Towards Personalized Modeling of Cerebral Aneurysms and Disease Evolution

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Towards Personalized Modeling of Cerebral Aneurysms and Disease Evolution

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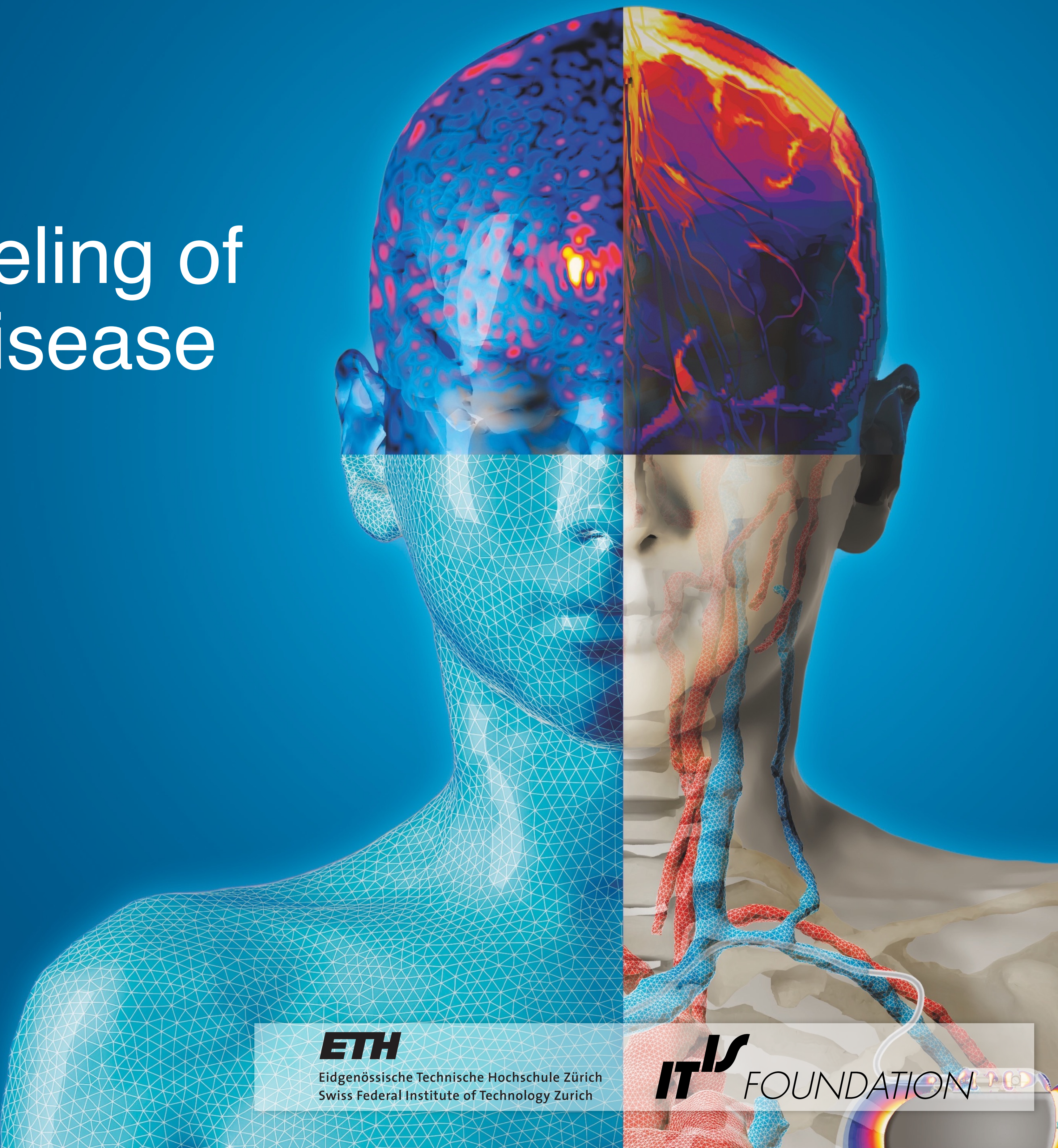
ETH Zurich & IT'IS Foundation



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- Personalized Model Generation
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Acknowledgments

Prof. Dr. Sven Hirsch (ZHAW, Switzerland)

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- disease evolution models

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- CFD validation and WSSAR metric

Dr. Alessandro Alaia

- FSI

Sim4Life Developers

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The AneuX Project

The AneuX Project

improve the assessment of aneurysm rupture risk through

- imaging
  - segmentation
  - vessel geometry
- statistics & learning
  - rupture risk probability through shape description
- disease evolution modeling
  - fluid & structure dynamics
  - wall constituent evolution
- aim: to improve the support for treatment decisions

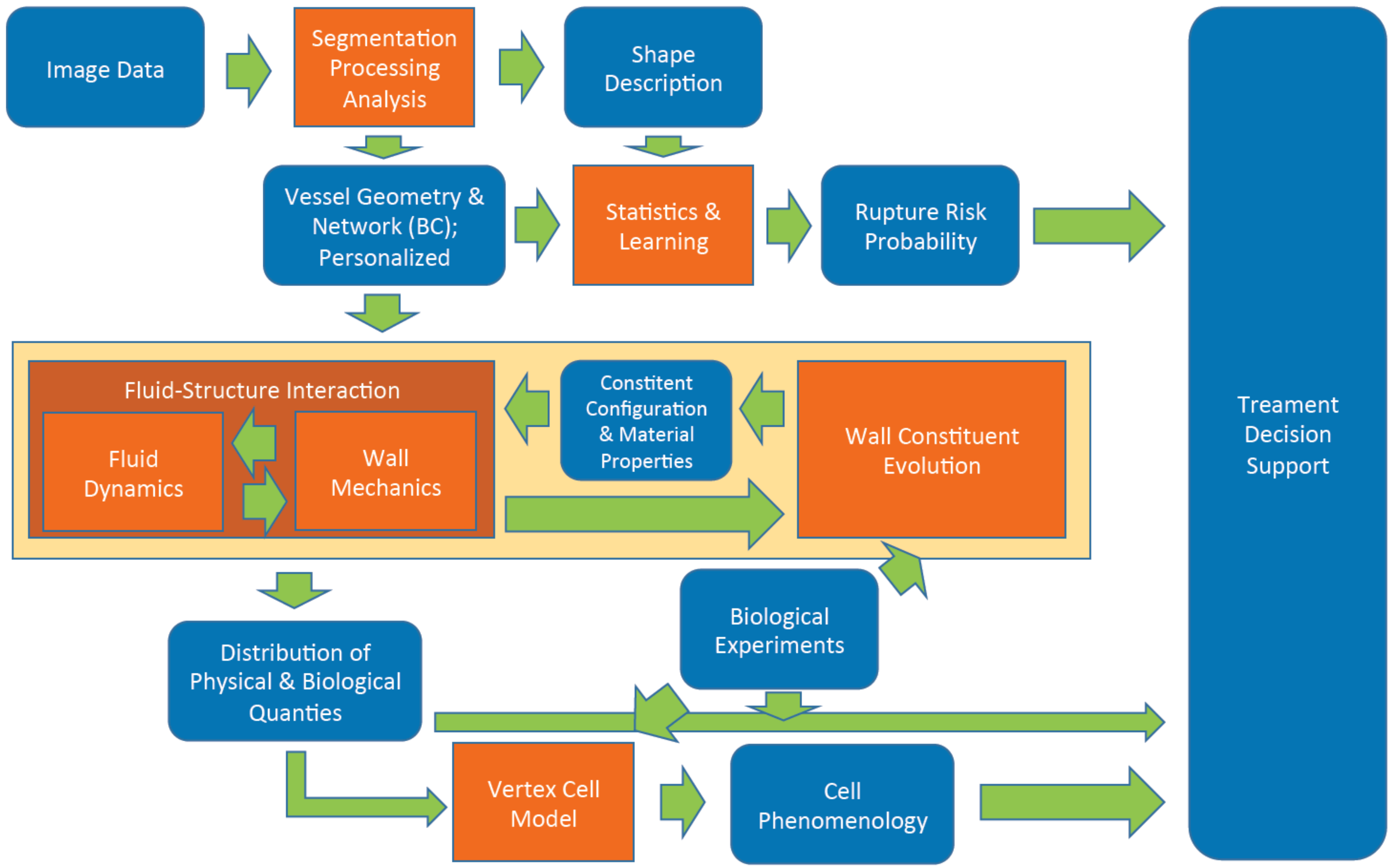

Figure: Data (blue) and processes (orange): image data is transformed into patient-specific input for shape-based and simulation-based assessment of rupture risk; biological experiments provide input for models of wall evolution and cell phenomenology, as well as the interpretation of the simulation results in terms of treatment decision support.

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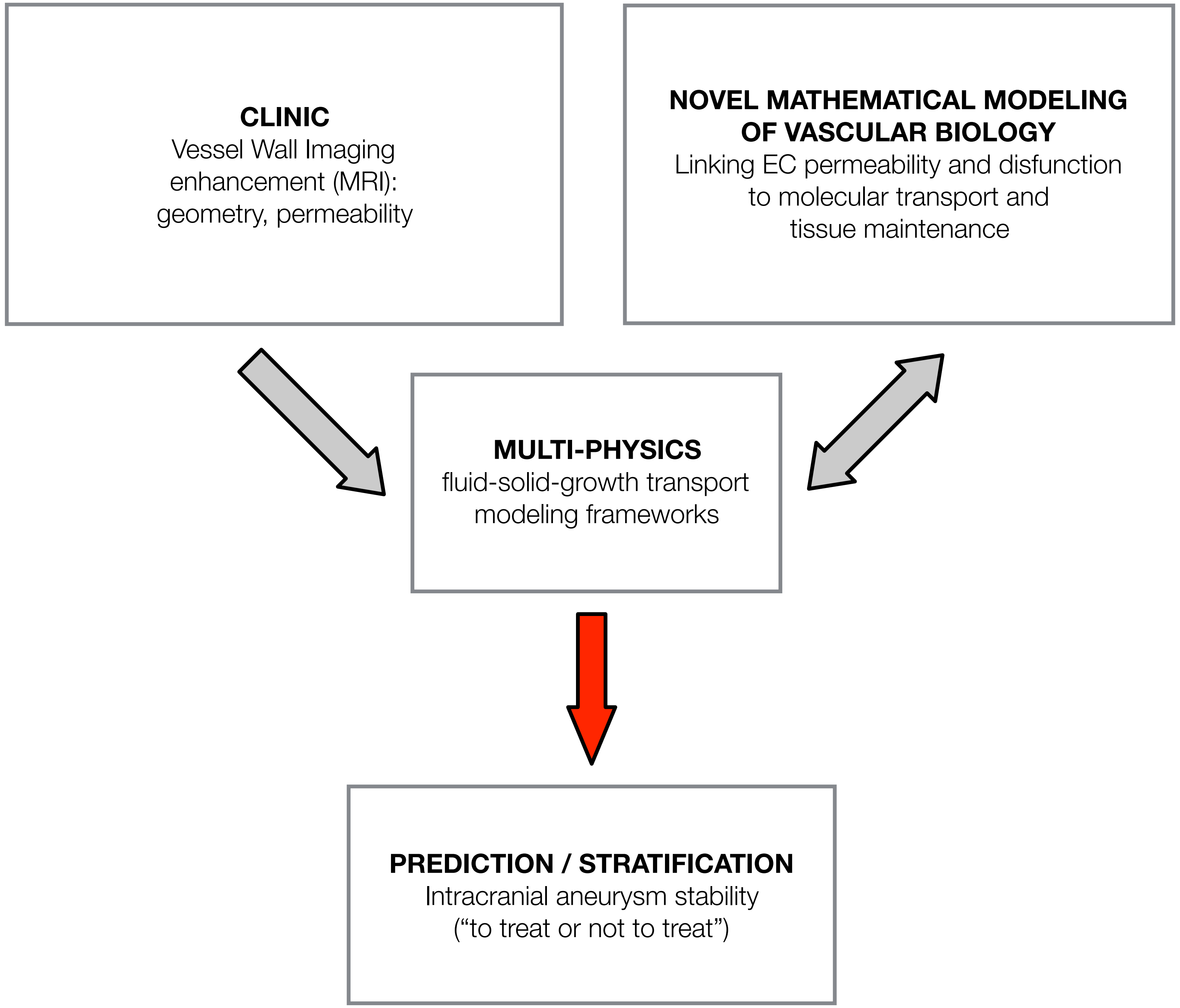
The Need for Computational Tools …

to treat or not to treat?

- more aneurysms are being detected because of developments in imaging technology
- high interventional costs
- value of the proposed framework: integrated tool, from imaging segmentation to disease evolution models



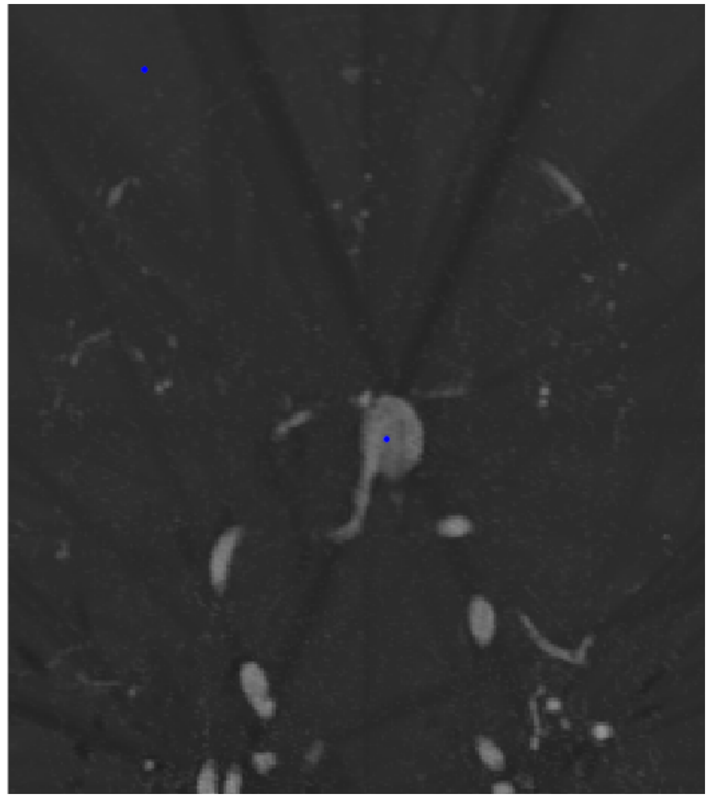
Personalized Model Generation

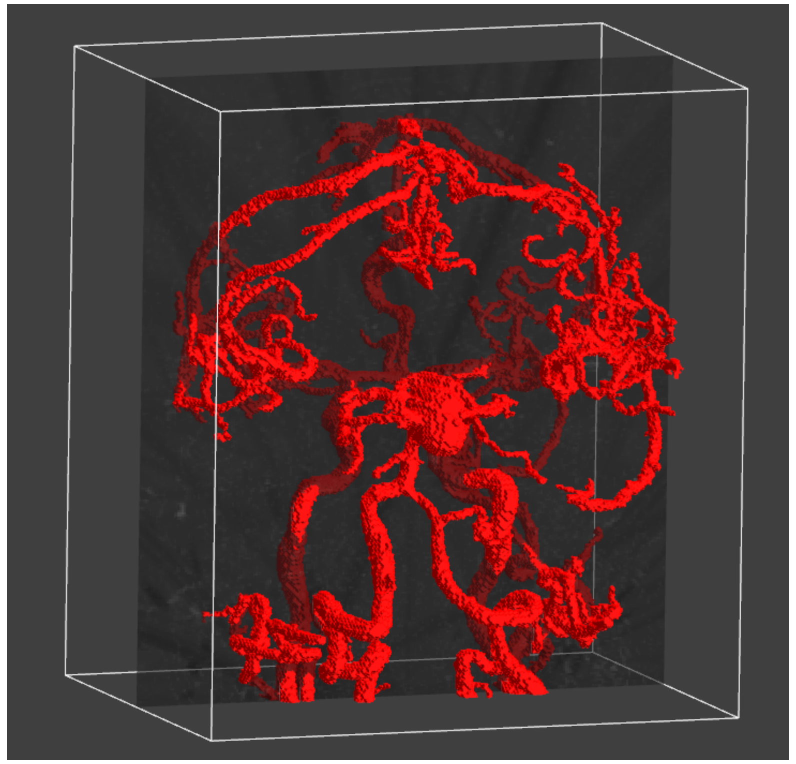
vessel segmentation

Personalized Model Generation

vessel segmentation

- line-shape profiles
  - preprocessing, automatic
  - looking at neighborhood of each pixel —> likelihood
- differential image foresting transform
  - set source points for regions
  - splits images into regions based on strength of connectedness
  - adds possibility for corrections
  - extend segmentation to previously not detected vessels





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Disease Evolution Modeling I: Fluid-Structure Interaction (FSI)

definition

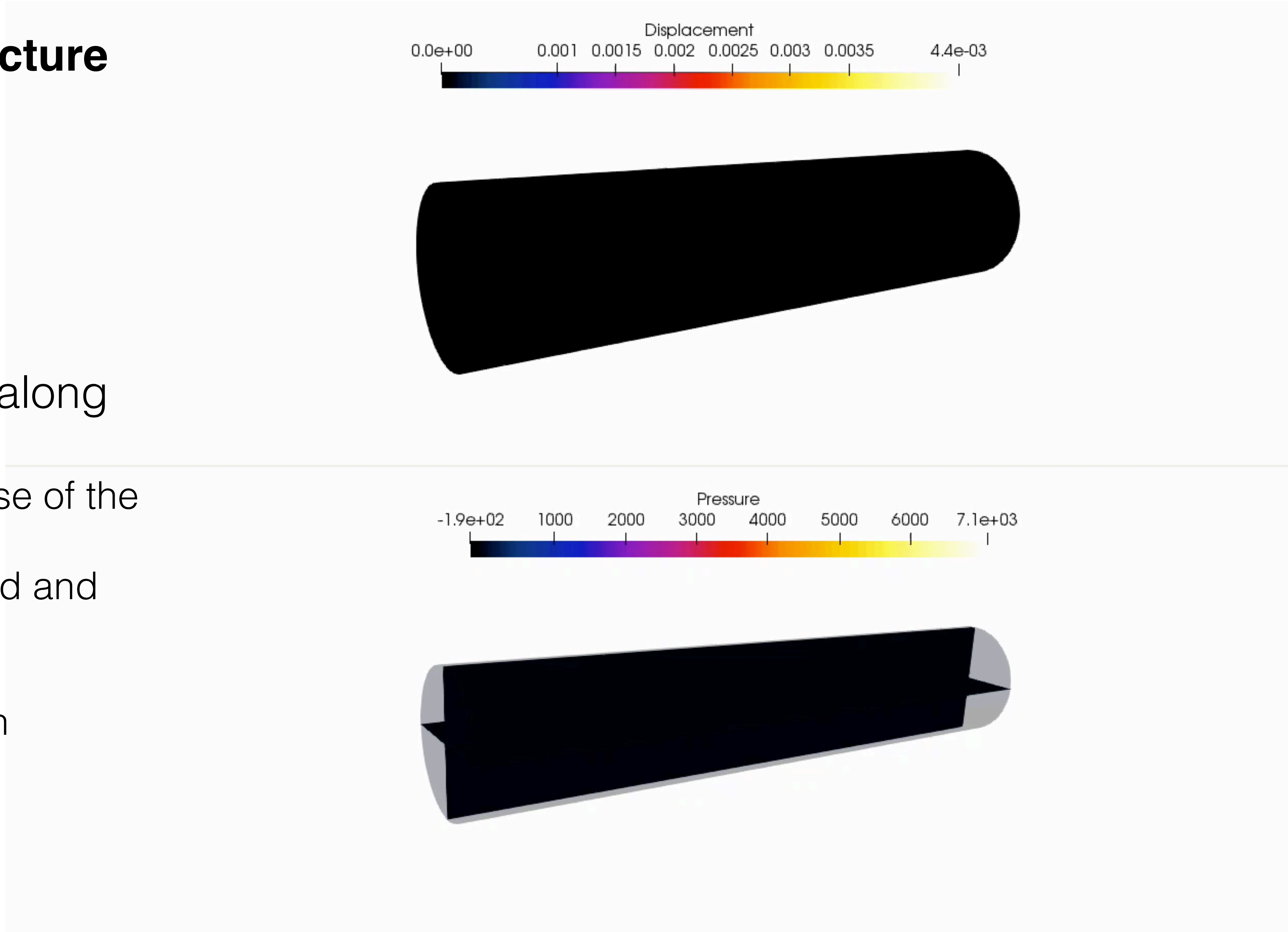
solver features

3D/1D coupling

What Is Fluid-Structure Interaction (FSI)?

interaction of some deformable structure with the neighboring fluid

- computational fluid dynamics (CFD)
  - flow characterization assuming rigid walls.
- finite element analysis (FEA)
  - computational structural dynamics (CSD)
- inherits the CFD and FEA challenges, along with
  - “extra” convective effect in the fluid because of the moving domain
  - the “added-mass effect”: ratio between fluid and solid densities
  - the need for specialized solvers
  - more complex issues with mesh generation



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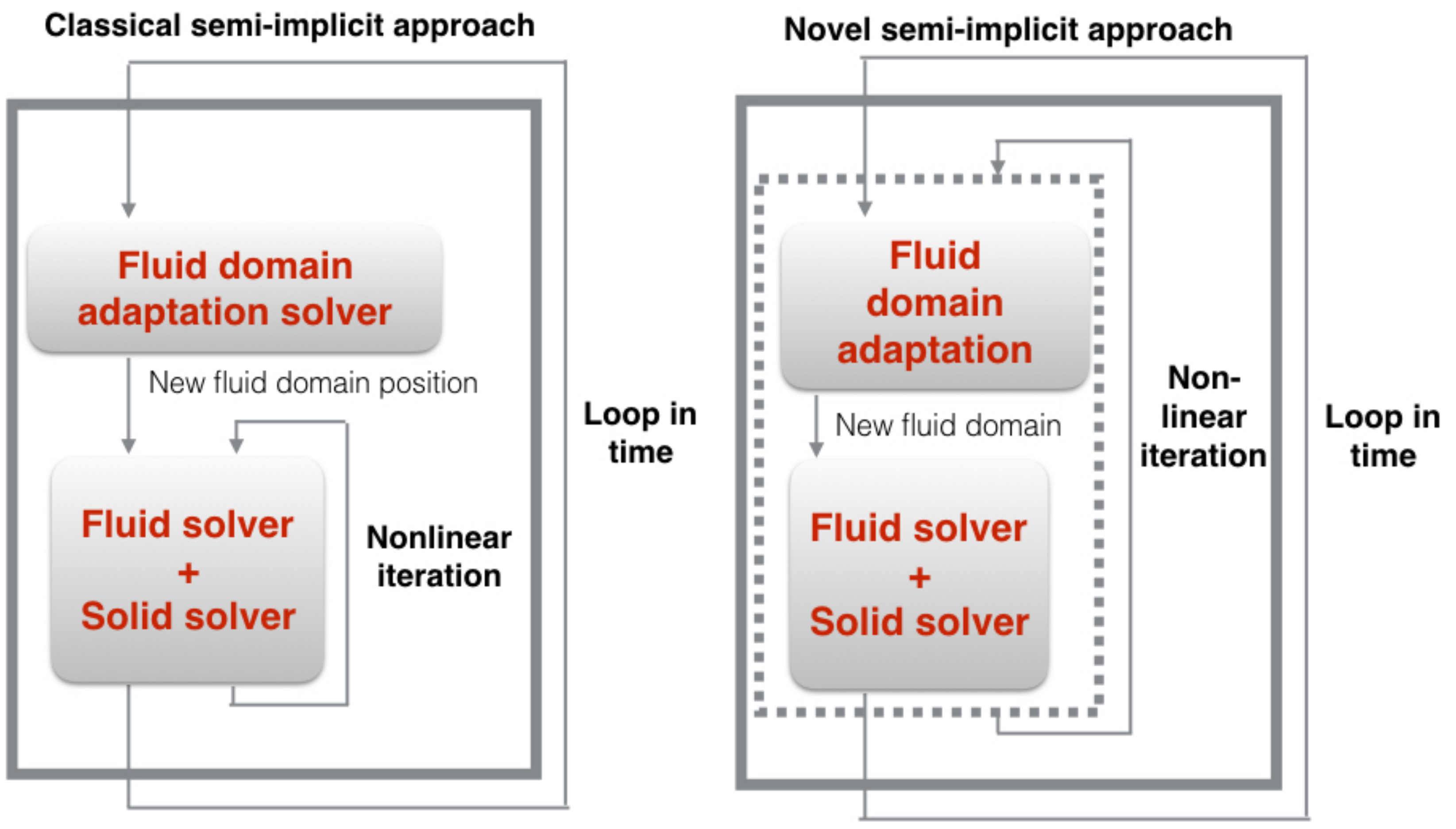
Our FSI Solver features

- PETSc-based, HPC enabled, support to hybrid conformal meshes
- solid solver
  - support to anisotropic constitutive laws
  - supports nearly incompressible materials through the three-fields formulation
- fluid solver
  - supports the Variational Multi-scale Stabilization (VMS) method, which enables P1 elements for velocity and pressure
  - preconditioners: SIMPLE, SIMPLEC, LSC, full and upper Schur factorization
  - 3D / 1D coupling
- why is it valuable?
  - novel semi-implicit approach
  - likely novel coupling of VMS (Fluid) with linear prismatic elements (Solid), which enables P1 elements for all fields



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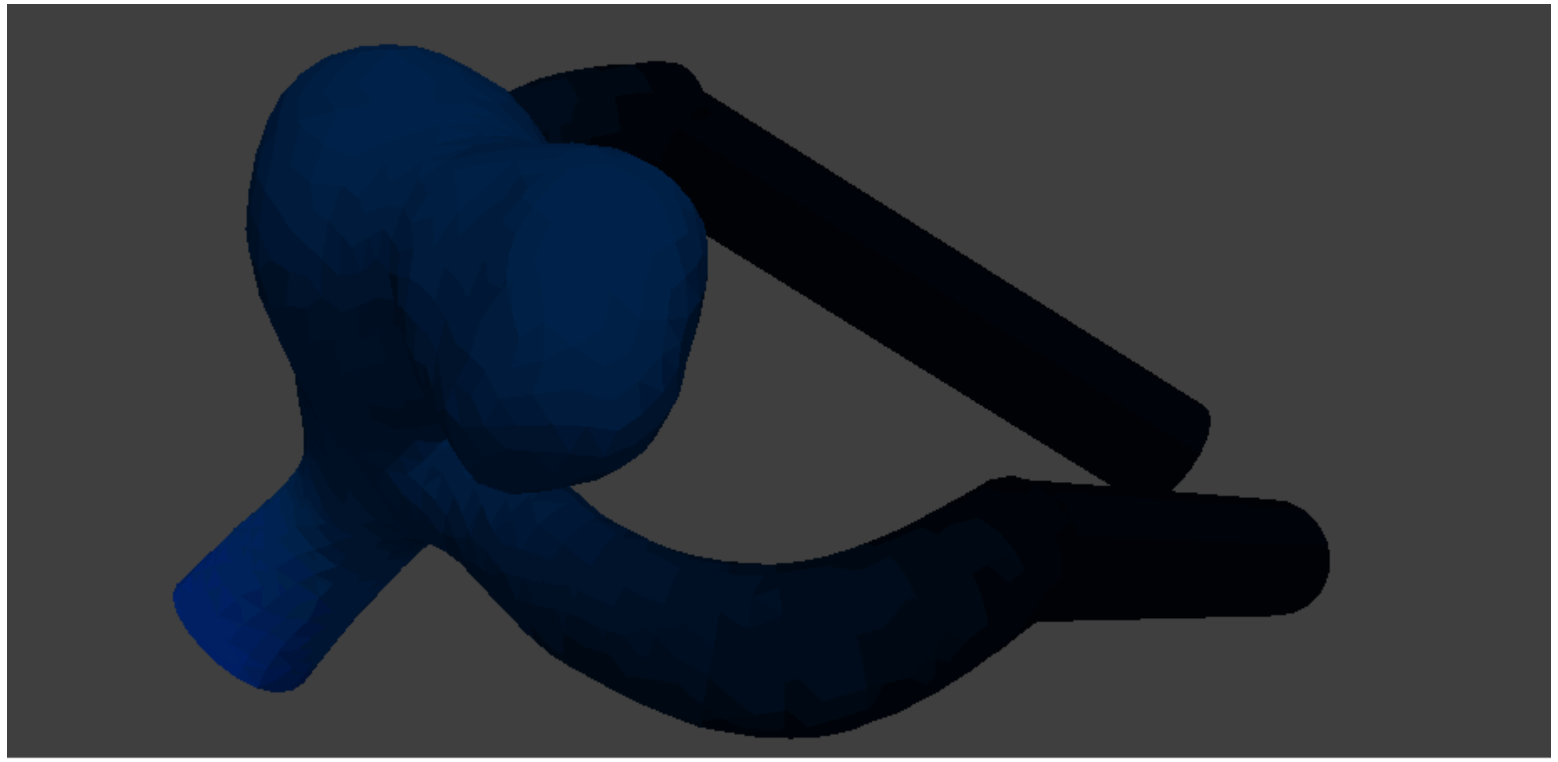
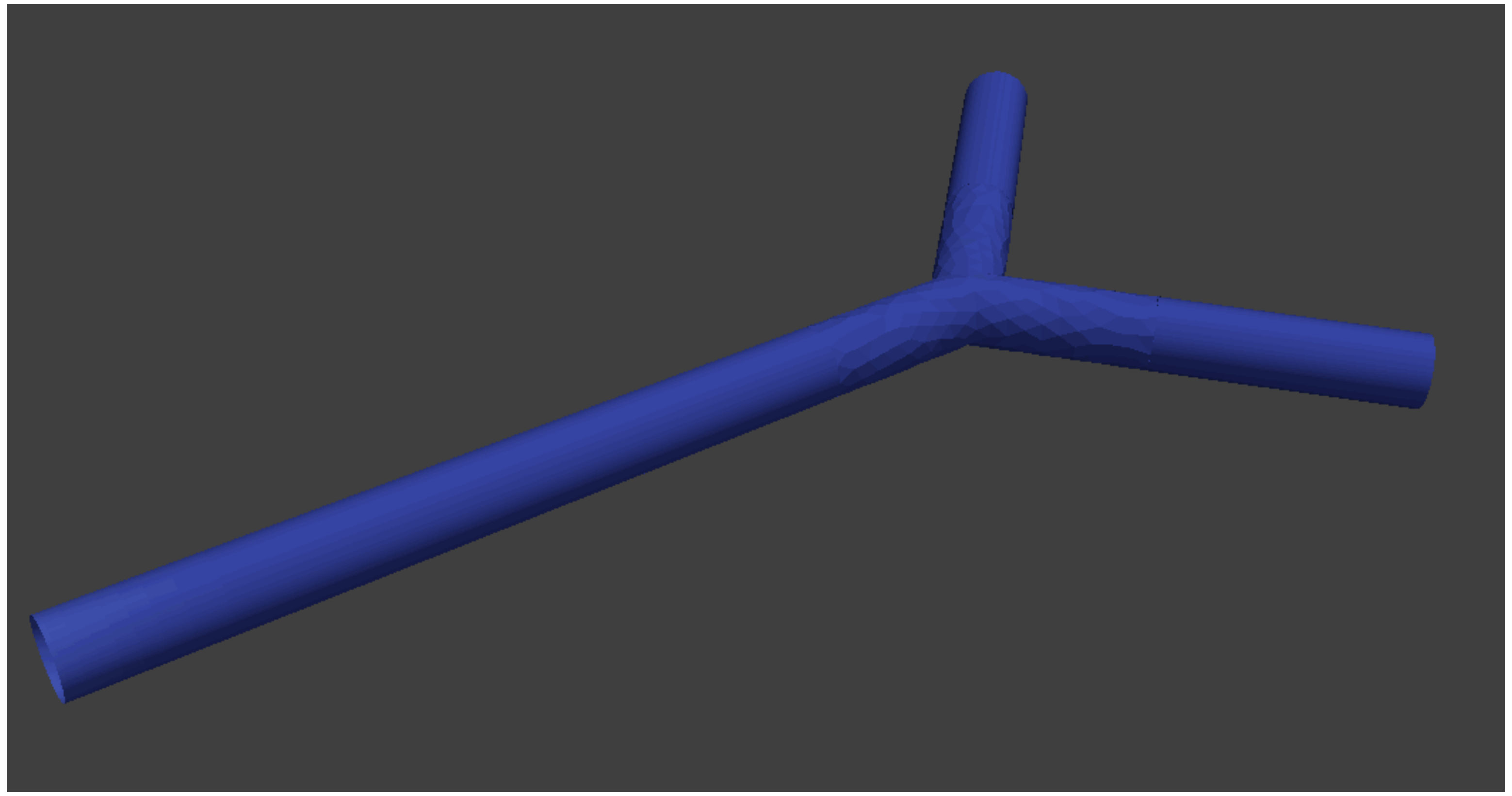
3D/1D Coupling

it reduces the size of the complex domain

- aneurysm: 3D domain of interests
  - 1D segments used as boundary conditions
- coupling:
  - imposing pressure on both domains
  - residual calculated based on flow-rates
  - approx. 2 to 4 iterations per time-step





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Disease Evolution Modeling II: Modeling of Cerebral Aneurysms

assumptions for structural analysis

aneurysms evolution models

Python framework in Sim4Life

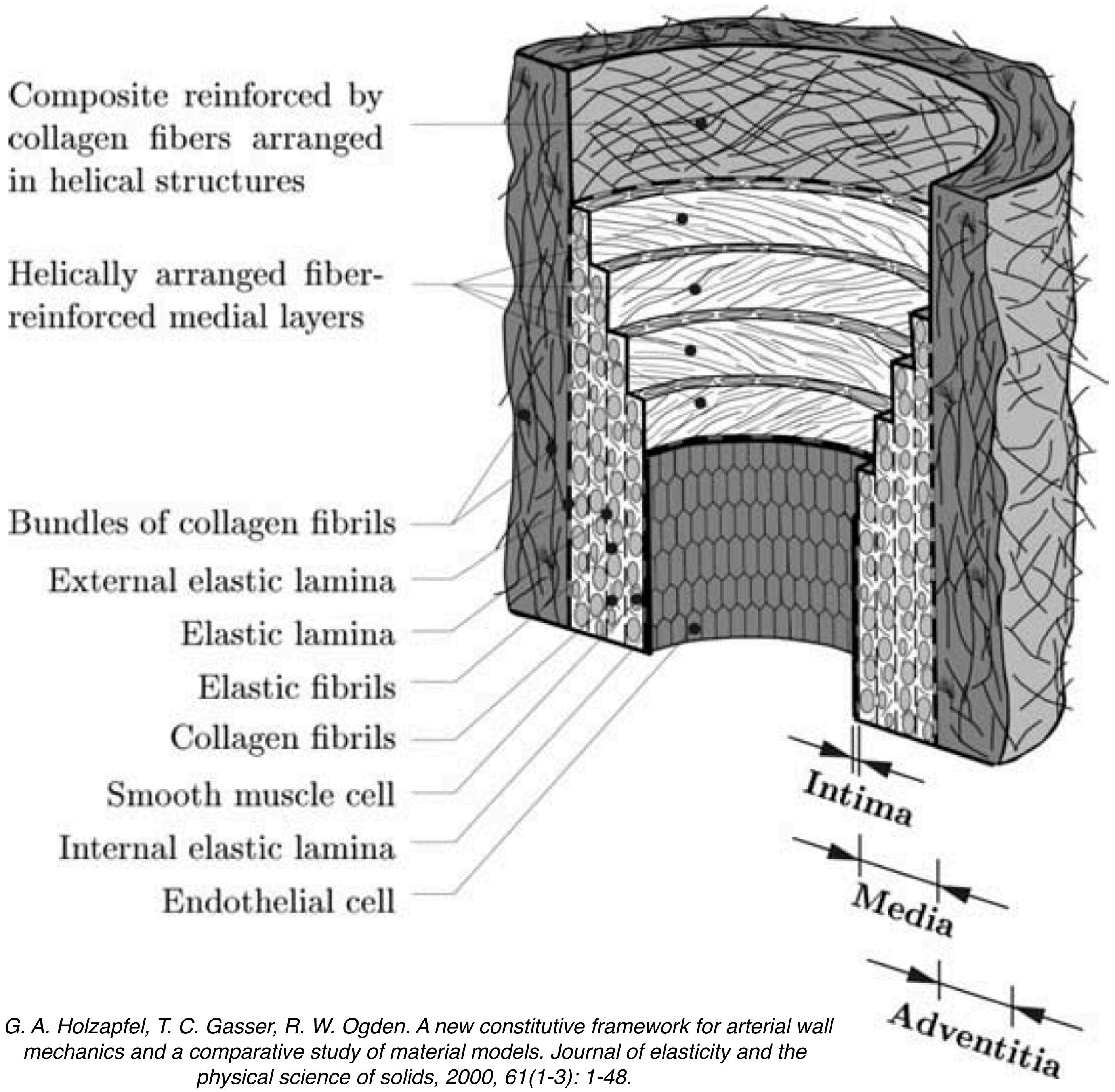
examples

Assumptions for Structural Analysis

an artery is composed of three layers

- intima:
  - only one layer of endothelial cells
  - is responsible for mechano-transduction
  - has no mechanical role
- media: helically arranged fiber-reinforced layer with
  - elastin, collagen fibers and smooth muscle cells
  - bears most of the loads
- adventitia: helically arranged fiber-reinforced layer with
  - mostly collagen fibers
  - in a healthy state, it is a protective sheath

- internal elastic lamina
  - separates the intima and the medial layers



G. A. Holzapfel, T. C. Gasser, R. W. Ogden. A new constitutive framework for arterial wall mechanics and a comparative study of material models. Journal of elasticity and the physical science of solids, 2000, 61(1-3): 1-48.

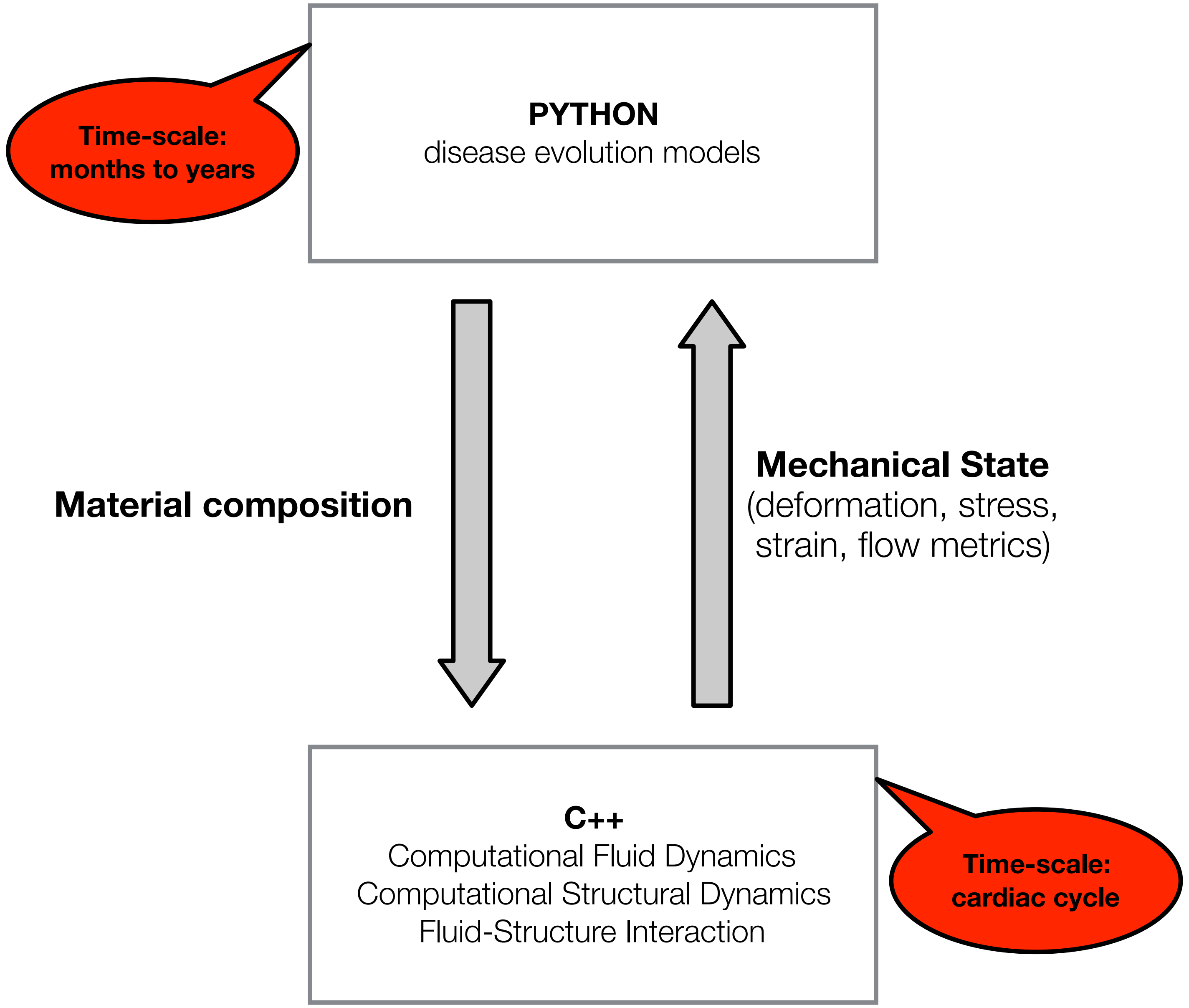
Aneurysm Evolution Stages

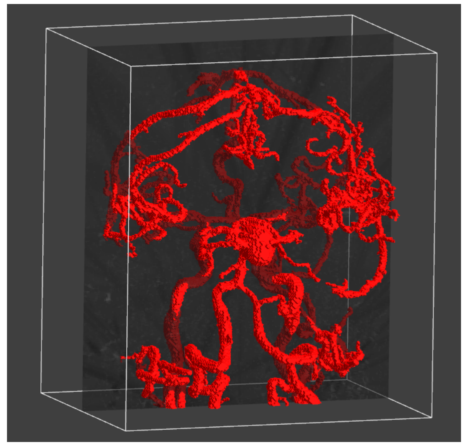
- inception: "*initial apoptosis in vascular smooth muscle cells within the vessel wall and disruption of the internal elastic lamina*"
- enlargement: collagen fiber remodeling and medial layer degeneration
  - the adventitia layer changes its role, from a protective sheath to the main load bearer
- stabilization and/or growth/rupture:
- the hemodynamic environment seems to impact all three stages

A. M. Robertson & P. N. Watton. Mechanobiology of the Arterial Wall. Transport in Biological Media, 2014: 275-347.

N. Etminan, et al. Cerebral aneurysms: Formation, progression and developmental chronology. Stroke Res. 2014, April, 5(2): 167-173.

Python Framework in Sim4Life





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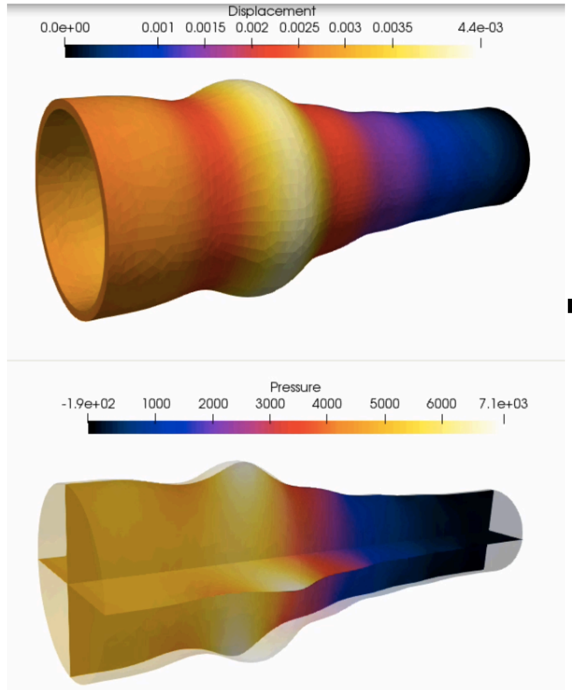

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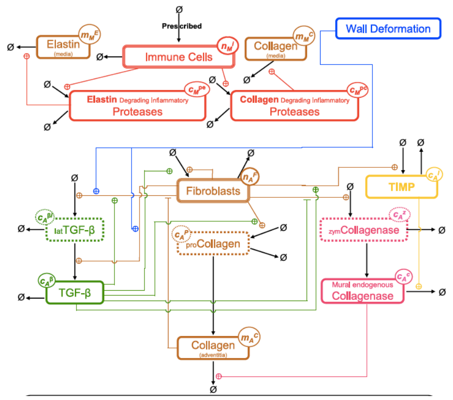

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PYTHON

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Aneurysm analysis

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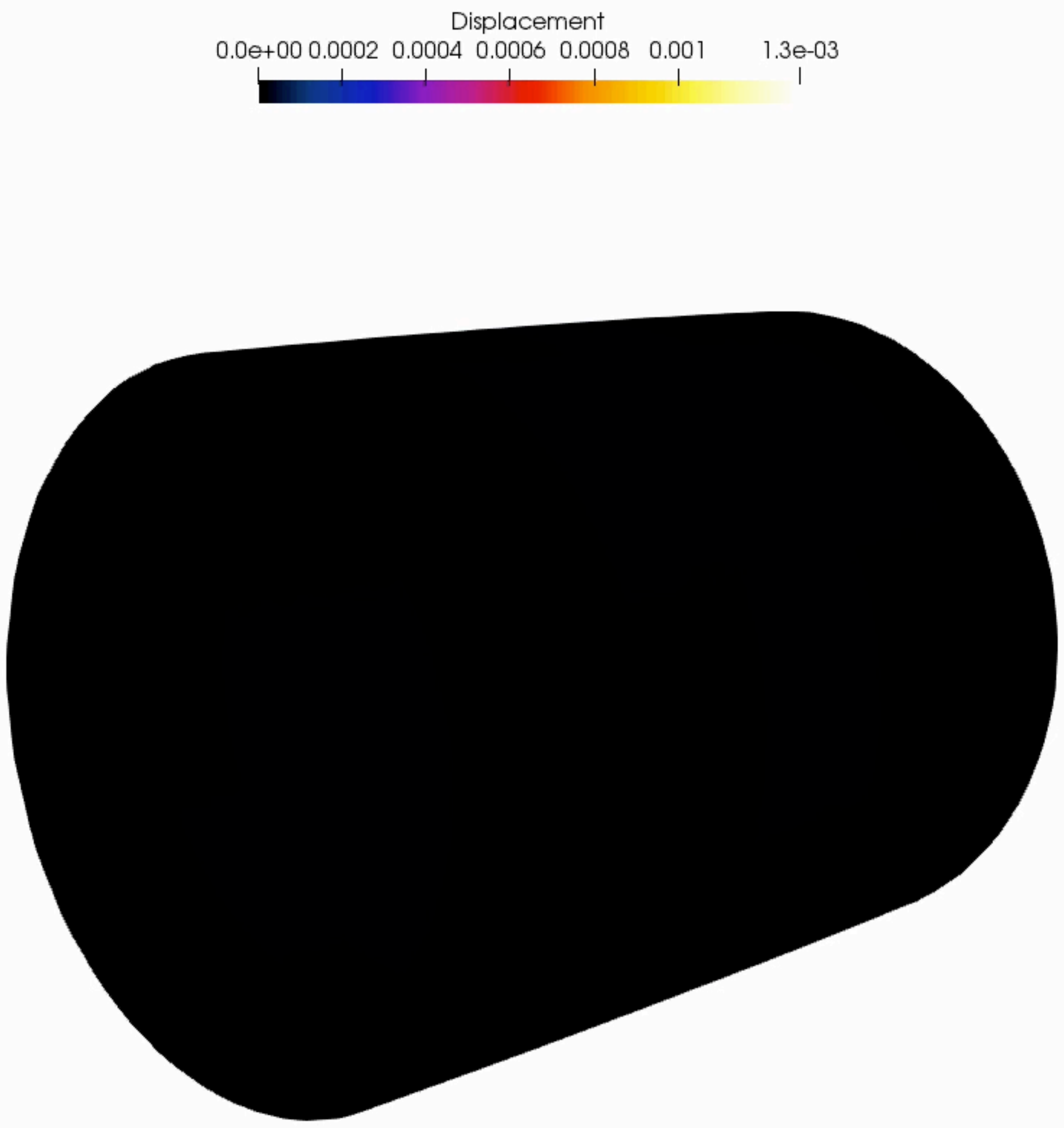
Verification case 1

idealized geometry to verify the modeling framework

- medial layer degradation (loss of elastin and smooth muscle cells): specified in a controlled area
  - 90% degraded after 1 year.
- aim: enlargement in the area where the layer degrades, followed by stabilization size caused by the collagen growth to maintain homeostasis.

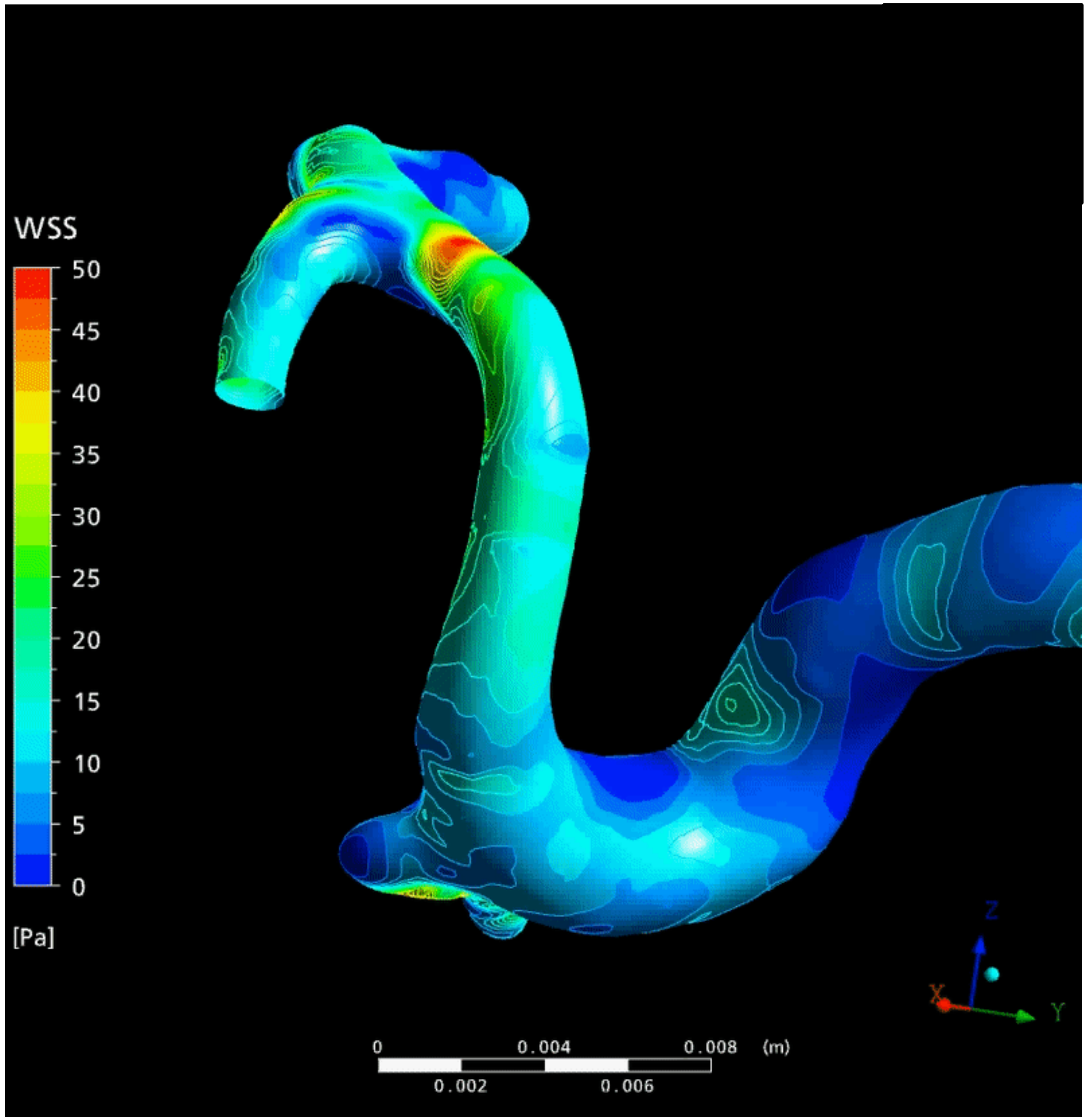


P. N. Watton et al. Coupling the hemodynamic environment to the evolution of cerebral aneurysms: computational framework and numerical examples. Journal of Biomechanical Engineering (2009) 131: 101003-1 - 101003-13

Verification case 2 (in progress)

patient-specific geometry to verify the coupling with flow metrics

- medial layer degradation (loss of elastin and smooth muscle cells): coupled to the spatial heterogenous low WSS
- aim: enlargement in the area where the elastin degrades, followed by stabilization caused by the collagen growth to maintain homeostasis.

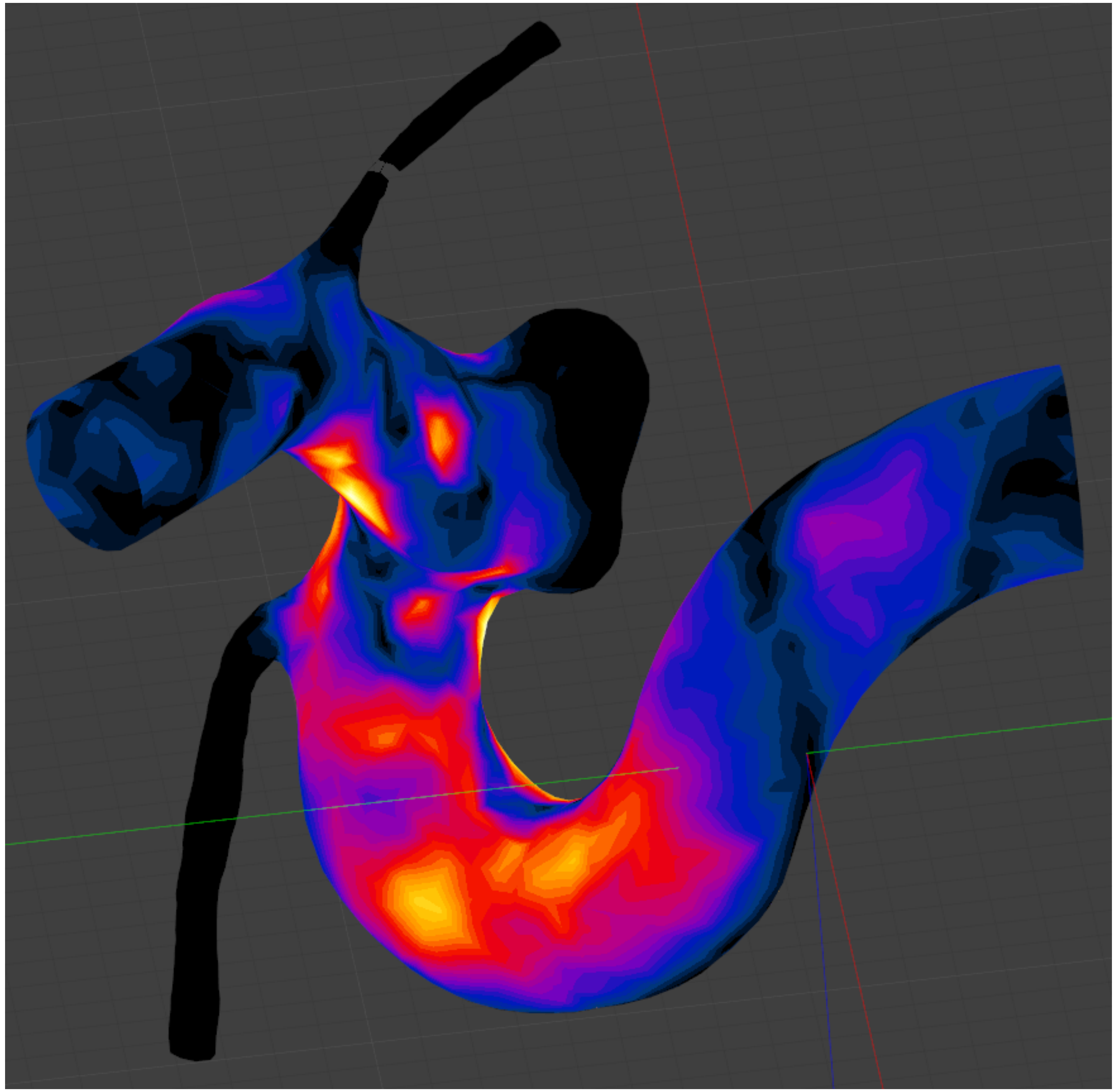


P. N. Watton et al. Modelling evolution and the evolving mechanical environment of saccular cerebral aneurysms. Biomech Model Mechanobiol (2011) 10: 109-132

Application case (next step)

patient-specific geometry of clinical relevance

- aim: focus on aneurysm growth and stabilization
- growth and remodeling linked to cyclic deformation and endothelial cells morphology



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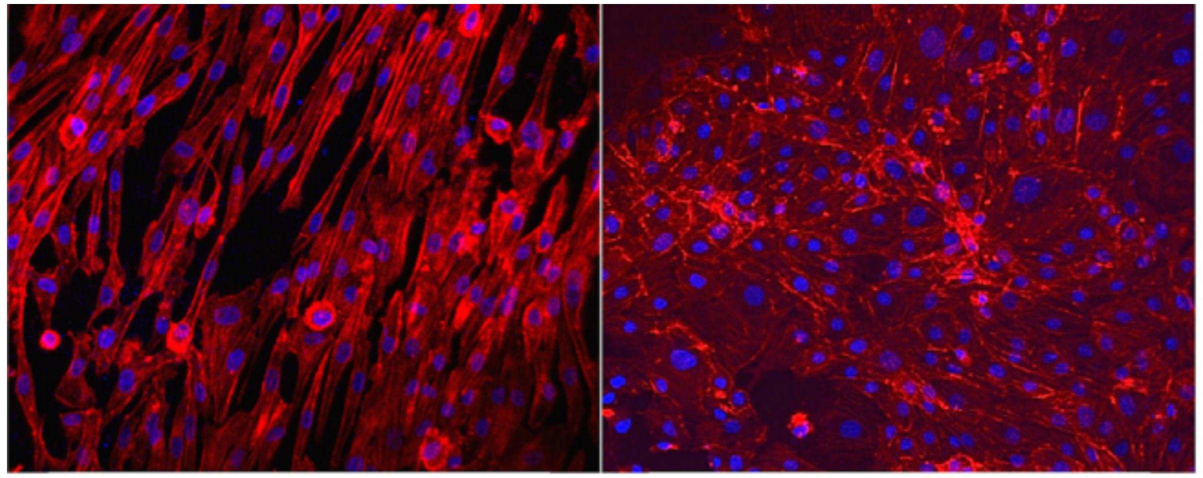
Application case: Flow-Biochemical Coupling

the state of the constituents is influenced by the hemodynamic environment

- biochemical pathway: endothelial cells morphology —> endothelial permeability —> aneurysm growth / stabilization

Parent artery: spindle shaped

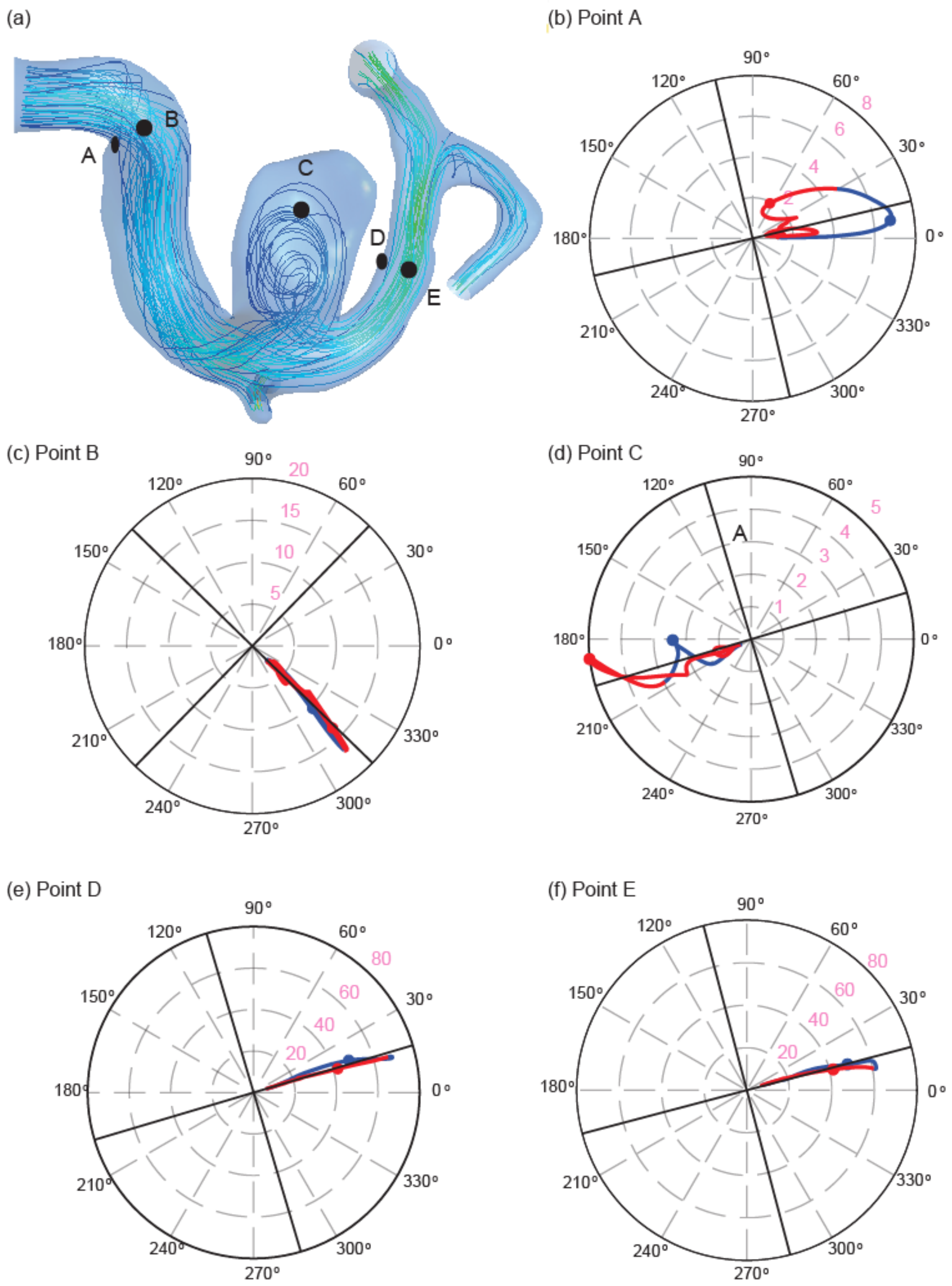


Aneurysm: irregular

N. Kaneko et al.. A patient-specific intracranial aneurysm model with endothelial lining: a novel in vitro approach to bridge the gap between biology and flow dynamics. Journal of NeutroInterventional Surgery (2017) 0: 1 - 5.

- Shear Stress Rosettes: behavior of the WSS vector in a point over one cardiac cycle (Namrata Gundiah's lab)

- flow-biochemical pathway: WSSAR —> endothelial cells morphology



C. Vais Krishna, P. Watton, N. Gundiah, et al.. Shear Stress Rosettes captures the complex flow physics in diseased arteries. Journal of Biomechanics, to appear.

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Conclusions

- novel framework under development with functionalities from imaging manipulation to support for disease evolution models
  - from vessel segmentation to fully functional meshes, incl. prism layers
  - support to advanced mechanical tissue models
  - extensible Python scripts for disease evolution modeling
  - framework for cell phenomenology studies
- framework will focus on the differentiation between stable and unstable aneurysms
- current state of the model
  - thick-wall model of the arterial wall
  - G&R linked to cyclic deformation and transient hemodynamics
  - fibril distribution function and adaptation of collagen fabrics
- discussion & next steps:
  - multi-physics is in place but it needs more sophisticated representations of mechanobiology
  - general application to G&R of soft tissues