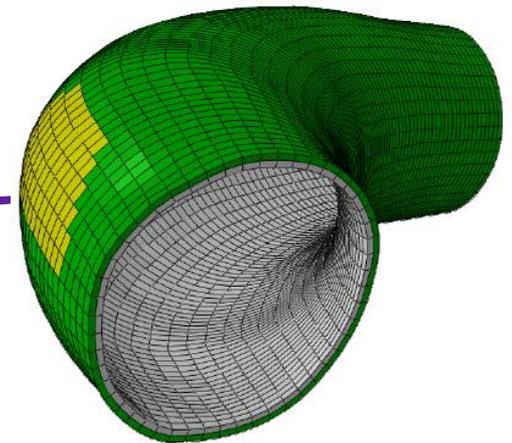
Finite-element simulations

Growth and remodeling of a two-layer patient-specific human ATAAs due to elastin loss

$$W = \varrho_t^e (\bar{W}^e(\bar{I}_1^e) + U(J_{el}^e)) + \sum_{j=1}^n \varrho_t^{c_j} W^{c_j}(I_4^{c_j}) + \varrho_t^m W^m(I_4^m)$$

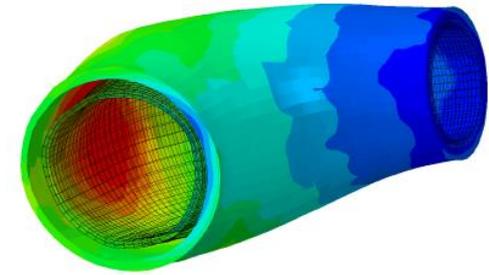
$$\dot{\varrho}^e = -\frac{\varrho^e(\mathbf{X}, t)}{T^e} - \frac{D_{\max}}{t_{\text{dam}}} \varrho^e(\mathbf{X}, 0) e^{-0.5 \left(\frac{X_3}{L_{\text{dam}}} \right)^2 - \frac{t}{t_{\text{dam}}}}$$

**Localization function
around the point of
TAWSS max**



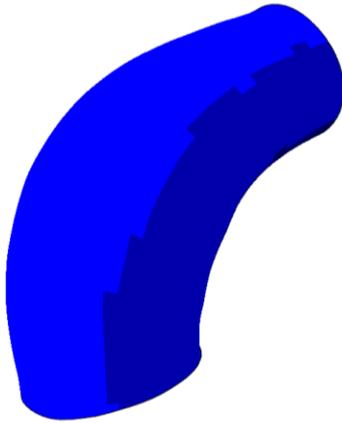
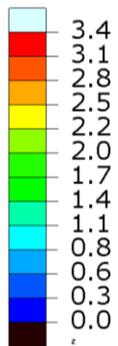
Patient-specific predictions

Growth and remodeling of a two-layer patient-specific human ATAAs due to elastin loss

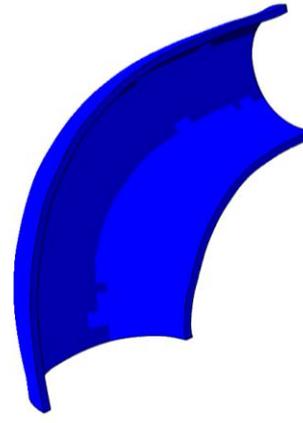
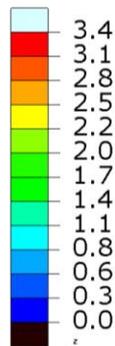


Small growth parameter

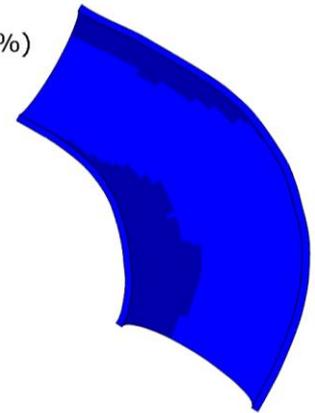
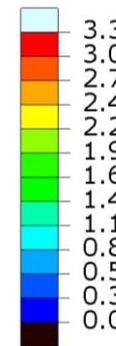
SDV69
(Avg: 75%)



SDV69
(Avg: 75%)



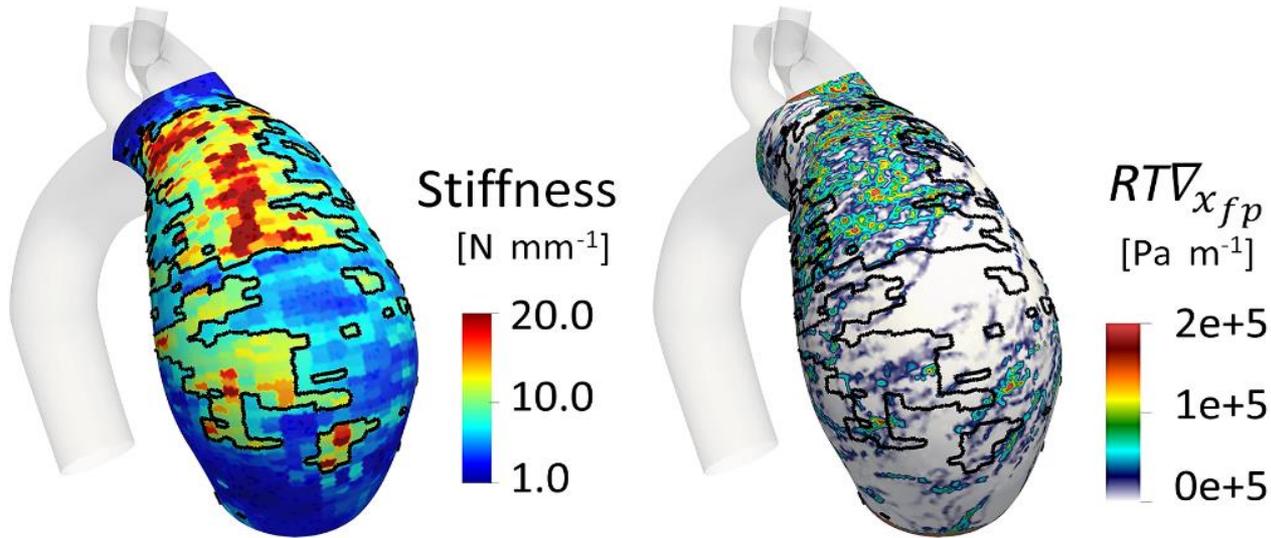
SDV69
(Avg: 75%)



Normalized Thickness

Mousavi et al, BMMB (2019)

Some patients show local stiffness increase correlated with local hemodynamics



De Nisco, G., ... & Morbiducci, U. (2020). Medical Engineering & Physics, 82, 119-129.



POLITECNICO
DI TORINO

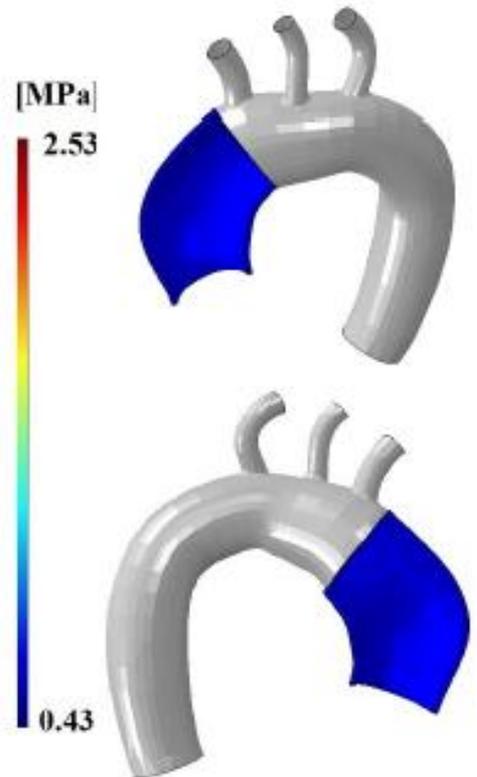


Patient-specific vascular adaptation

$$\dot{q}^j(t) = q^j(t) k_{\sigma}^j \frac{\sigma^j(t) - \chi * \sigma_h^j}{\chi * \sigma_h^j}$$

$$\chi = 1$$

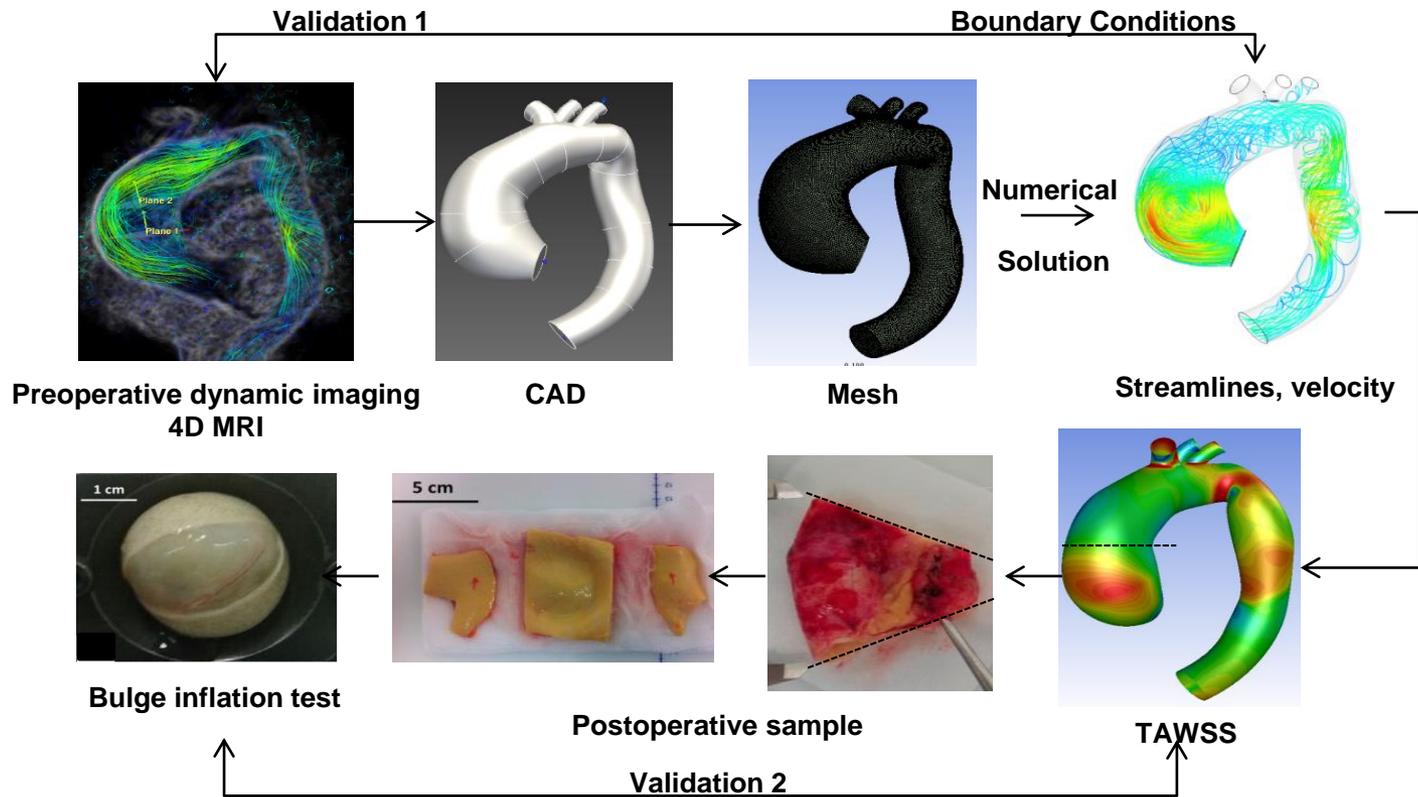
Tangent stiffness
after
10 years



$$\dot{q}^j(t) = q^j(t) k_{\sigma}^j \frac{\sigma^j(t) - \chi * \sigma_h^j}{\chi * \sigma_h^j}$$

TOWARDS INDUSTRIAL APPLICATIONS: AUGMENTED MEDICAL IMAGING

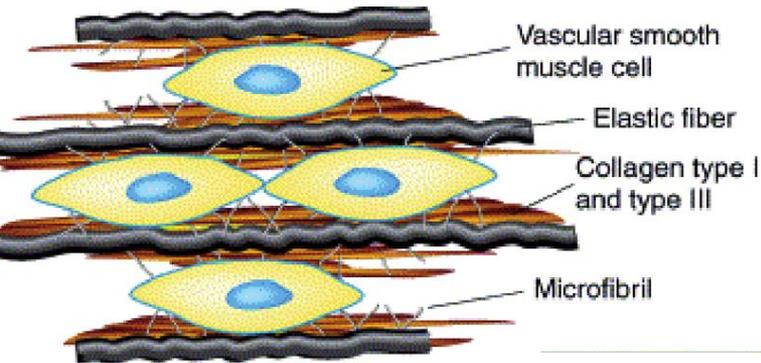
The maintenance of tensional homeostasis in the tissue is critical but also patient-specific



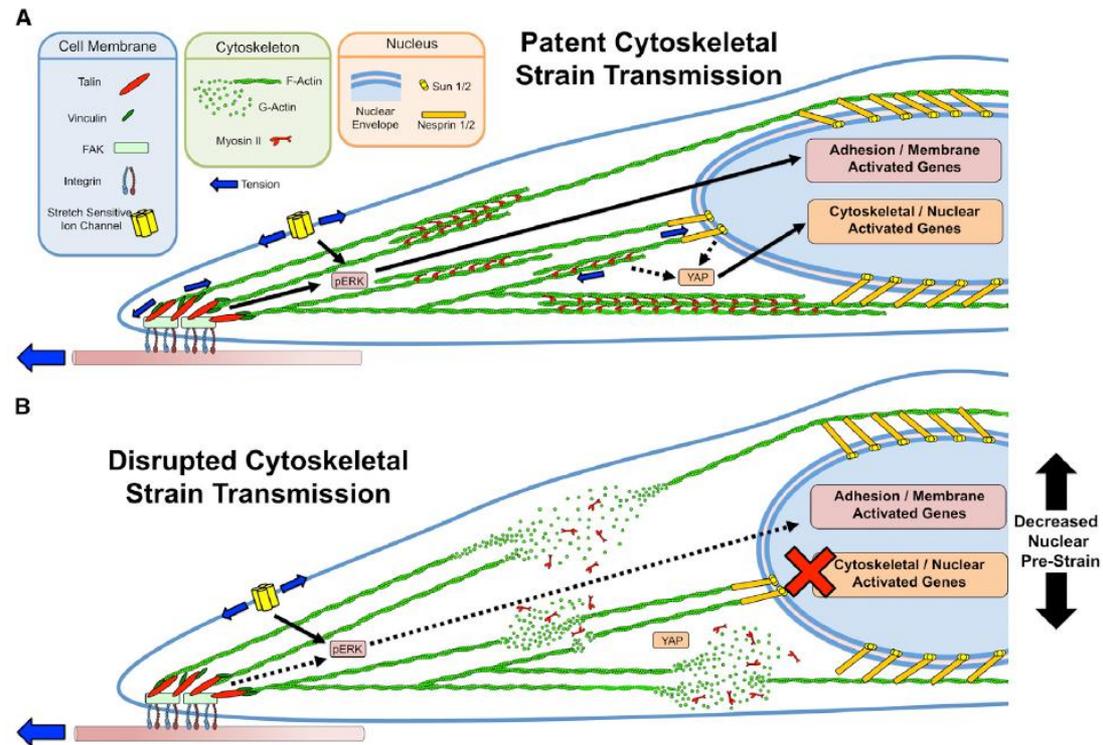
OUTLINE

- PART I: Industrial applications of continuum mechanics models in cardiovascular medicine
- PART II: The need of combining data driven and continuum mechanics models in cardiovascular mechanobiology
- **PART III: Towards continuum mechanics of tensional homeostasis down to the subcellular level**

Introduction to mechanobiology

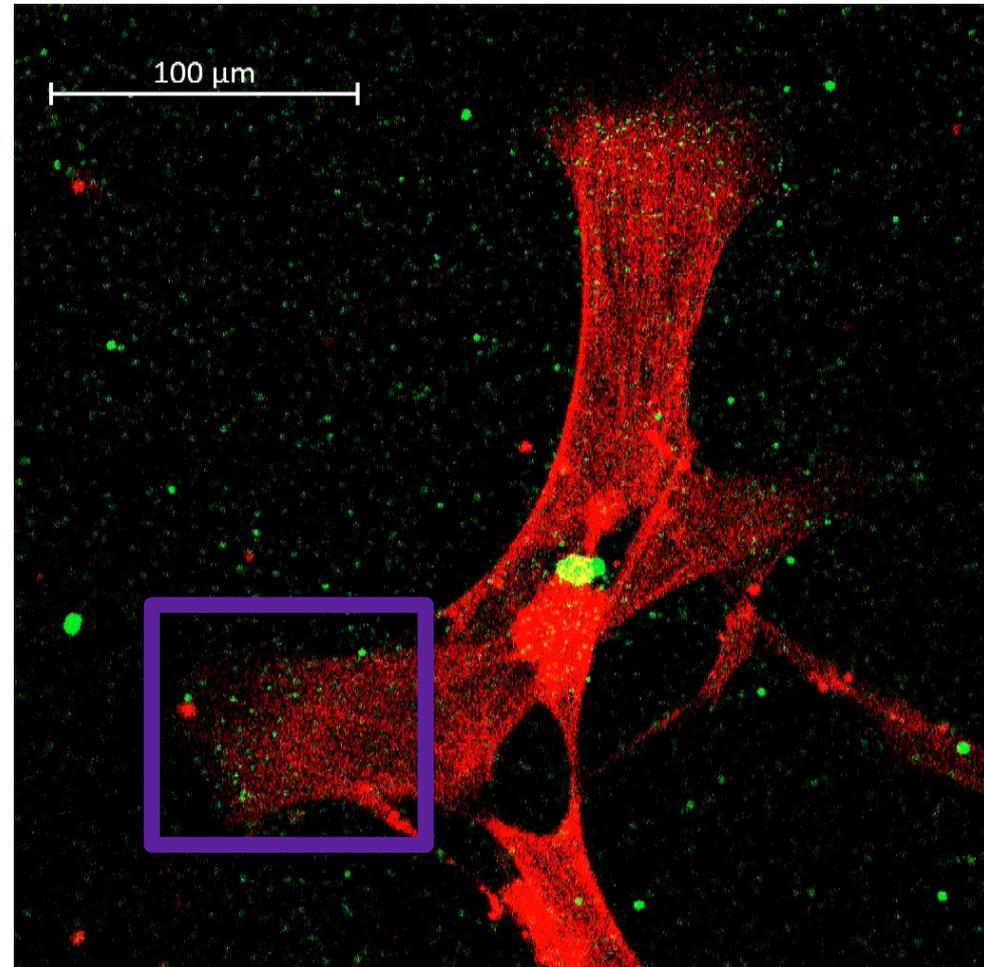
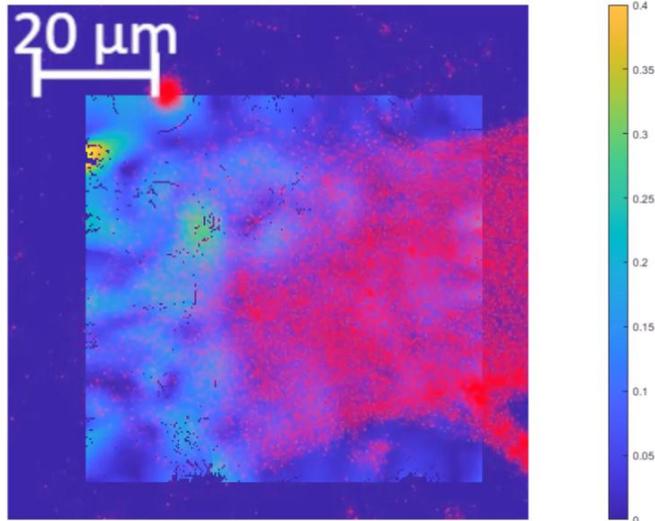


Driscoll et al, Biophysical Journal, 2015



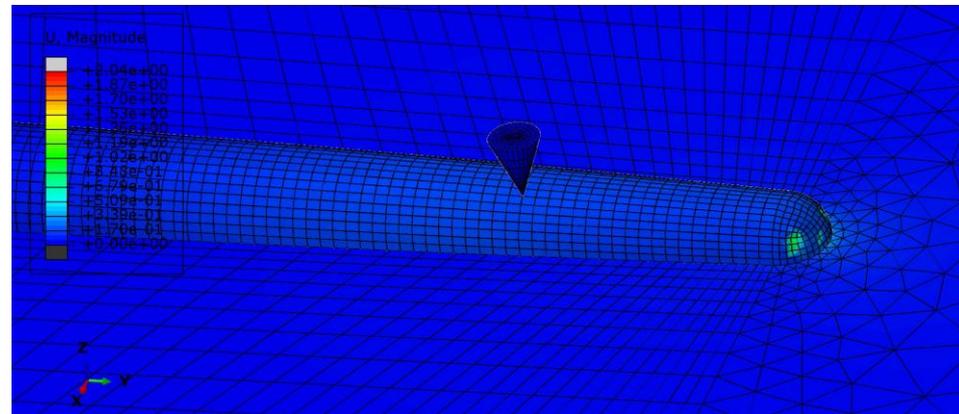
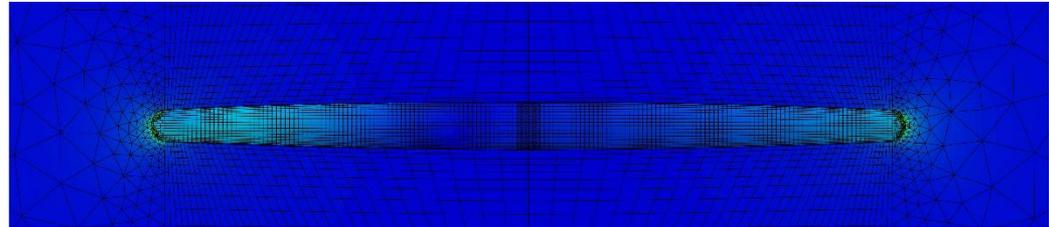
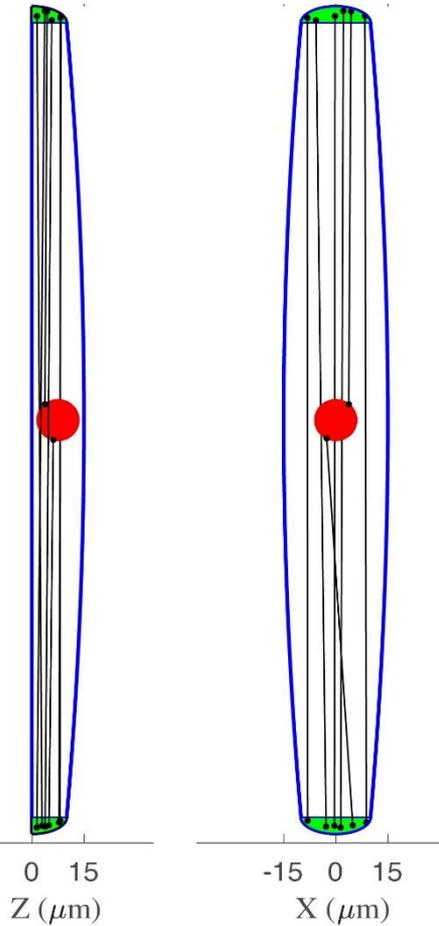
Major role of smooth muscle cells in mechanoregulation

Monitoring mechanobiology of live SMCs

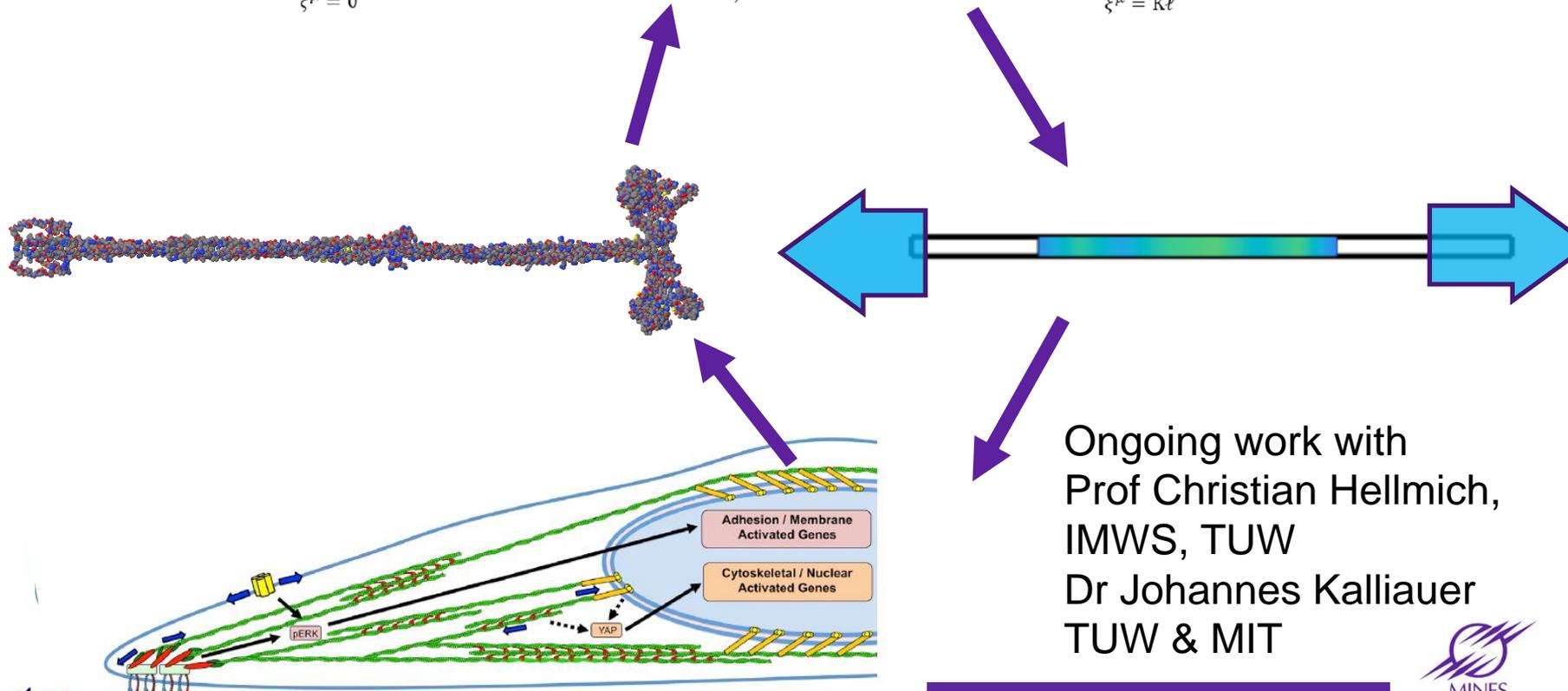
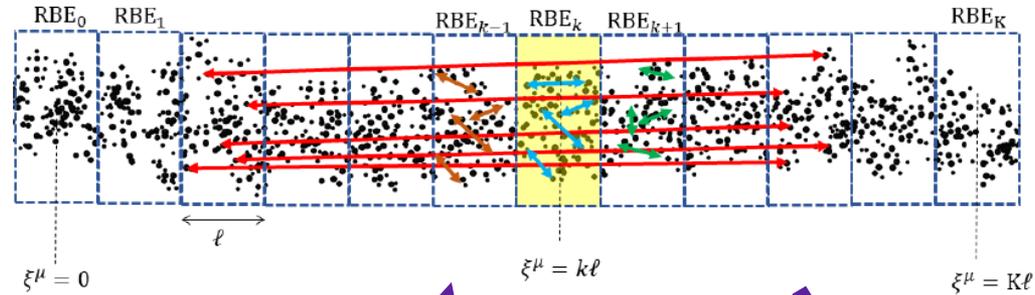


**Confocal microscopy +
DIC combined with
Siractin staining on living
cells**

Finite Element model of SMCs



HOMOGENIZATION OF PROTEINS INTO BEAMS



Ongoing work with
 Prof Christian Hellmich,
 IMWS, TUW
 Dr Johannes Kalliauer
 TUW & MIT

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- Federica Galbiati
- Francesco Bardi
- Solmaz Farzeneh
- Francesca Condemi
- Cristina Cavinato
- Jérôme Molimard
- Baptiste Pierrat
- Claudie Petit
- Marzio Di Giuseppe
- Jay Humphrey
- Christian Cyron
- Fabian Braeu
- Ambroise Duprey
- Jean-Pierre Favre
- Jean-Noël Albertini
- Salvatore Campisi
- Magalie Viallon
- Pierre Croisille
- Joannes Kalliauer
- Christian Hellmich

