# Image-based modeling of the cardiovascular system

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**CEMRACS 2015 Summer School**
**CIRM - Luminy**
**July 20th – 21st 2015**

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COLLEGE OF ENGINEERING & MEDICAL SCHOOL
COMPUTATIONAL VASCULAR BIOMECHANICS LAB
UNIVERSITY OF MICHIGAN

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University of London

# Outline

- Lecture 1: Introduction to function and modeling of the CV system
- Lecture 2: Techniques for Parameter Estimation in the CV system
- Lecture 3: Simulation of Transitional Physiology
- Lecture 4: Advanced Topics, Clinical Applications and Challenges

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# Lecture 2:
# Techniques for Parameter Estimation in the CV system

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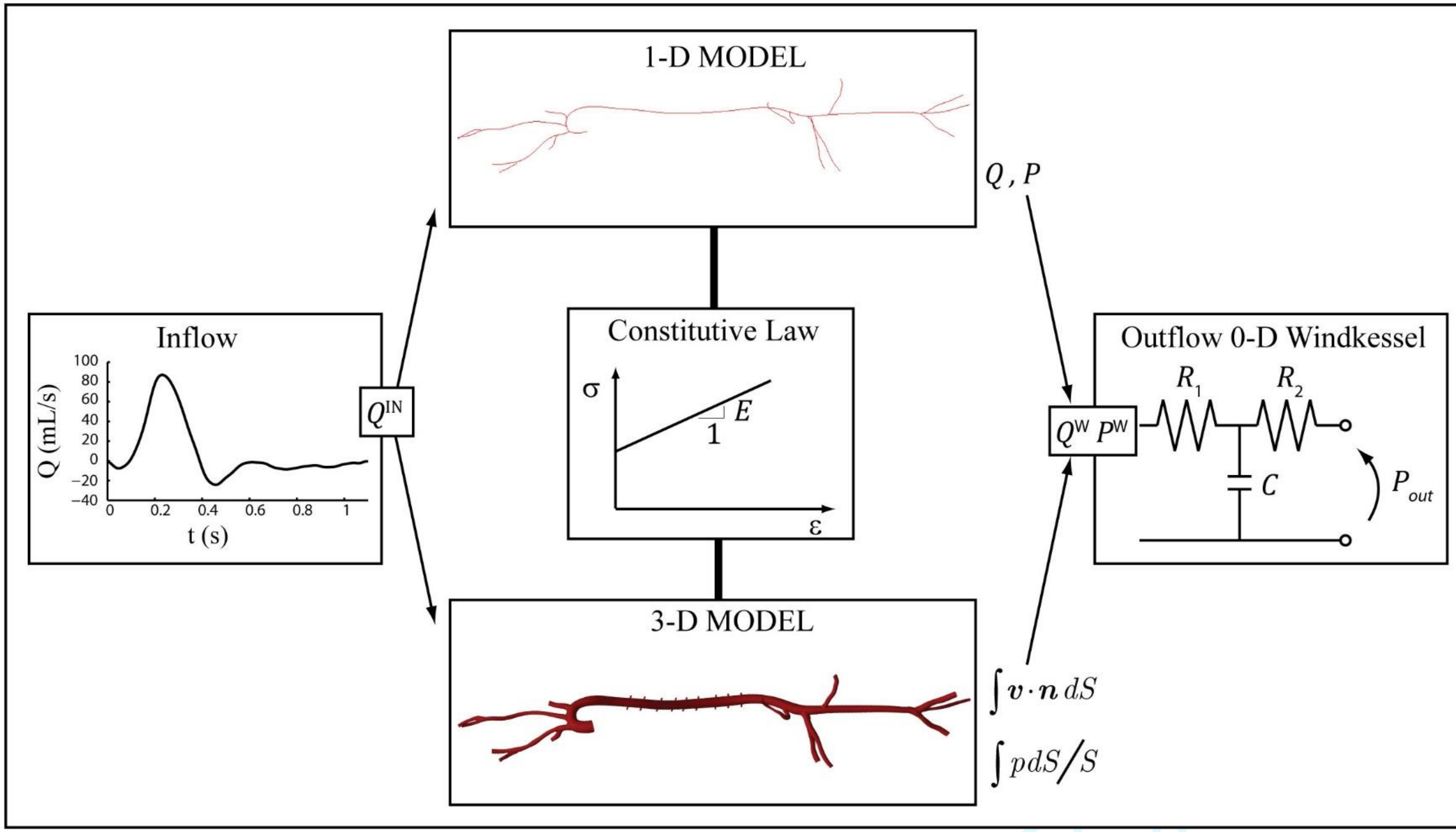
# A combined 1D-3D framework for fast parameter estimation




Xiao, Alastruey, Figueroa, IJNMBE, 2014.

- 1-D "equivalent" surrogate model
- Identical inflow and Windkessel outflow BC
- Equivalent linear elastic vessel wall constitutive law

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# A combined 1D-3D framework for fast parameter estimation

Cross-sectional area     Average axial velocity

Mass conservation:

$$\frac{\partial A}{\partial t} + \frac{\partial (AU)}{\partial x} = 0$$

Frictional force/length

Momentum conservation:

$$\frac{\partial U}{\partial t} + U\frac{\partial U}{\partial x} + \frac{1}{\rho_\mathrm{f}}\frac{\partial P}{\partial x} = \frac{f}{\rho_\mathrm{f} A}$$

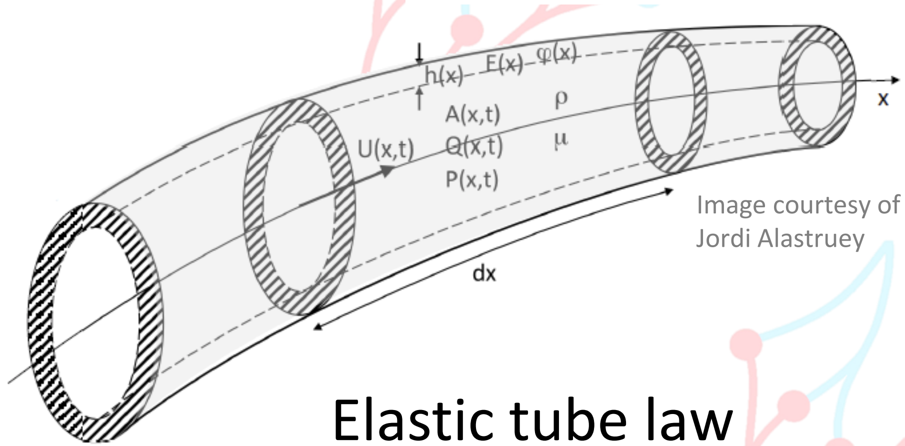


Image courtesy of Jordi Alastruey

Elastic tube law

$$P = P_\mathrm{d} + \frac{4}{3}Eh\frac{r - r_\mathrm{d}}{(r_\mathrm{d})^2} = P_\mathrm{d} + \frac{\beta}{A_\mathrm{d}}(\sqrt{A} - \sqrt{A_\mathrm{d}}), \qquad \beta = \frac{4}{3}\sqrt{\pi}Eh$$

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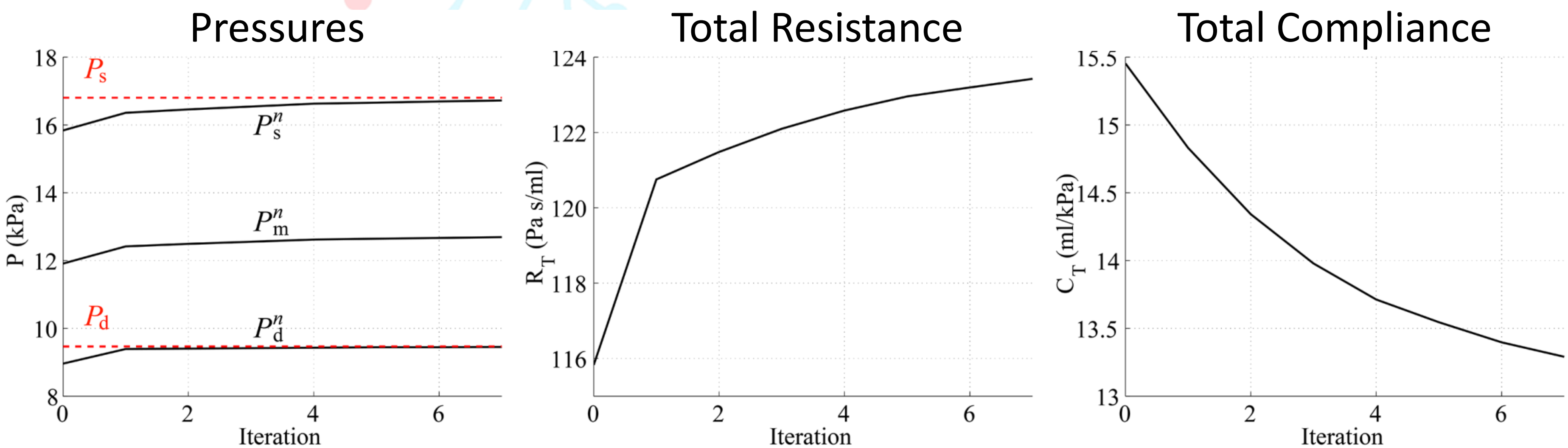
# Iterative approach for tuning outflow BCs in 1D model




$$R_T^{n+1} = R_T^n + \frac{\Delta P_m^n}{\overline{Q}_{in}}$$

$$\Delta P_m^n = P_d - P_d^n$$

Target diastolic pressure

Diastolic pressure after the *n*th 1-D simulation

$$C_T^{n+1} = C_T^n - \frac{Q_{max} - Q_{min}}{(P_{pulse}^n)^2} \Delta t \Delta P_{pulse}^n$$

$$\Delta P_{pulse}^n = P_{pulse} - P_{pulse}^n$$

Target pulse pressure

Pulse pressure after the *n*th 1-D simulation

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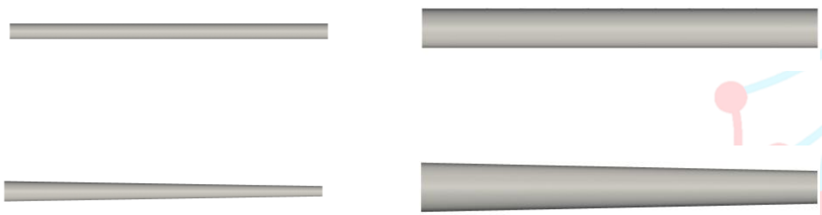
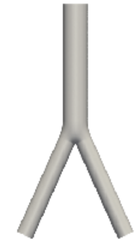
# 1D/3D Comparison: Idealized Geometries

**Straight and tapered Carotid/Aorta**



**Curved Aorta**

**Bifurcation**



**Full Aorta**

- Comparisons using idealized geometries
- “Best-case-scenario” for 1-D model assumptions

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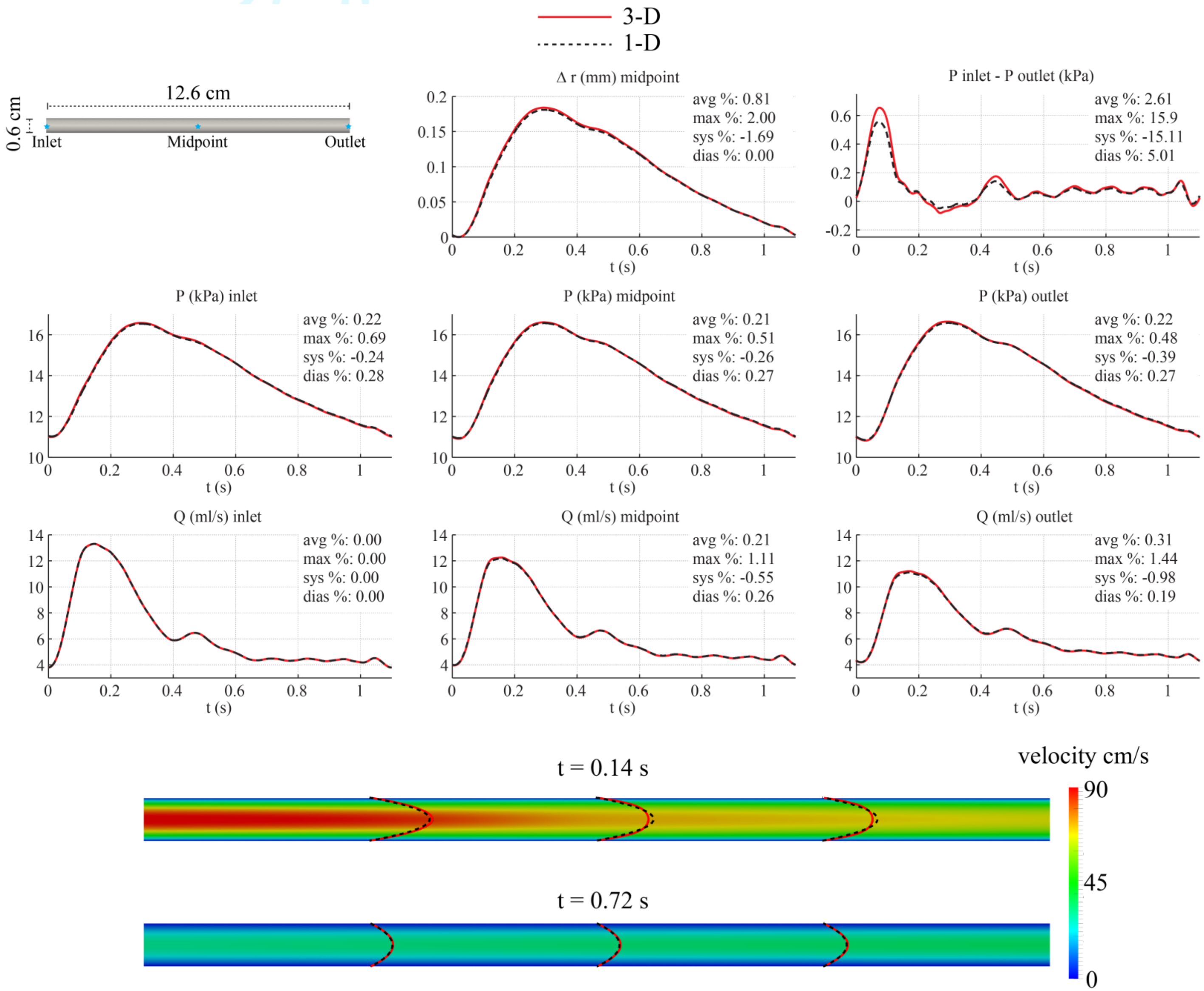
# 1-D/3-D Comparison: Idealized Carotid

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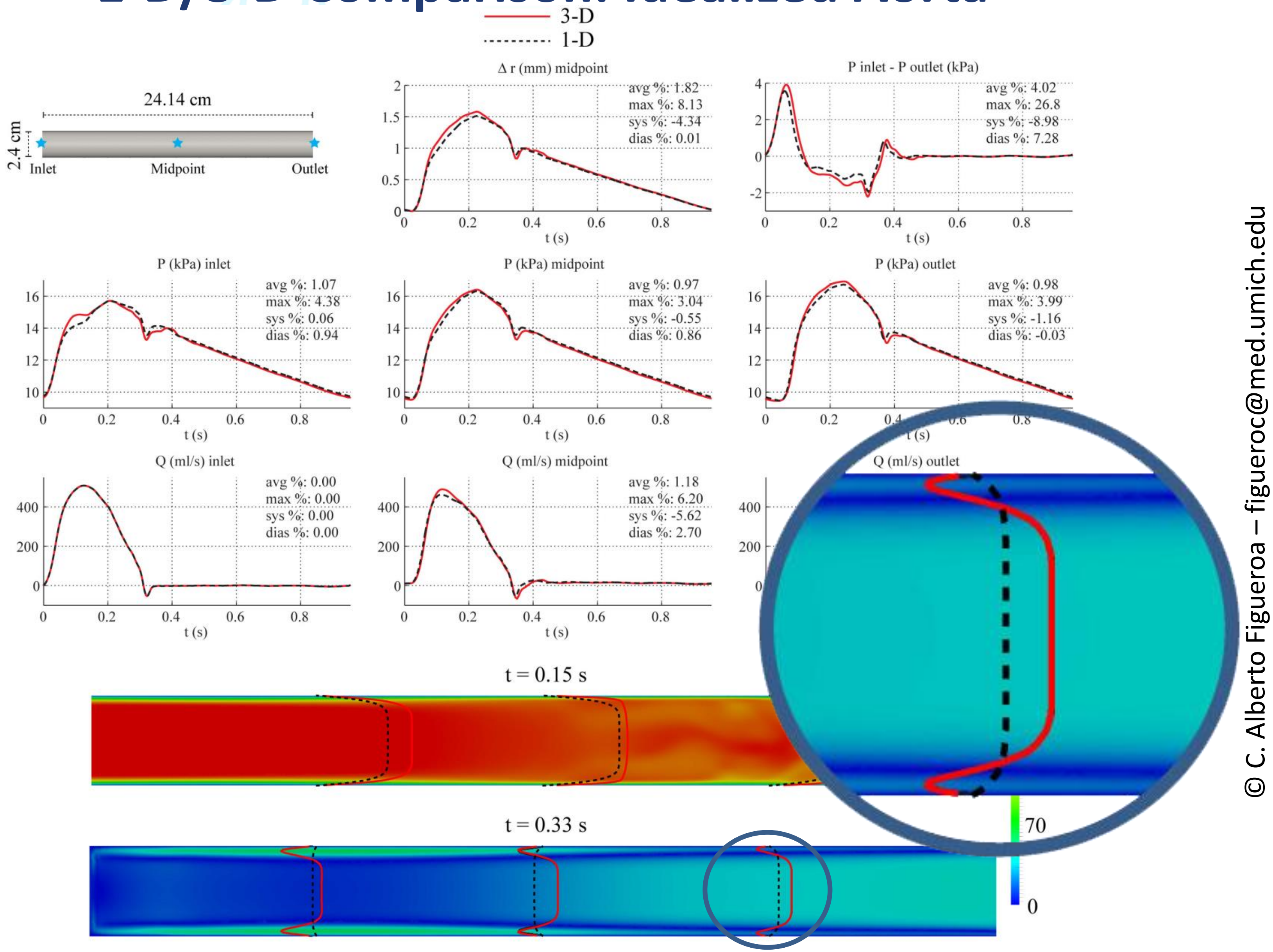
# 1-D/3-D Comparison: Idealized Aorta

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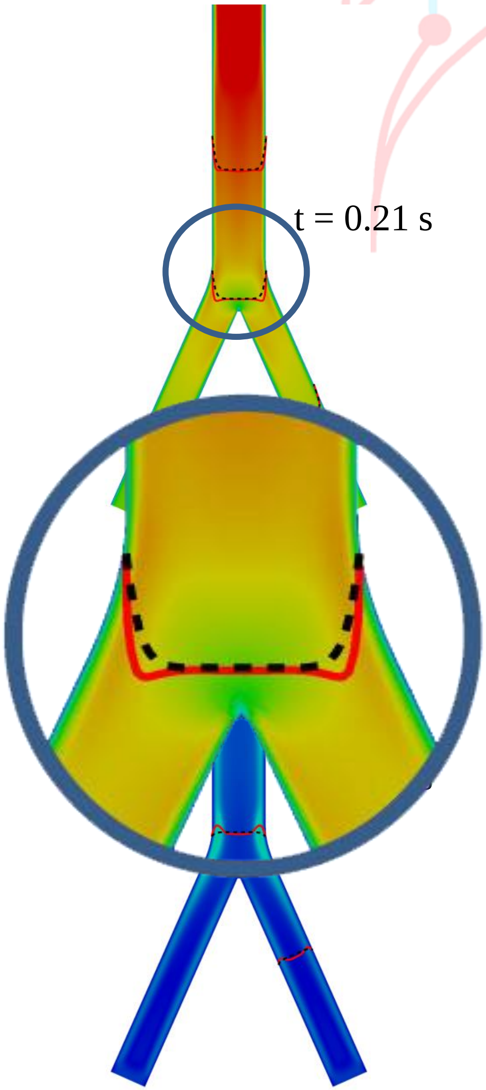
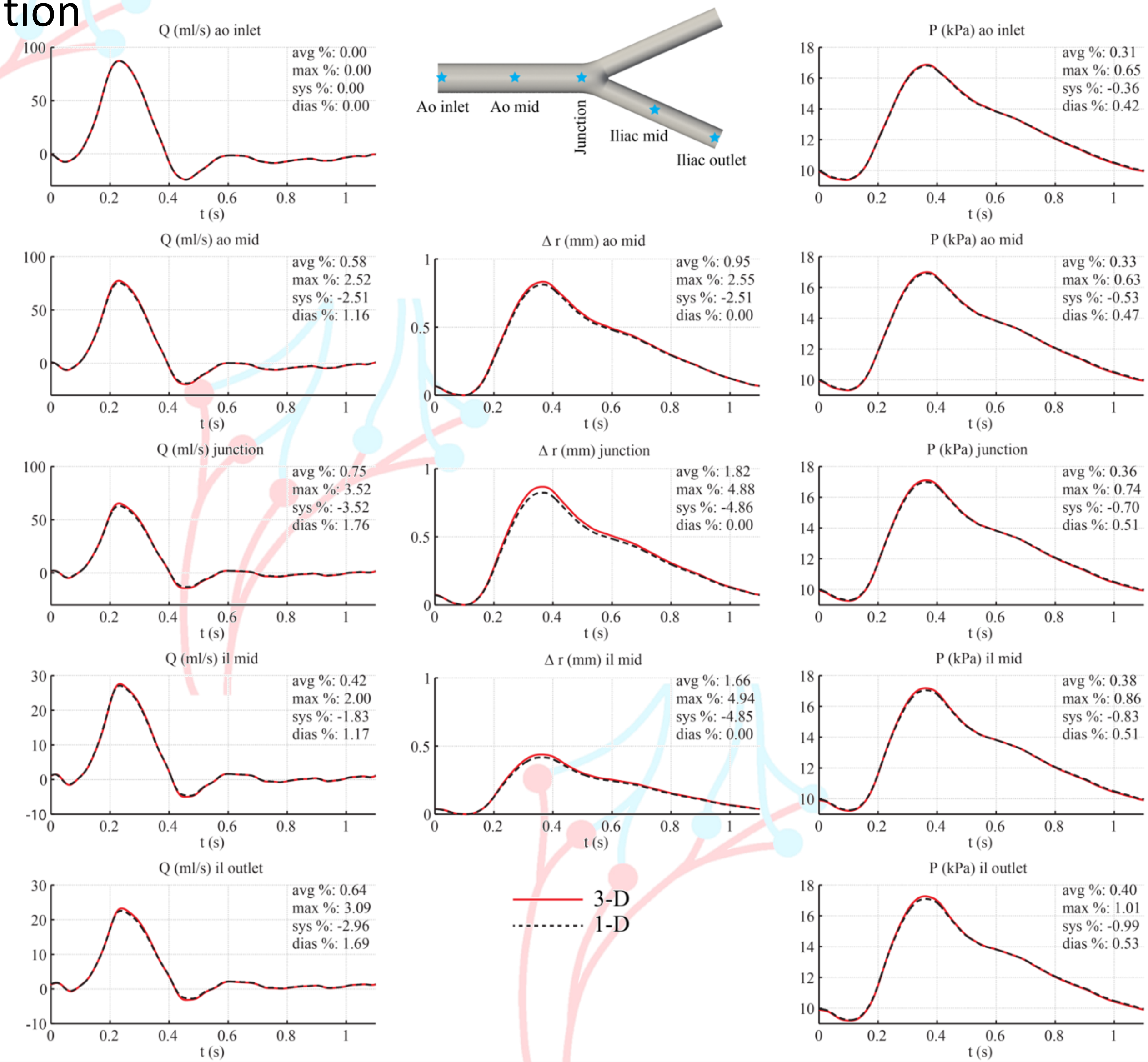
# 1-D/3-D Comparison: Idealized Bifurcation

Idealized aortic bifurcation

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# 1D/3D Comparison: % Errors in Flow and Pressure

| Cases | Flow | Pressure |
|---|---|---|
| straight carotid | 0.31 | 0.22 |
| tapered carotid | 0.38 | 0.34 |
| straight aorta | 1.74 | 0.98 |
| tapered aorta | 1.9 | 1.22 |
| larger diameter aorta | 1.62 | 0.64 |
| low-flow aorta | 1.58 | 0.75 |
| curved aorta (1 plane) | 1.91 | 0.97 |
| curved aorta (3 planes) | 1.92 | 1 |
| aortic bifurcation | 0.64 | 0.4 |

Good agreement between 1D and 3D

On average, relative errors less than 2% over cardiac cycle

Largest errors near peak systole

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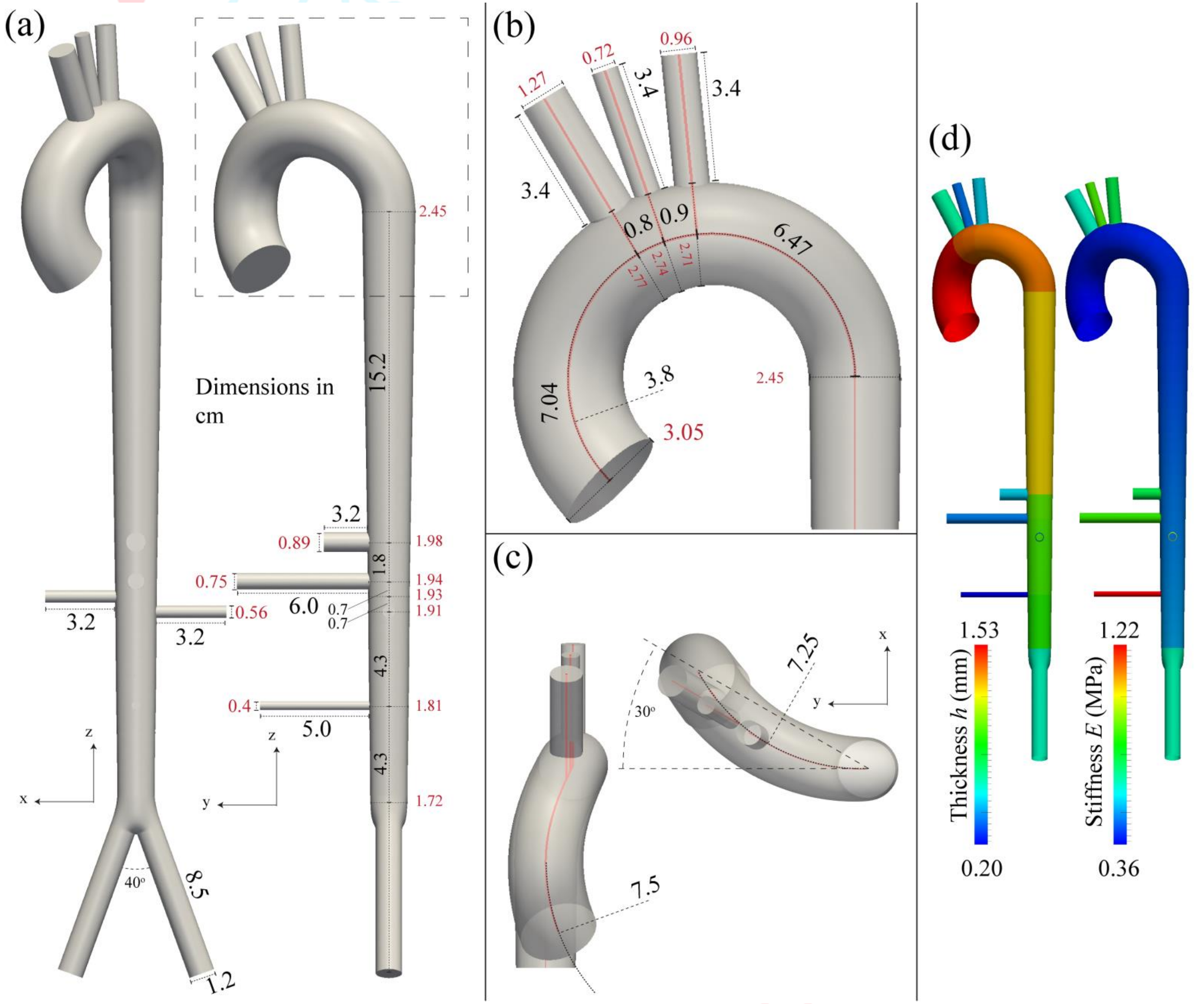
# 1D/3D Comparison: Idealized Full Aorta

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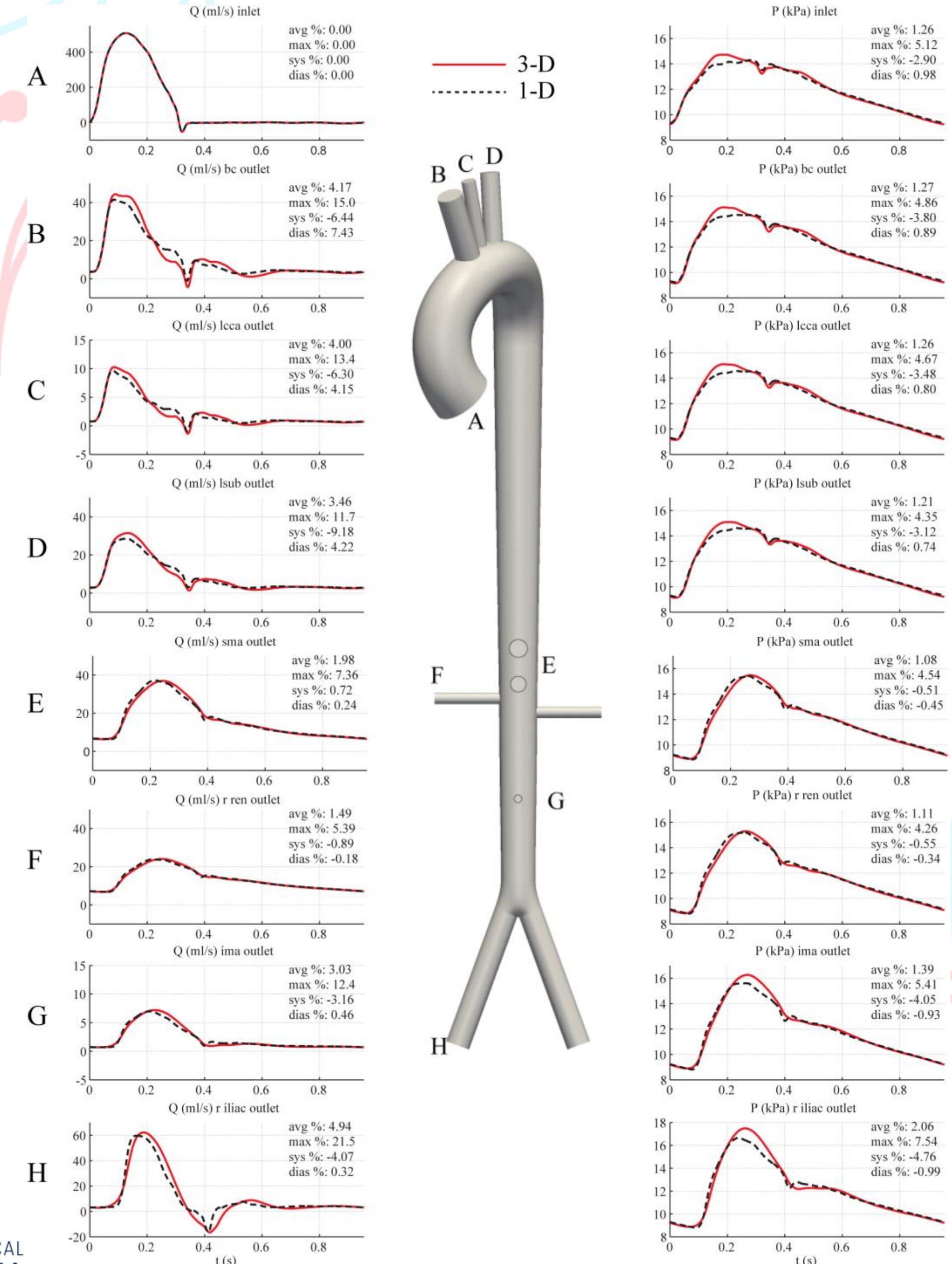
# 1D/3D Comparison: Idealized Full Aorta

Outlet Flows




Outlet Pressures

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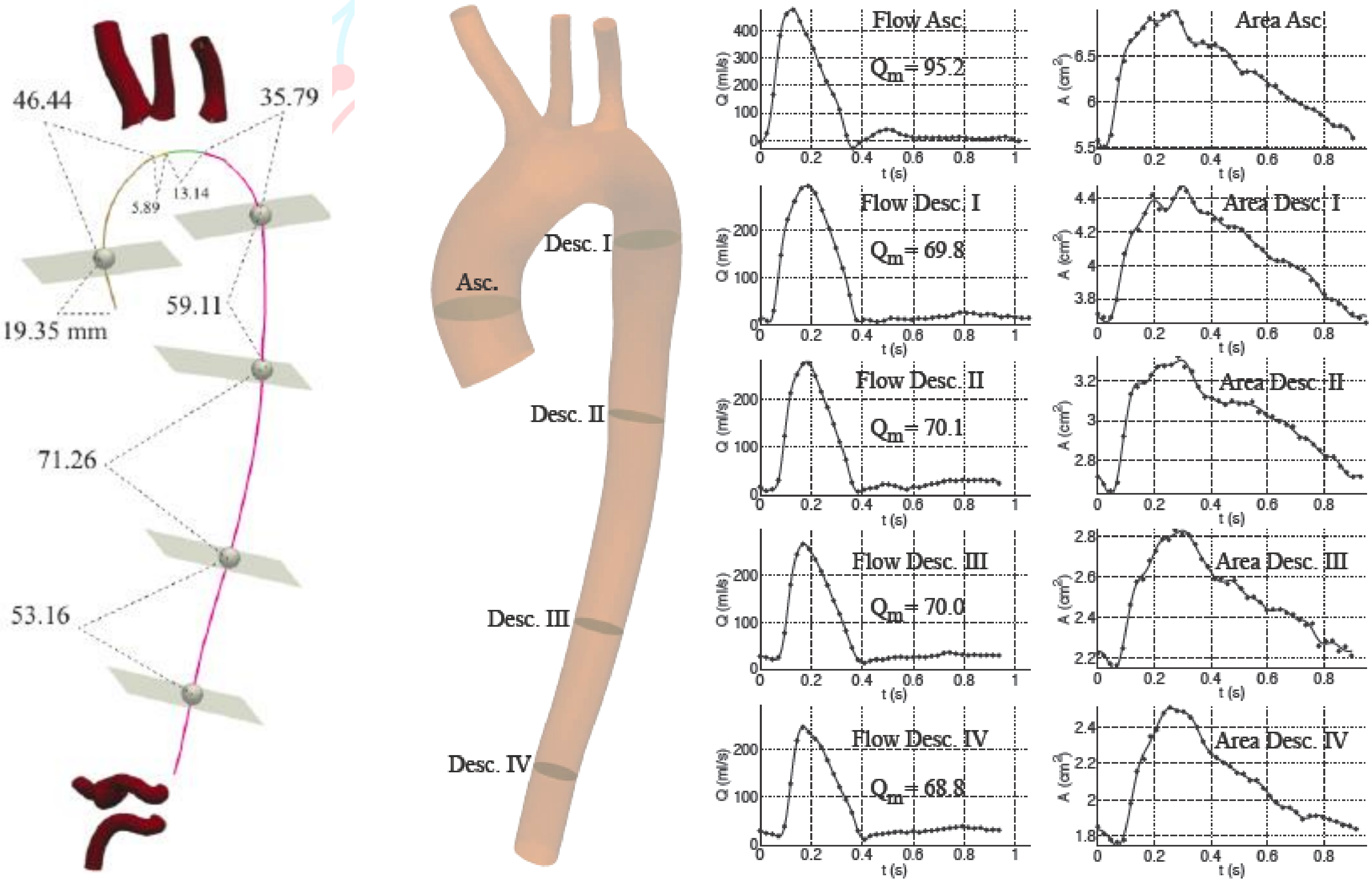
# 1D/3D Comparison: Patient-Specific Aorta




Alastruey, Xiao, Schaeffter, Figueroa, In preparation

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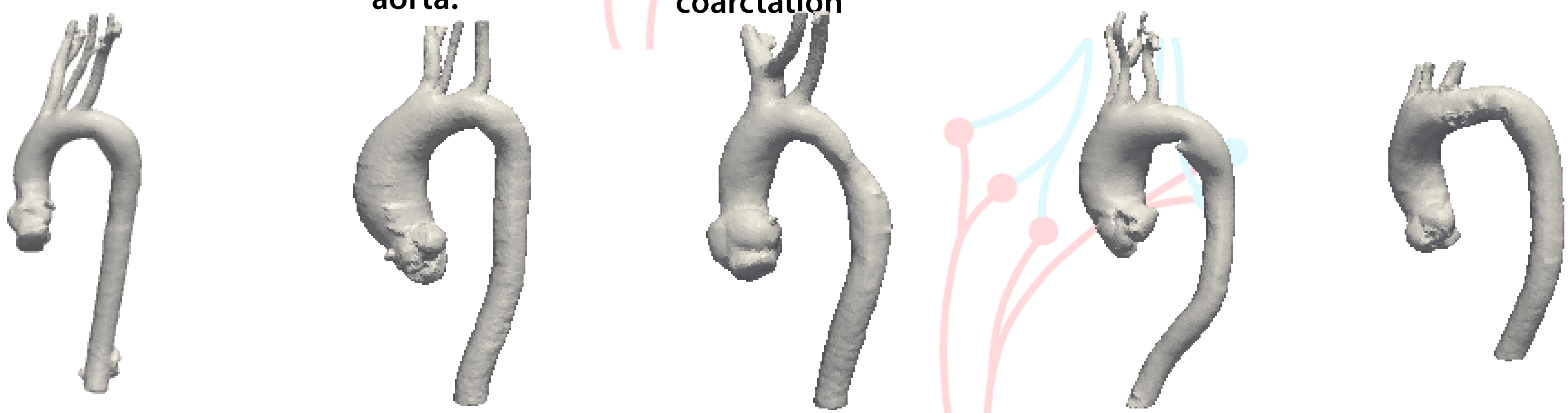
# So far it's all been outflow BCs… What about the wall?

**Methods for <u>Non-Invasive</u> Assessment of Arterial Stiffness**

| 37yo male | 48yo male | 49yo male | 55yo female | 68yo male |
|---|---|---|---|---|

| Healthy aorta | Aneurysmal dilatation of the ascending aorta. | Aneurysmal dilatation of the aortic root. Repaired coarctation | Aneurysmal dilatation of the ascending aorta | Calcification of the transverse aortic wall |
|---|---|---|---|---|



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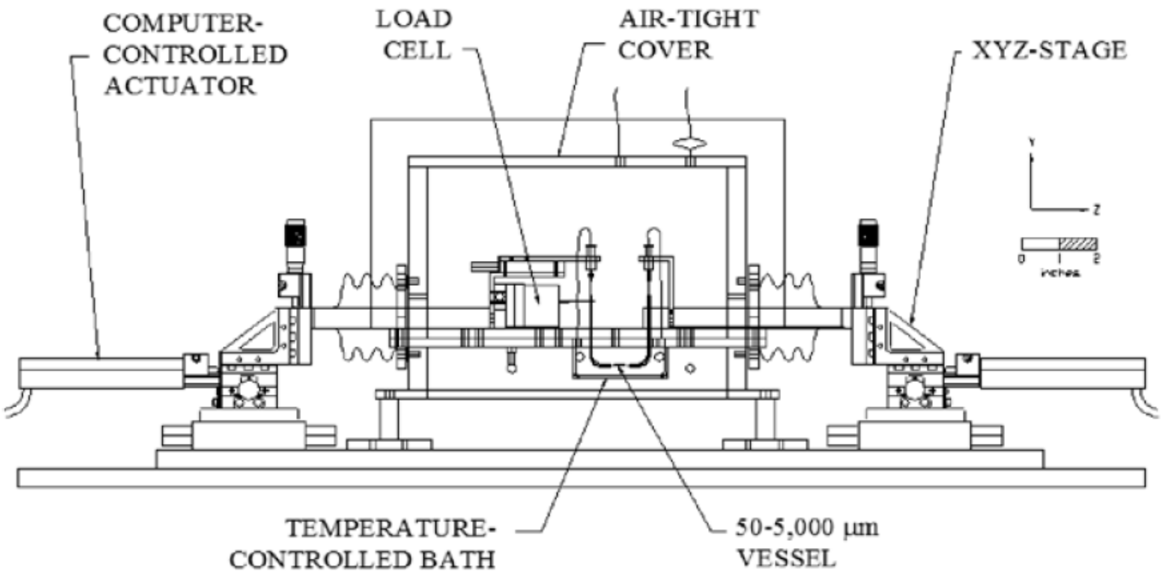
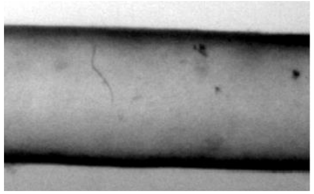
Xiao and Figueroa, in preparation

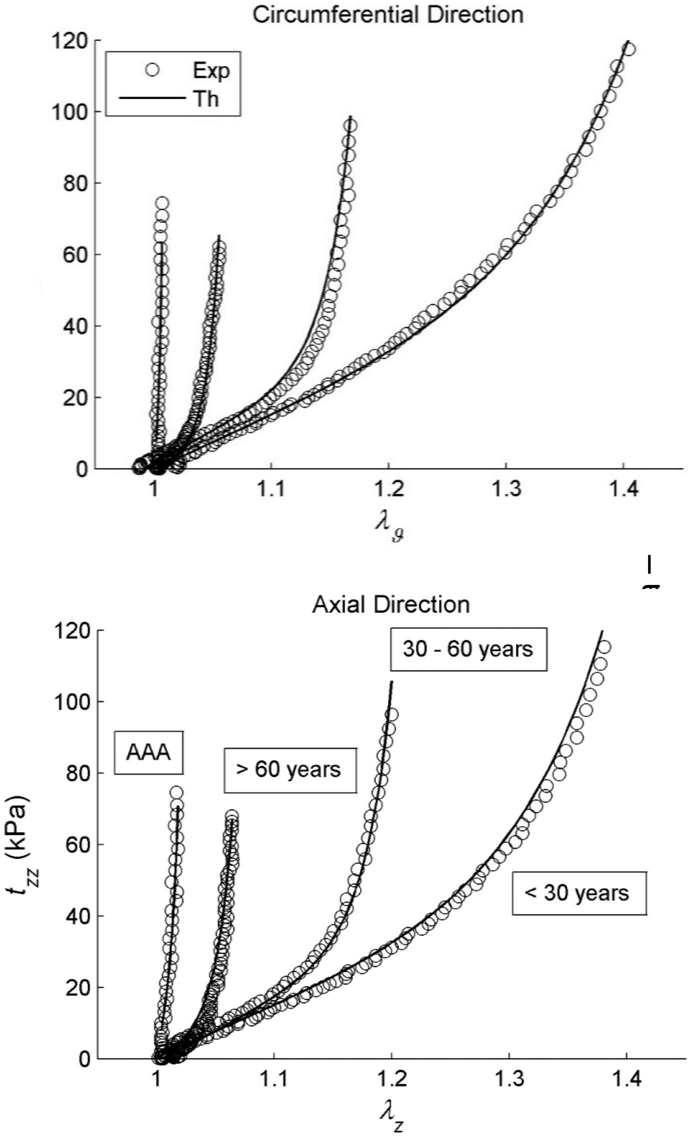
# Methods: Image-based Modeling of Hemodynamics

**Methods for <u>Invasive</u> Assessment of Arterial Stiffness**



Gleason et al., J Biomech Eng 2004




Ferruzzi et al., J Roy Soc Inter 2010

# Case study: Pressure Gradients in Aortic Coarctation

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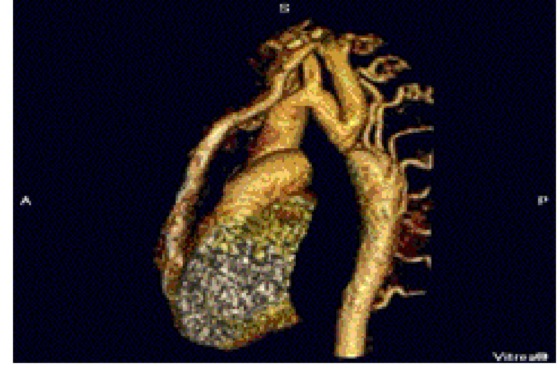
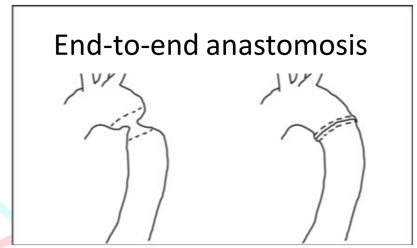
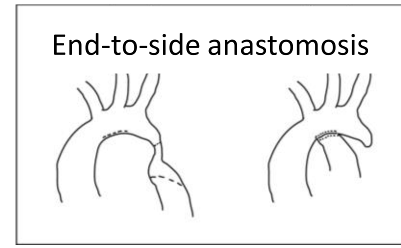
- **Aortic Coarctation (CoA)**
  - 8%-11% of congenital heart defects
    (10 000 patients annually in Western world)
  - Treatment: alleviate blood pressure (BP) gradient through the coarctation
  - Open repair or stenting






- **Diagnosis and treatment planning: importance of BP metrics:**
  - BP at rest:
    - Catheter-driven transducer (accurate but **invasive**)
    - Sphygmometer (less accurate but non-invasive)
    - Doppler ultrasound imaging (Bernoulli's equation)
  - BP at stress (pharmacologically-induced):
    - Catheter-driven transducer (accurate but **invasive**)
  - Current putative treatment guideline: **BP gradient > 20 mmHg at rest**

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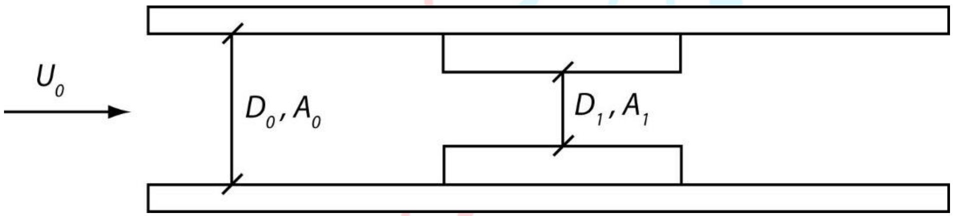
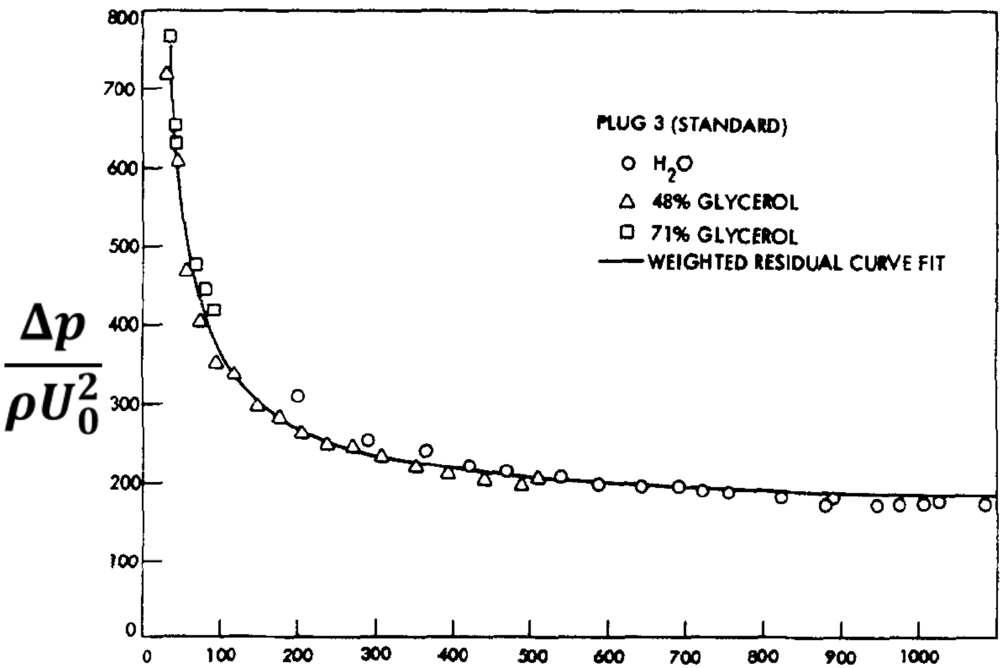
# Pressure gradient (drop) through a stenosis




Seeley & Young, J Biomech, 1976




$$Re = \frac{D_0 U_0}{\nu}$$

$U_0$ : mean velocity unobstructed tube

$D_0$ , $A_0$ : Diameter/Area unobstructed tube

$D_1$ , $A_1$ : Diameter/Area obstructed tube

Reynolds number: $\boxed{Re = \frac{D_0 U_0}{\nu}}$

$\nu$: fluid viscosity

For medium-large ***Re***,

$$\boxed{\Delta p \sim constant \cdot \rho U_0^2 \sim constant \cdot Q_0^2}$$

**Pressure gradient has a complex, nonlinear dependency on flow**

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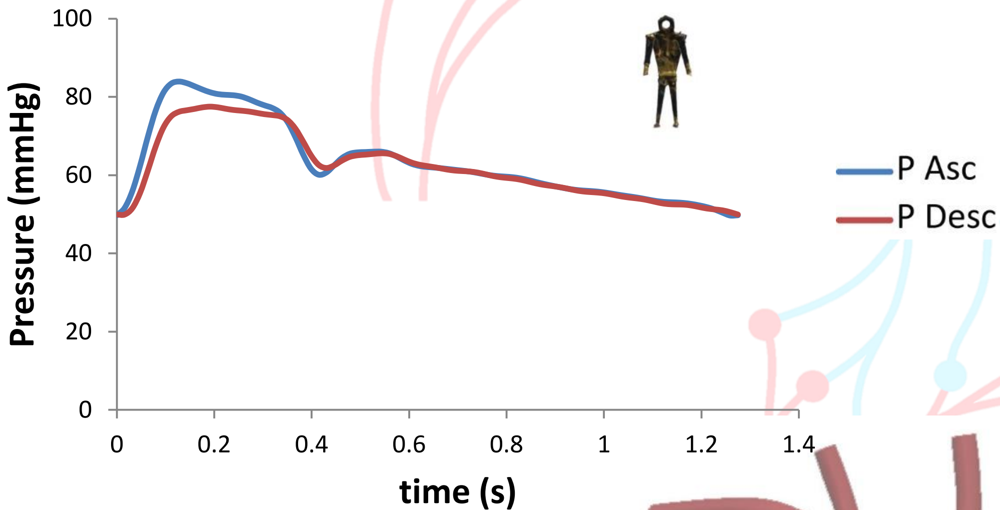
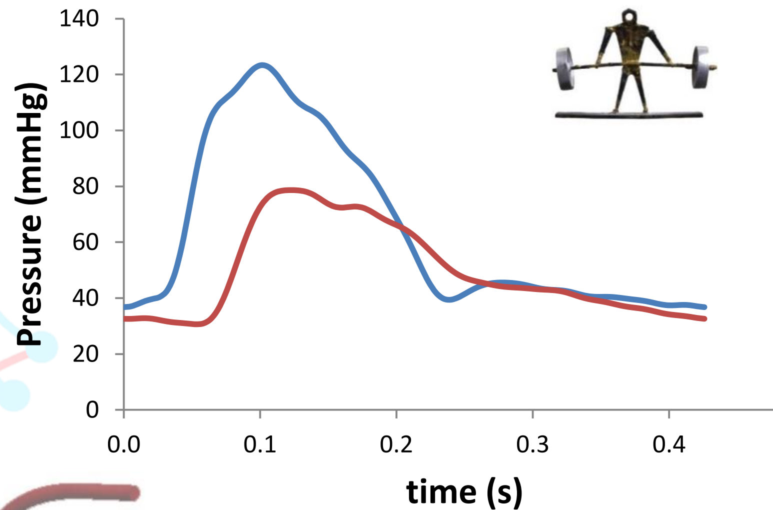
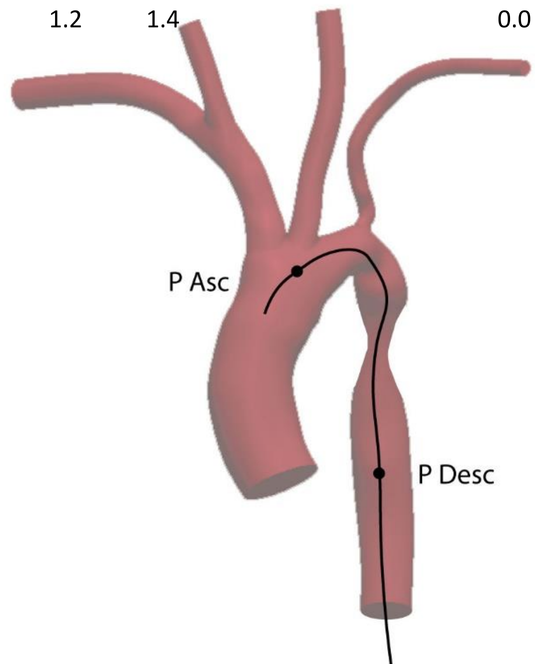
# Pressure gradient (drop) through a coarctation

- Pressure wire measurements at rest and stress

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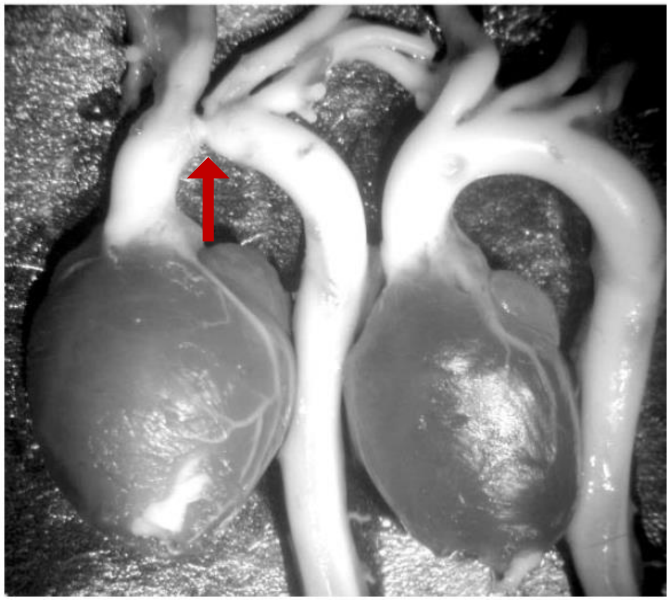
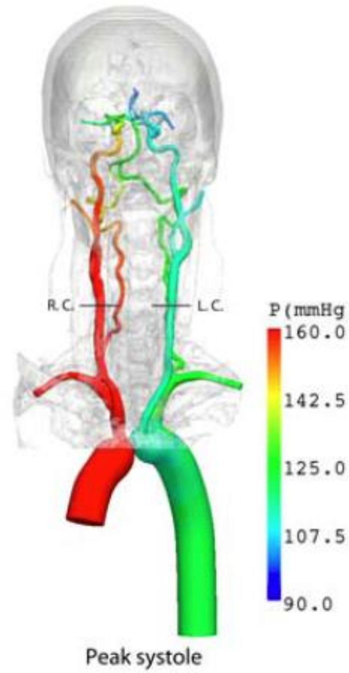
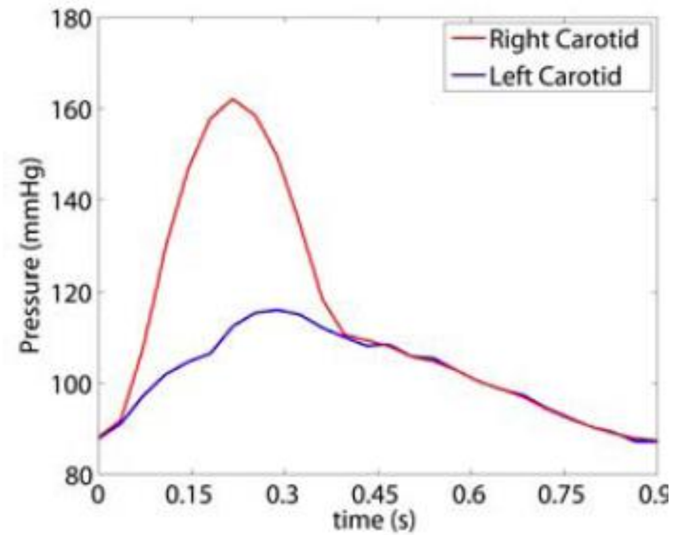
# Implications of abnormal pressure indices

- Lessons learned from animals models of hypertension



Li et al., Ultrasound in Med and Biol 2003




Coogan, Humphrey, Figueroa, Biomed & Model Mechanob 2013

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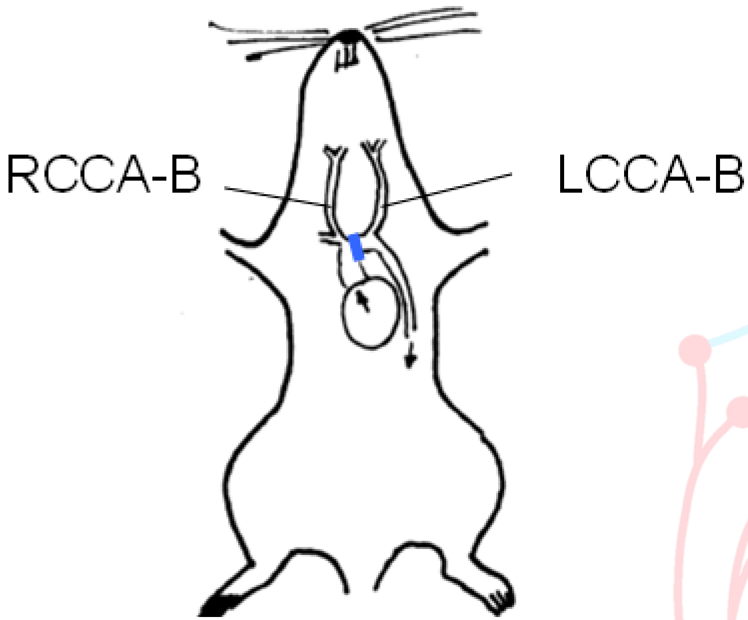
- Transverse **aortic banding** revealed that **vessel remodeling (thickening and stiffening**) is strongly correlated with changes in **pressure pulse**

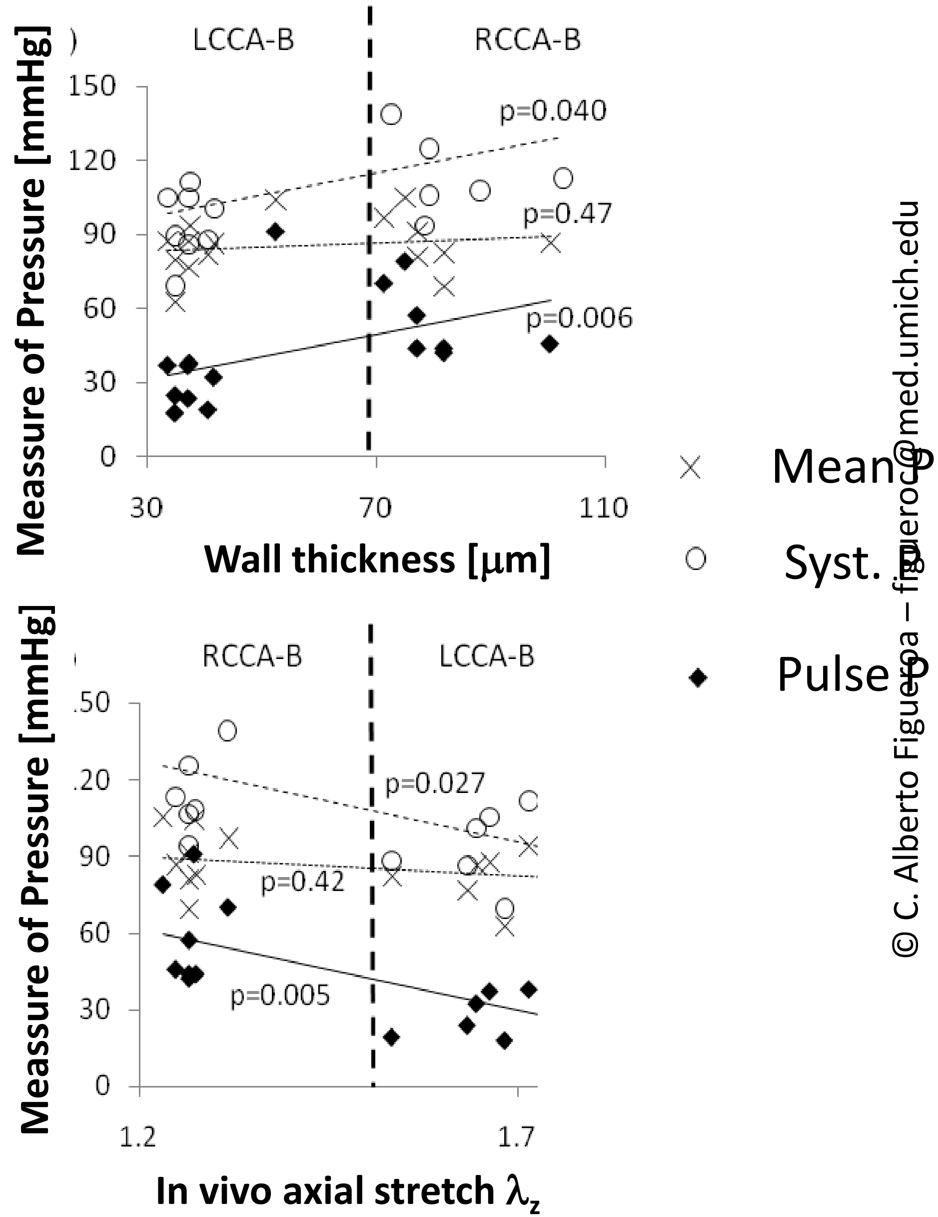
- Short time-courses also showed **marked changes in vascular structure**

# Implications of abnormal pressure indices




Eberth et al., J Hypertens 2009

- **Pulse pressure** is associated with **wall thickening**
- **Pulse pressure** is associated with **loss of axial stretch**

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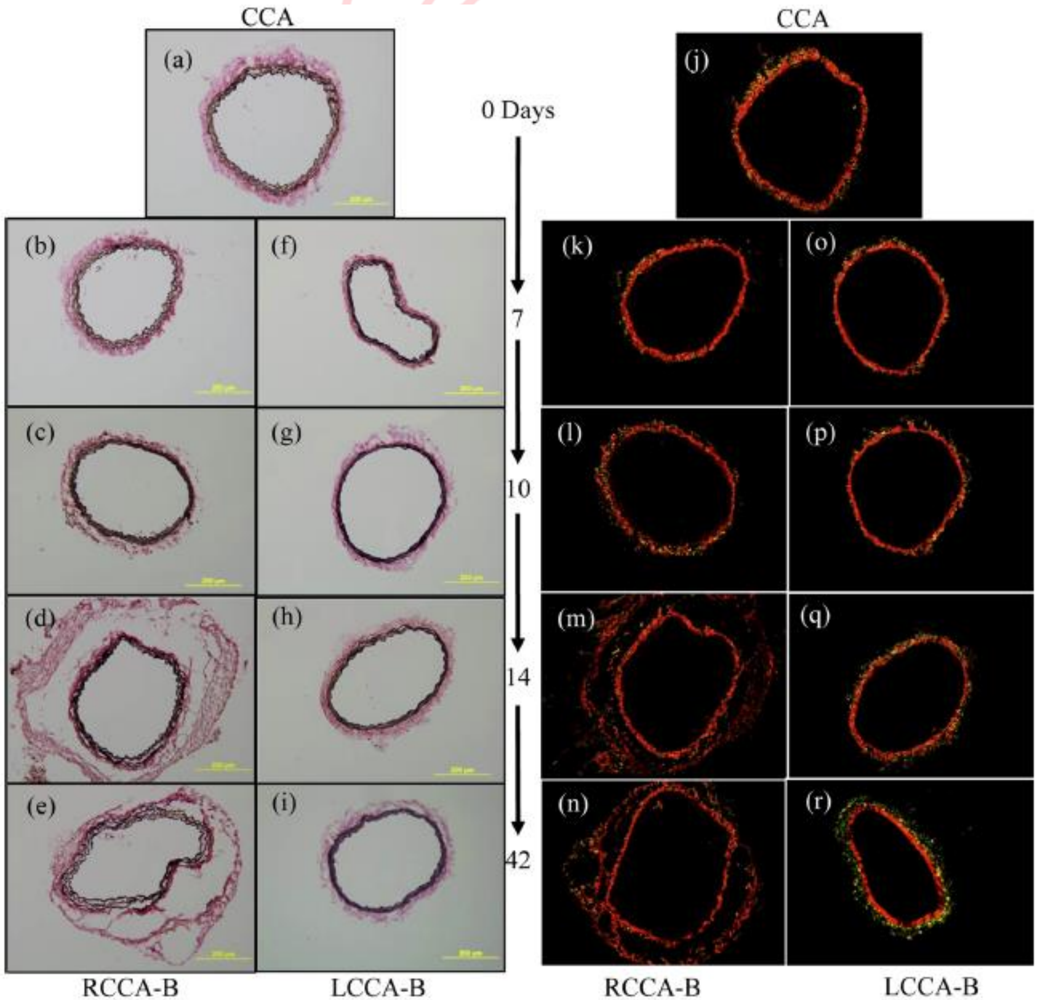
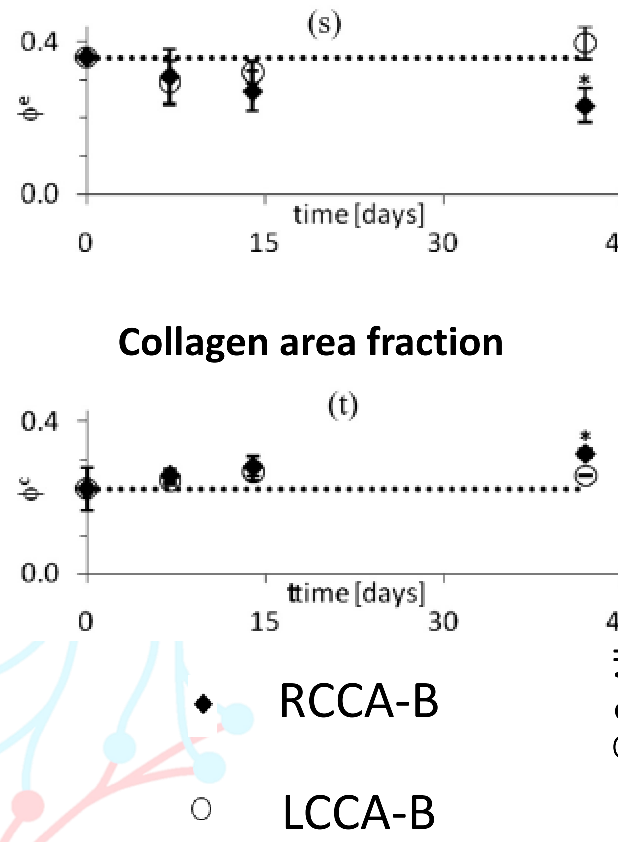
# Implications of abnormal pressure indices

- **Pulse pressure** is associated with **loss of elastin** and **collagen production**.




**Elastin area fraction**

**Collagen area fraction**




Eberth et al.,
Am J Physiol Heart Circ Physiol 2010

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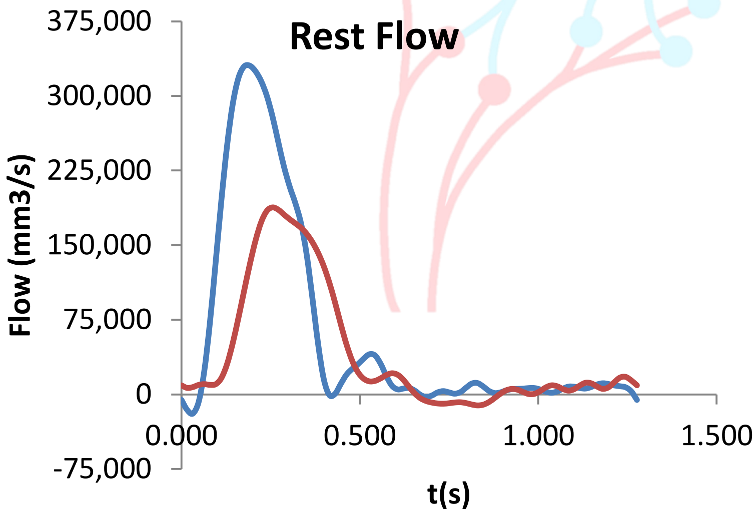
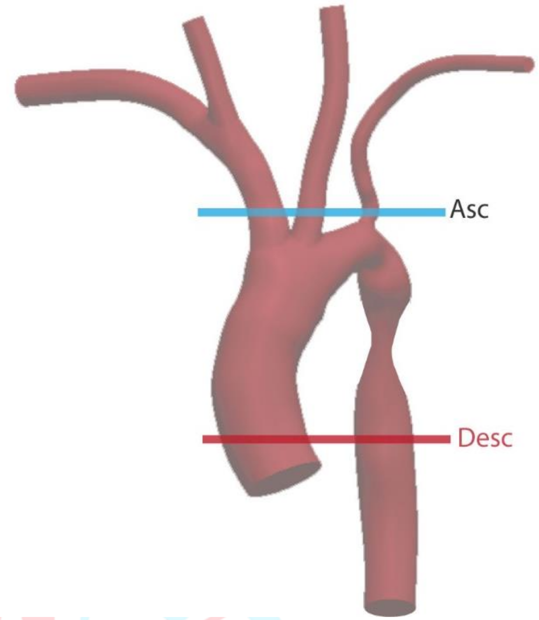
# CMR & pressure data in repair CoA patients at rest & stress

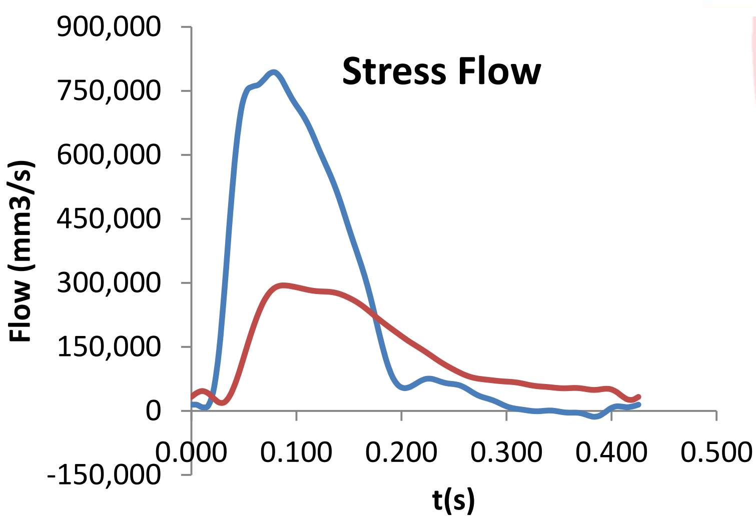
## 2D PC-MRI data





| | AscAo | Innominate | LCC | LS | DiaphAo |
|---|---|---|---|---|---|
| Total Flow (L/min) | 3.71 | 0.624 | 0.312 | 0.364 | 2.41 |
| % AscAo | 100 | 17 | 8 | 10 | 65 |




| | AscAo | Innominate | LCC | LS | DiaphAo |
|---|---|---|---|---|---|
| Total Flow (L/min) | 13.53 | 3.38 | 0.68 | 1.49 | 7.98 |
| % AscAo | 100 | 25 | 5 | 11 | 59 |

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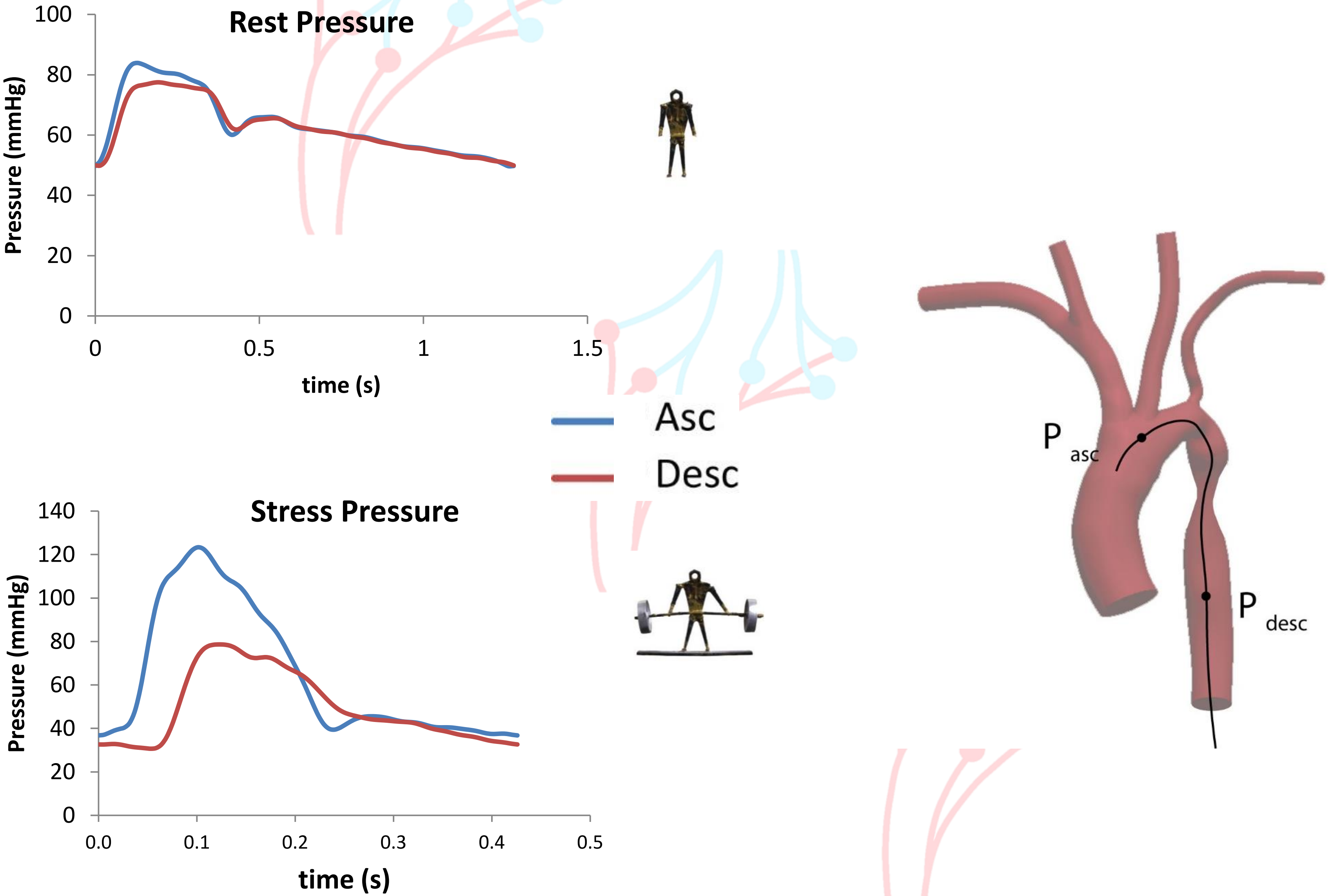
# CMR & pressure data in repair CoA patients at rest & stress

## Pressure wire data

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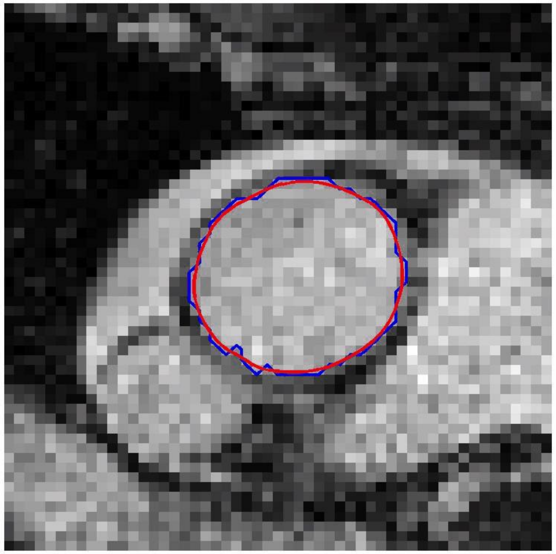
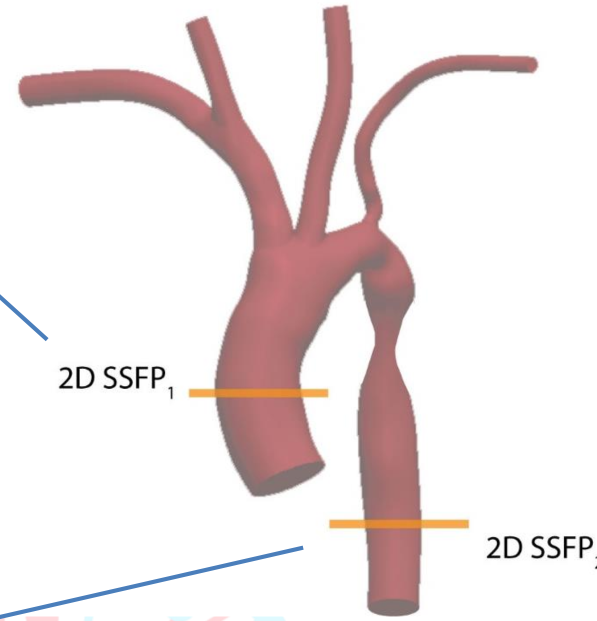
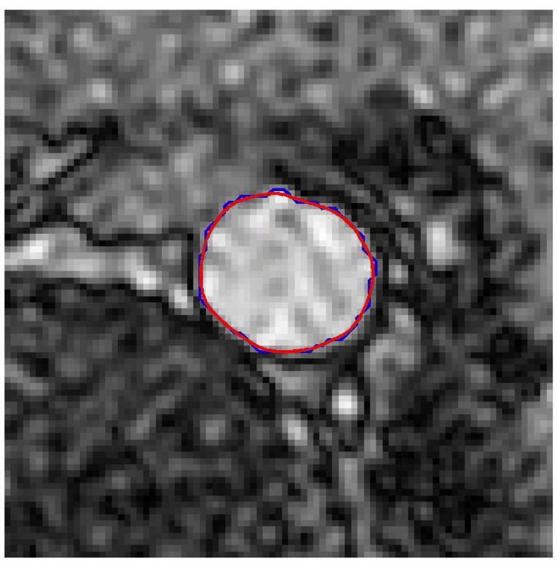
# CMR & pressure data in repair CoA patients at rest & stress

## 2D-SSFP data



**Ascending Aorta Distensibility**



**Descending Aorta Distensibility**

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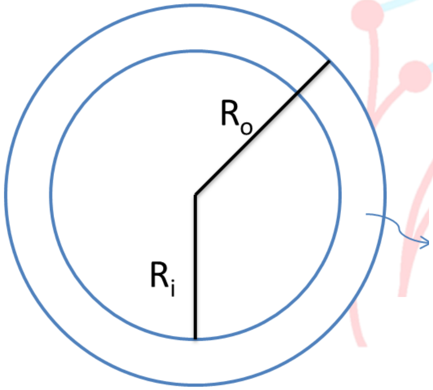
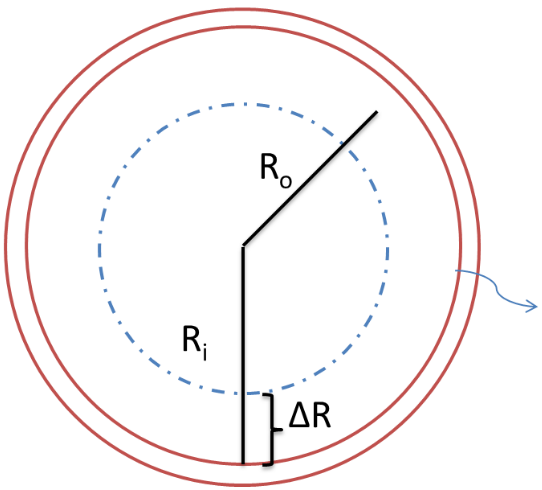
# Arterial Stiffness estimated from Pressure and Vessel Motion



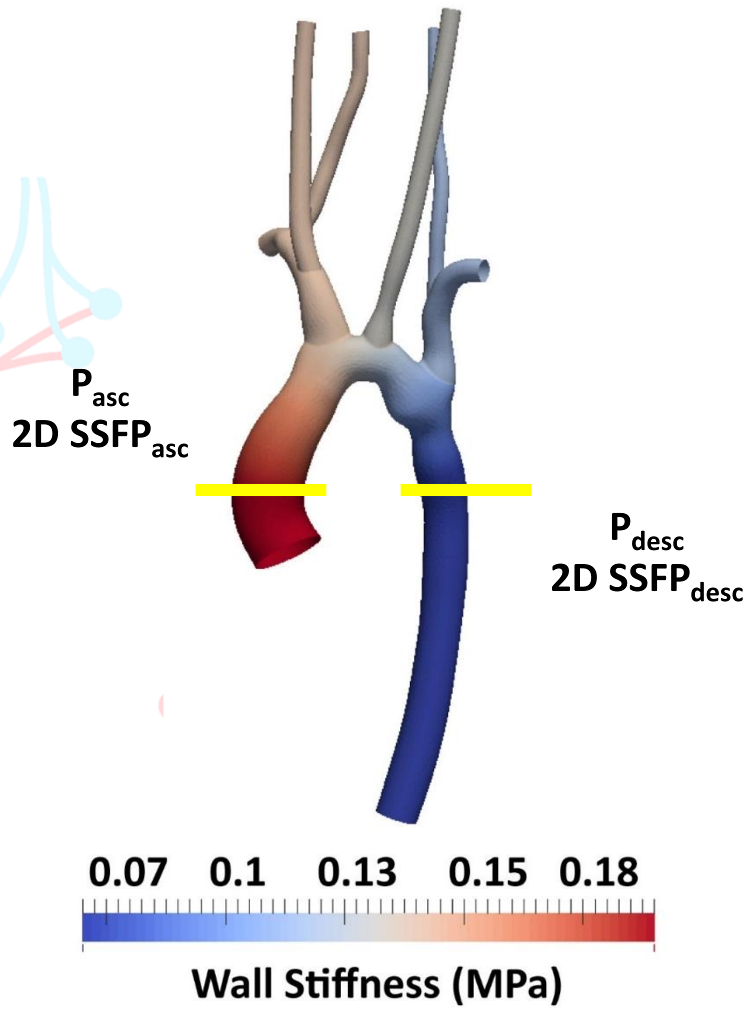

Diastolic Configuration




Systolic Configuration

$$E = \frac{1.5 \cdot \Delta P \cdot R_i^2 \cdot R_o}{\left(R_o^2 - R_i^2\right) \Delta R}$$

**Simultaneous knowledge of distensibility AND pressure is used to derived elastic properties**

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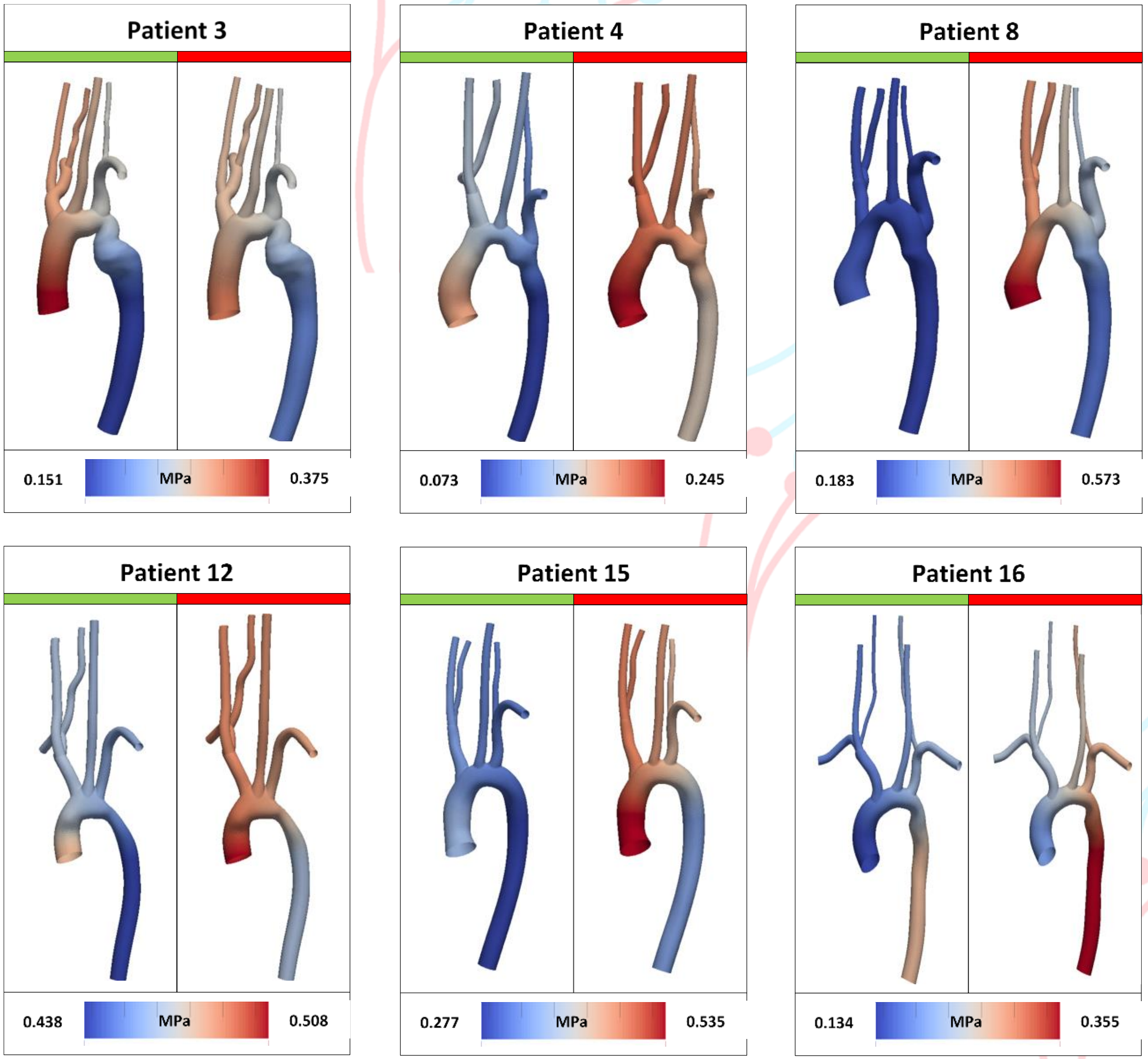
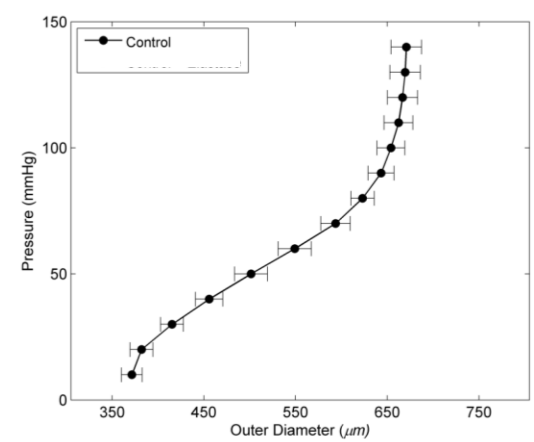
# Arterial Stiffness in repaired CoA patients at rest & stress

## Vessel stiffness increases with stress (pressure)

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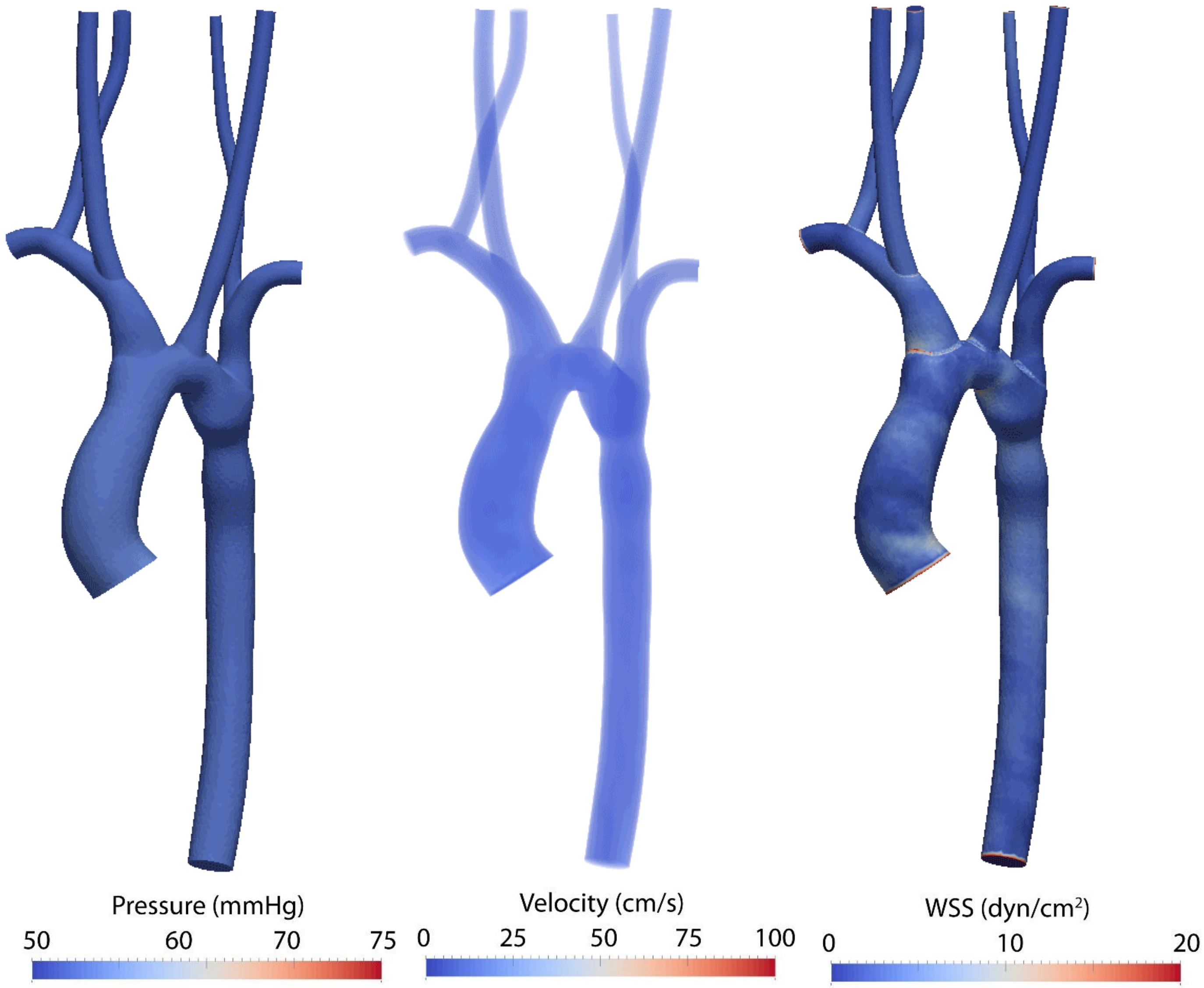
# Results – CFD predictions

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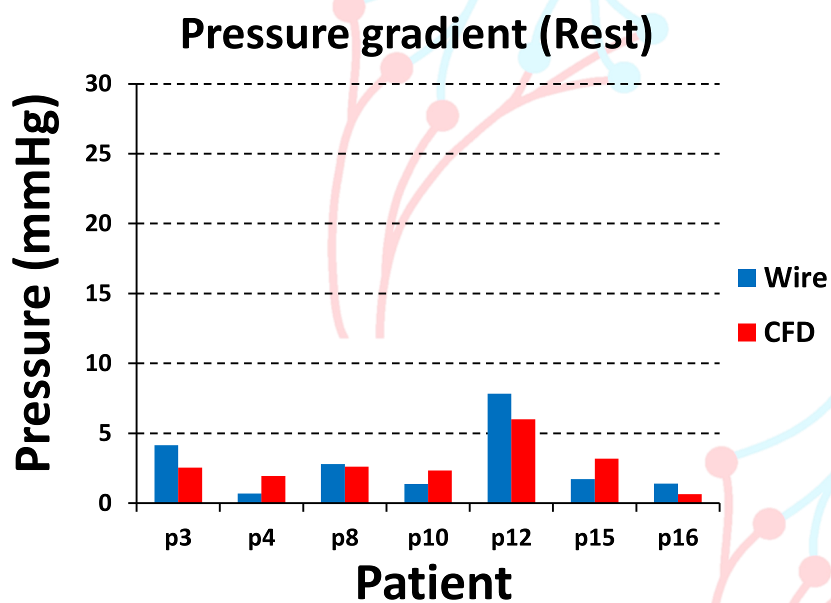
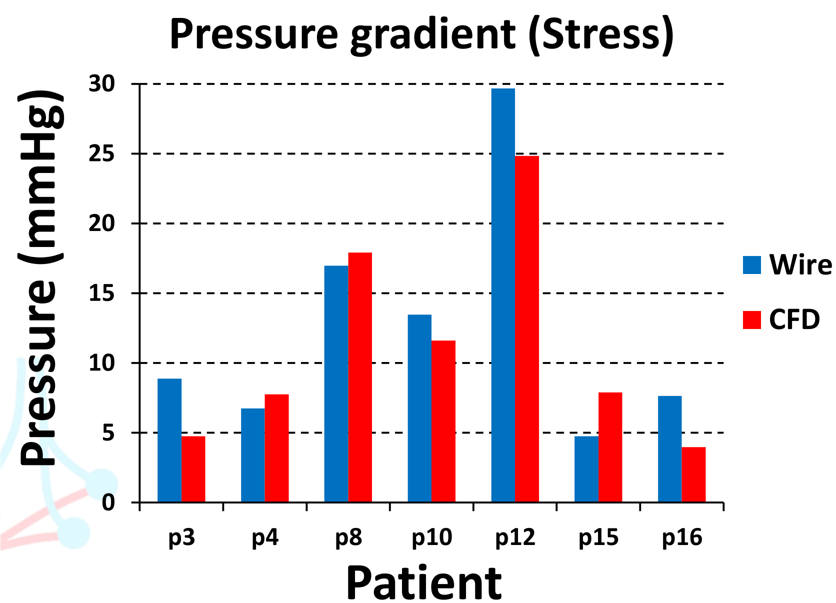
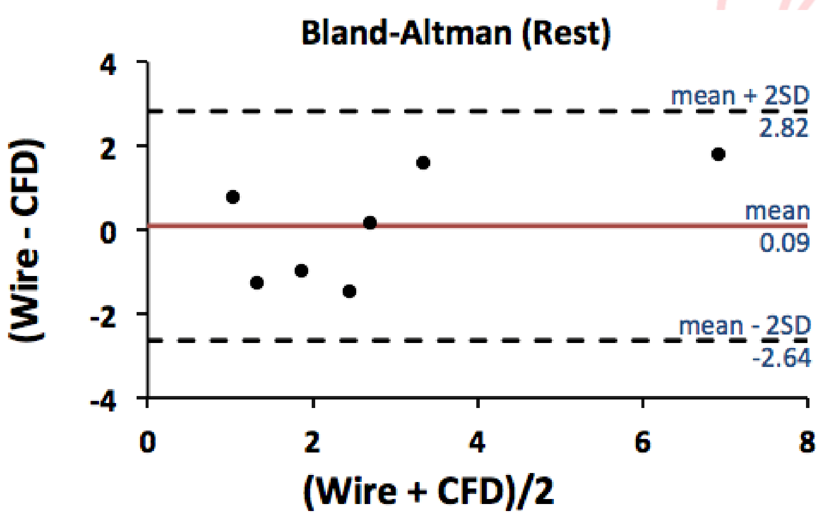
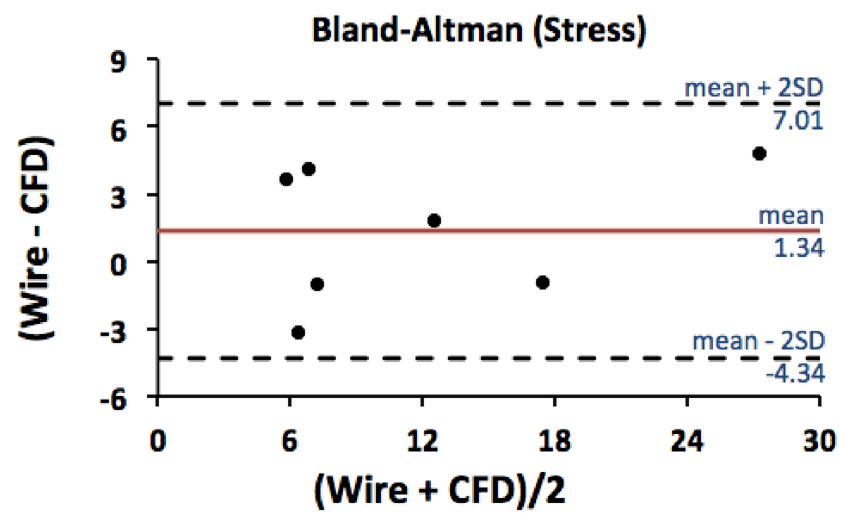
# Validation of computational predictions

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# Filtering Techniques for Parameter Estimation

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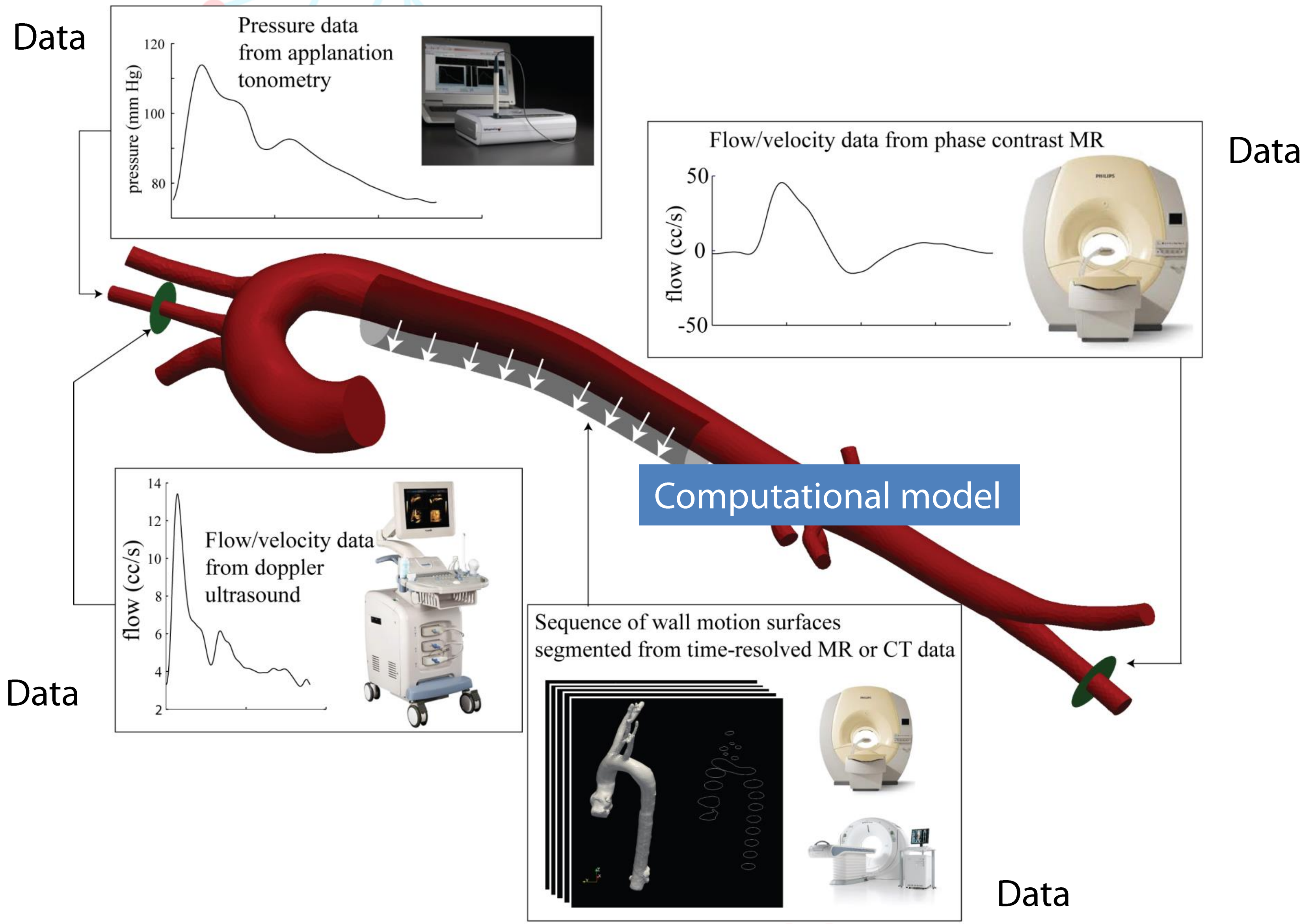
# 3D Data Assimilation Framework

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# Data Assimilation Framework

- Data assimilation: combine mathematical model with real-world measurements to produce estimate of "true state" of system (including the values of the model parameters)

- We adopted a sequential approach based on a reduced order unscented Kalman filter[1,2,3]

- The goal of this work is to explore applications in blood flow simulation in systemic arterial networks


1. Moireau et al. *ESAIM: Control, Optimisation and Calculus of Variations*. 2010
2. Chabiniok et al. *BMMB*. 2012
3. Bertoglio et al. *IJNMBE.* 2012


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# The Model and Augmented State

- The model (forward problem)

model operator (i.e. Navier-Stokes)

$$\dot{X} = A(X)$$

state

$$X(0) = X_0 + \zeta^X$$

initial uncertainty/error

- Augmented state

$$\chi = \begin{pmatrix} X \\ \theta \end{pmatrix}$$

parameters

$$\dot{\chi} = \mathcal{A}(\chi)$$

$$\chi(0) = \chi_0 + \zeta^\chi$$

Includes uncertainty in the parameters

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# State Variables and Parameters

velocities, pressures, accelerations, wall boundary displacements, 0-D model states

$$X_n = \{v_n, p_n, \dot{v}_n, u_n, P_{\mathrm{0D}}, \theta_n\}_n^T$$

Model parameters

$$\theta_n = [\underbrace{Eh^{(1)}, Eh^{(2)}, \ldots, Eh^{(n_{\mathrm{regions}})}}_{\text{Vessel wall stiffnesses}}, \underbrace{R_2^{(1)}, R_2^{(2)}, \ldots, R_2^{(n_{\mathrm{outlets}})}}_{\text{Windkessel resistances}}, \underbrace{C^{(1)}, C^{(2)}, \ldots, C^{(n_{\mathrm{outlets}})}}_{\text{Windkessel compliances}}]$$

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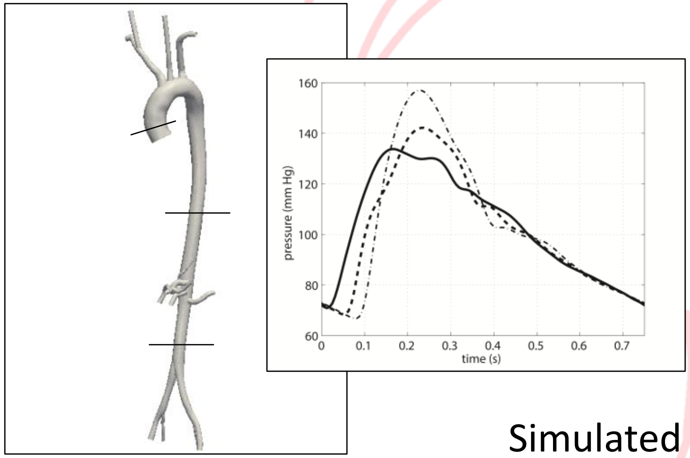
# Observation Error

$$Z = H(X) + \zeta^z$$

observation operator — $H(X)$

measurement error — $\zeta^z$



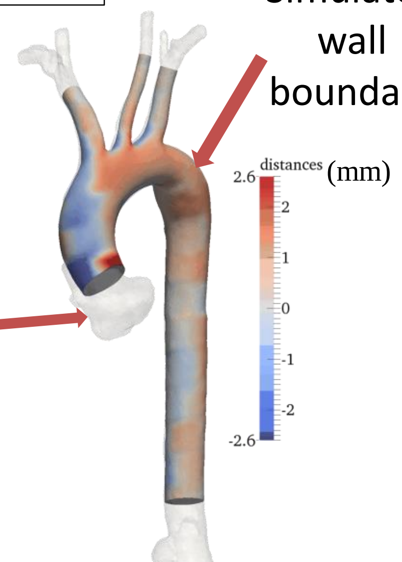

Cross-sectional averaged pressure and flow

$$H(X_n) = [Q_1, Q_2, \ldots, Q_{n_{\text{obs-Q}}}, P_1, P_2, \ldots, P_{n_{\text{obs-P}}}]_n^T,$$

$$Q_i = \int_{a_i} v(x, t_n) \cdot \vec{n} da$$

$$P_i = \frac{1}{\text{area}_i} \int_{a_i} p(x, t_n) da$$

Simulated wall boundary




Segmented data

Distance to a sequence of wall motion surfaces (interpolated linearly in time)

$$Z - H(X_n) = D(X_n) = \alpha_k \text{dist}(x + u, S_k) + (1 - \alpha_k)\text{dist}(x + u, S_{k+1})$$

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# Data-driven Estimation

**Goal:**
**Minimize discrepancy between model observations and real measurements**

$$\min_X J(X)$$

$$J(X) = \int_0^T (Z - H(X))^\top (W)^{-1} (Z - H(X))dt + (X(0) - X_0)^\top (P)^{-1} (X(0) - X_0)$$

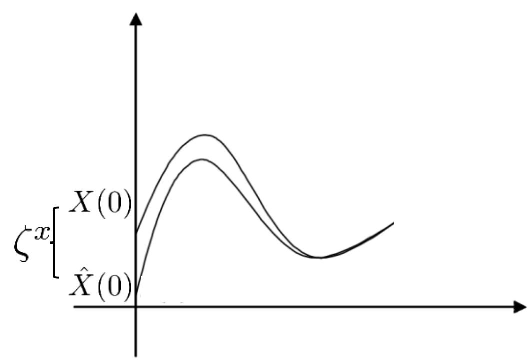
- "Variational" approach
  - Gradient-based minimization
  - Adjoint method

- "Sequential" approach

$$\dot{\hat{X}} = A(\hat{X}) + K\underbrace{(Z - H(\hat{X}))}_{\text{innovation}}$$

estimate

gain

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# Sequential Approaches

- Classical Kalman filter gives optimal estimates for linear models
- "Unscented" Kalman filter[1] is an effective extension to nonlinear models
- Reduced-order unscented Kalman filter[2] (ROUKF) enables estimation of an uncertain subset of augmented model states (i.e. the model parameters)
- A set of ($p$+1) "sigma points" (also called particles) samples the estimation-error probability distribution at each time step ($p$ is the # of parameters)
- In practice, this means running ($p$+1) concurrent simulations

1. Julier, S. *Proceedings of the 1995 American Control Conference*, 1995
2. Moireau et al., *ESAIM: Control, Optimisation and Calculus of Variations*, 2010

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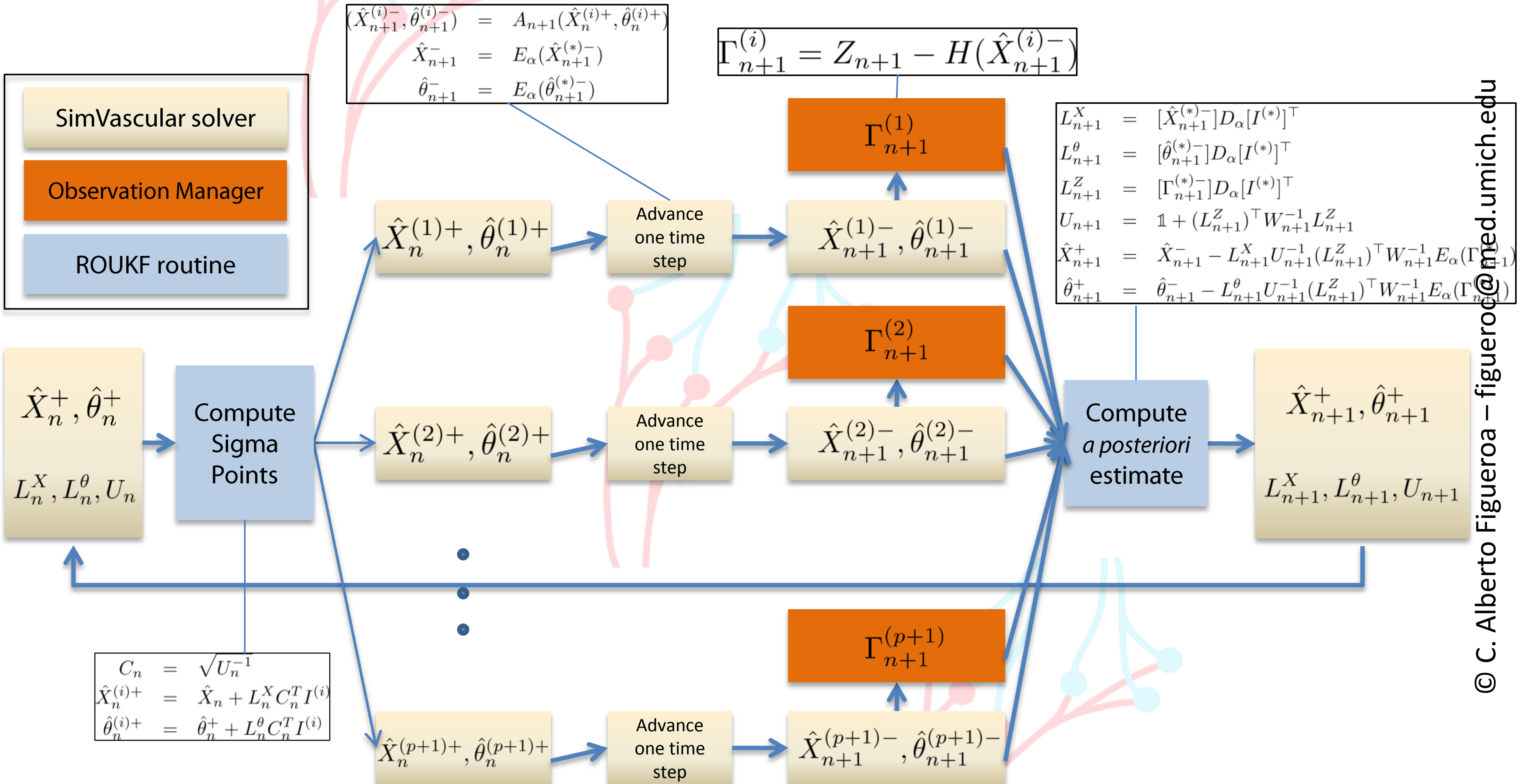
# Integration of Open-Source Data Assimilation Library

*Verdandi* *generic library for data assimilation*




$n \rightarrow n+1$

Xiao, Moireau, Schaeffter, Figueroa, in preparation

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# Application Examples

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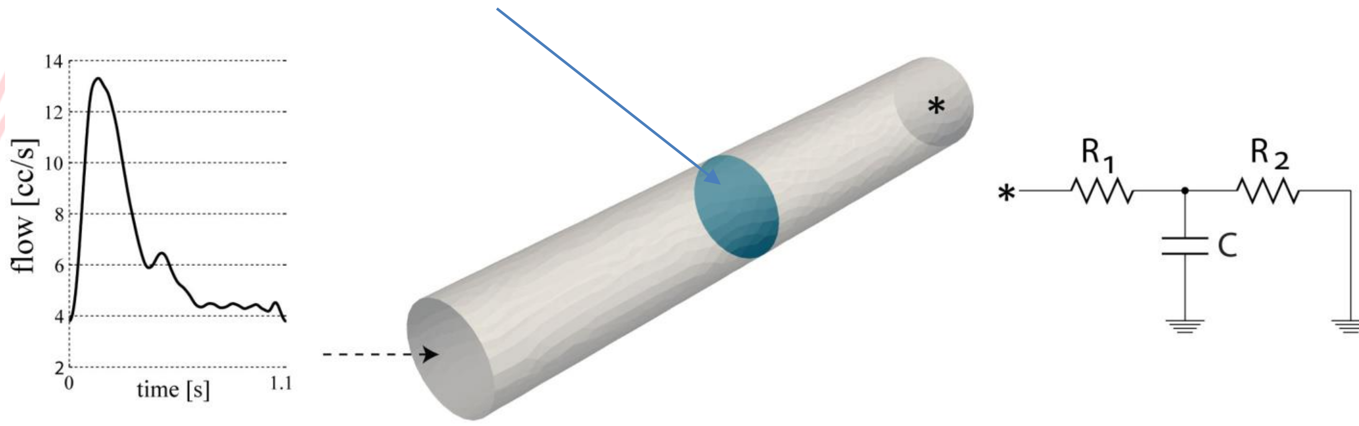
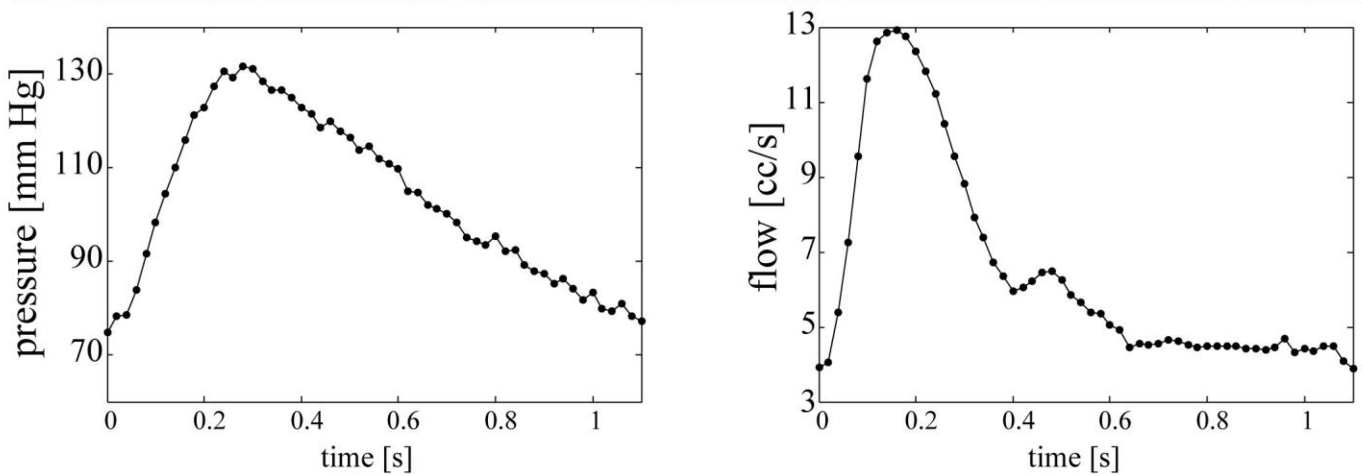
# Idealized Carotid: Estimation of Windkessel Parameters from P & Q

**Forward problem:**
Parameters values assumed to be known

Observation Plane




Extract “synthetic data” from simulation results




Synthetic pressure and flow data
+ Gaussian white noise, 40dB SNR

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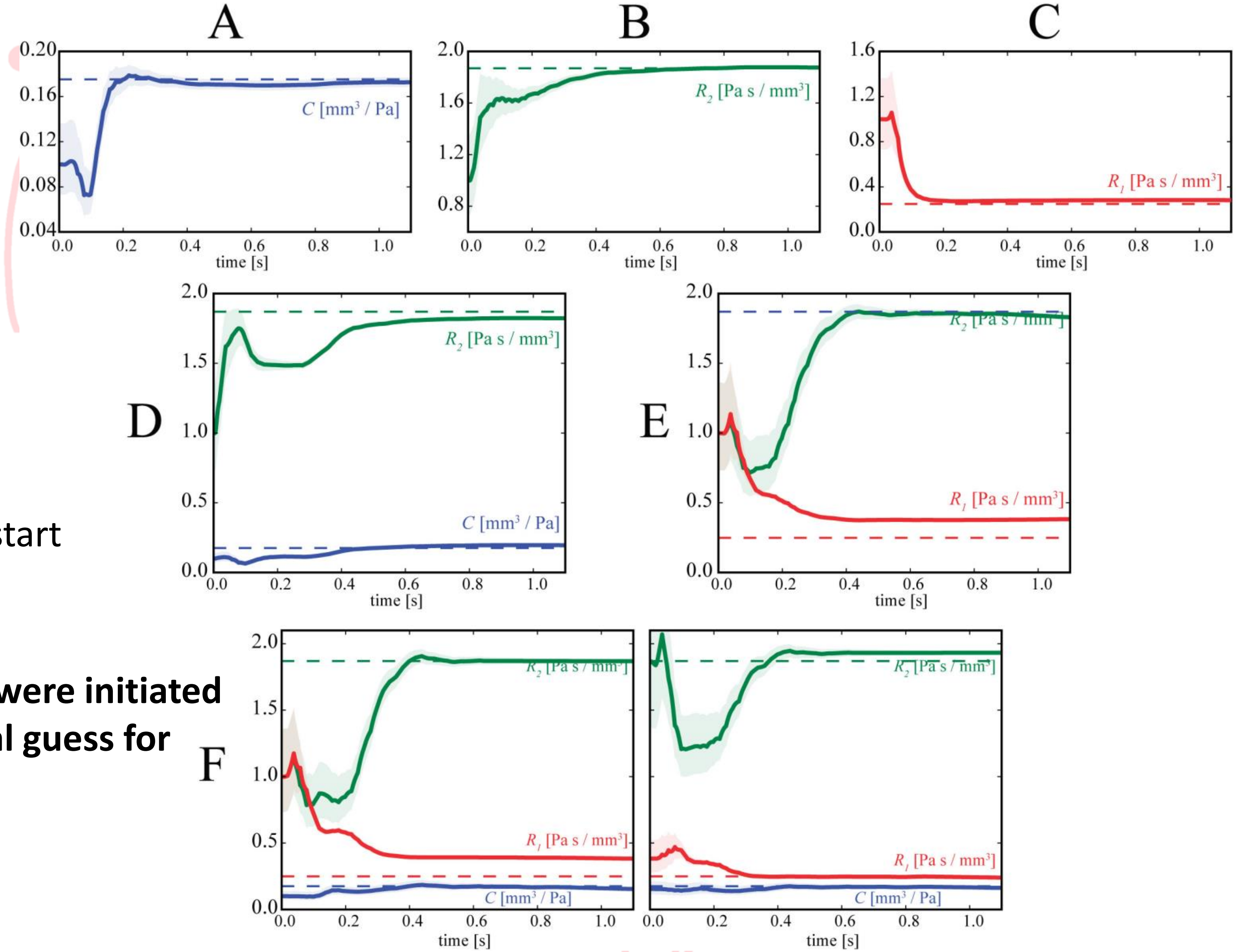
# Idealized Carotid: Estimation of Windkessel Parameters from P & Q

**7 different cases****

A: C only
B: $R_2$ only
C: $R_1$ only
D: $R_2$ and C
E: $R_1$ and C
F: all, including restart

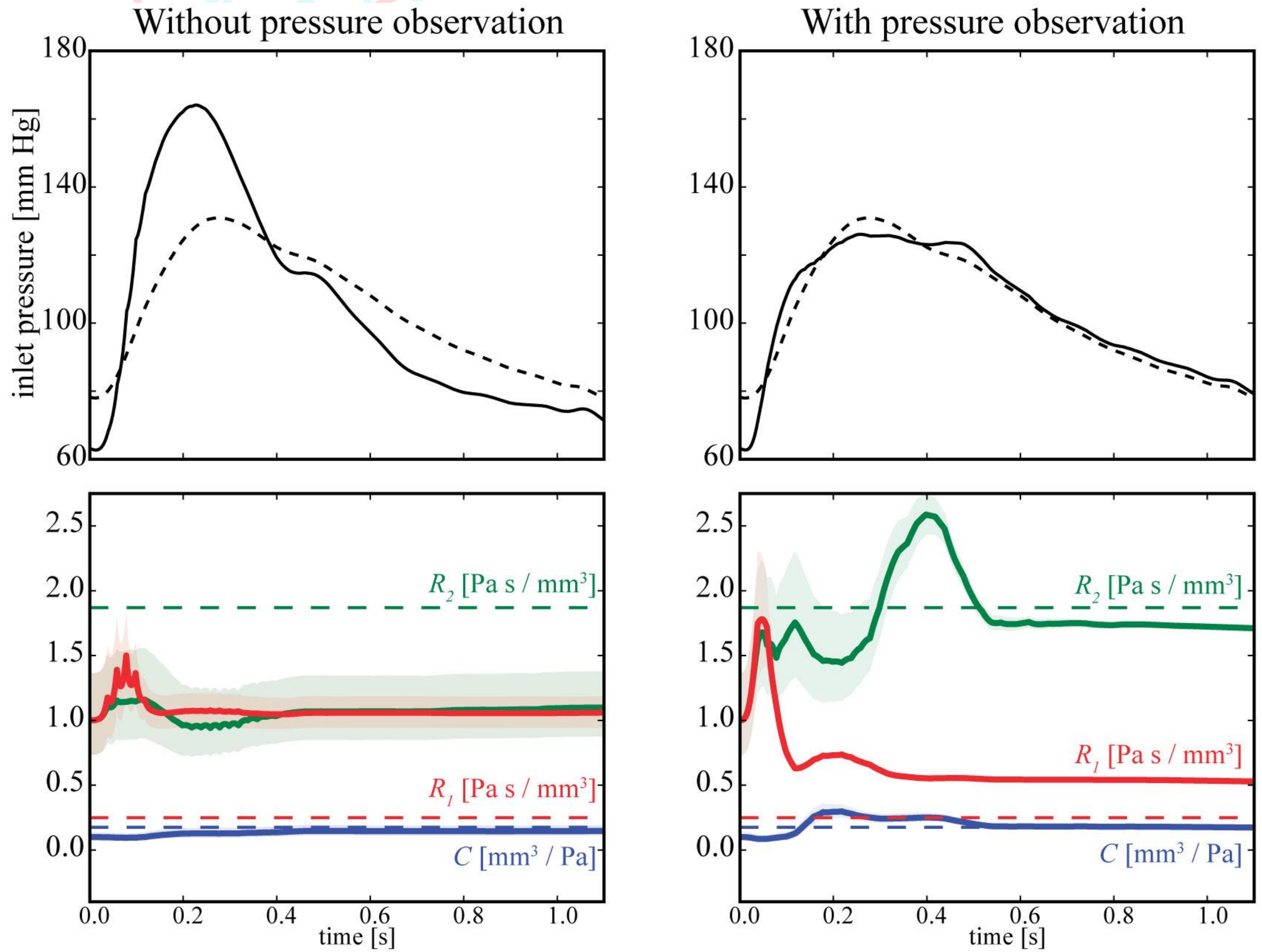



****All these cases were initiated using a good initial guess for the pressure state**

**Lesson:** If we have observations on Q & P, we can estimate any combination of the Windkessel parameters

# Idealized Carotid: Estimation of Windkessel Parameters from P & Q

**What happens if we don't have a good initial guess for the pressure field?**

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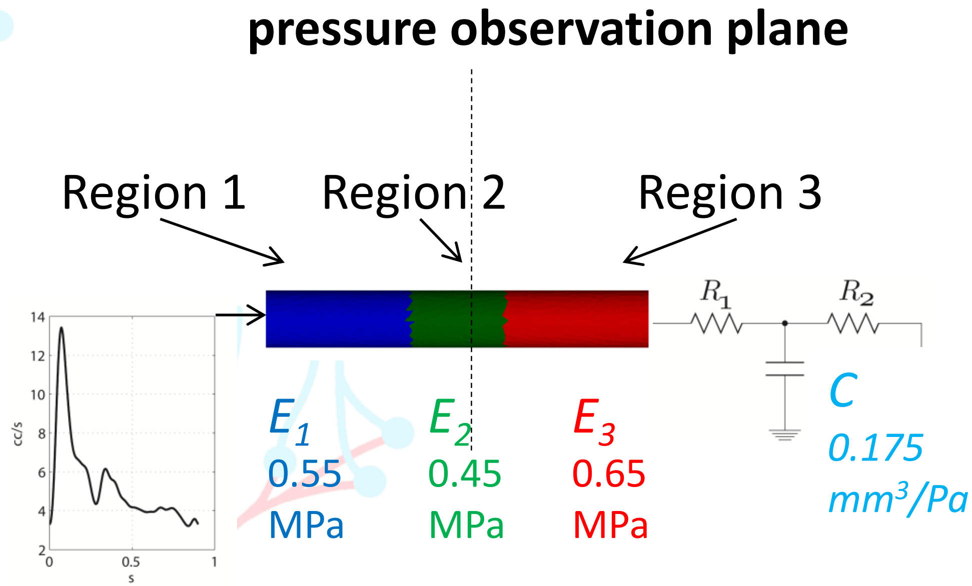
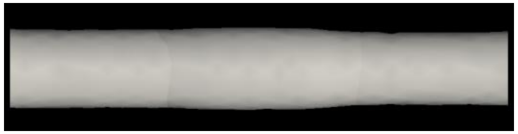
**Lesson:** If no observation on P, and bad initial guess on state of P, the Windkessel parameters are <u>not identifiable</u>

# Idealized Carotid: Estimation of Wall Stiffness + Distal Compliance

**Forward problem:** Parameters values assumed to be known

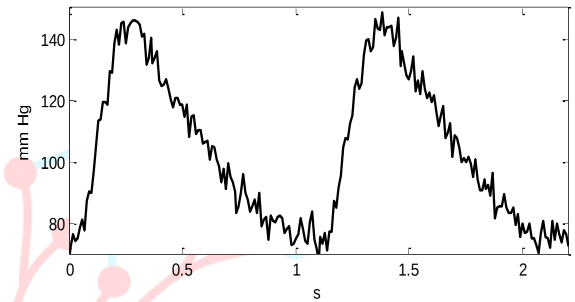



Extract "synthetic data" from simulation results



disp x2

Synthetic wall motion data




Synthetic pressure data +Gaussian white noise, 30dB SNR

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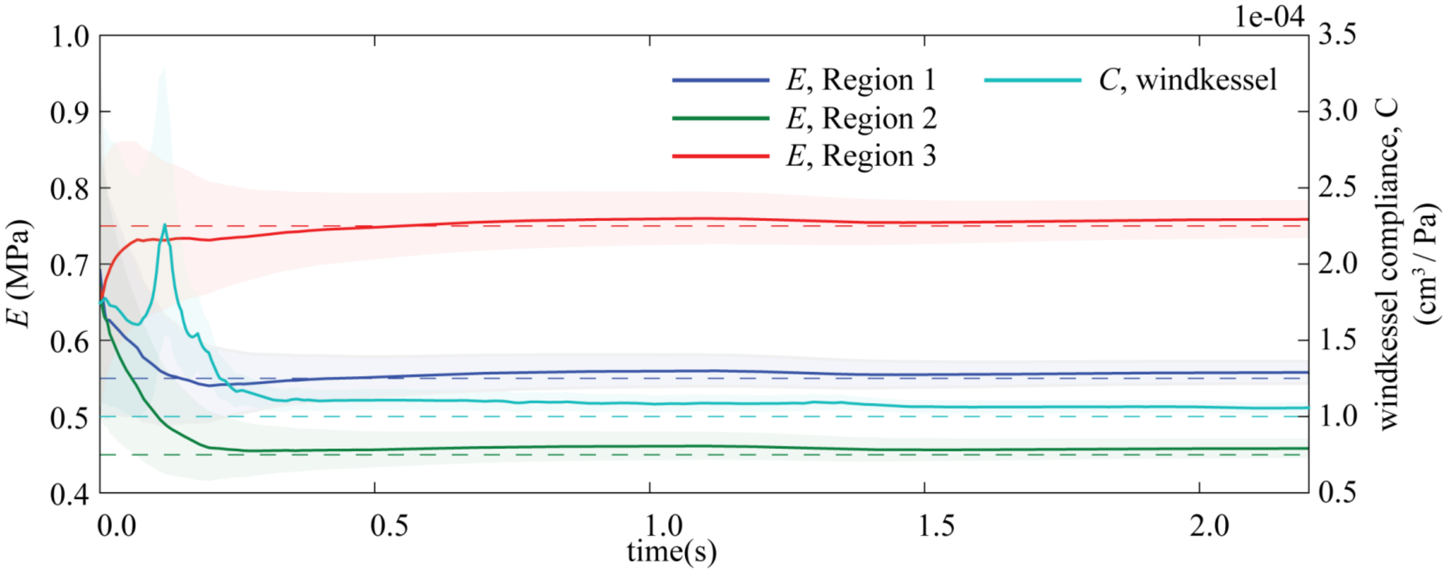
# Idealized Carotid: Estimation of Wall Stiffness + Distal Compliance




Estimation started with bad initial guesses for parameters but good for state of P

**Lesson:** If wall motion data and pressure observations are available, we can estimate the total compliance of the system, e.g.:

- The proximal compliance (vessel stiffness)
- The distal compliance (Windkessel)

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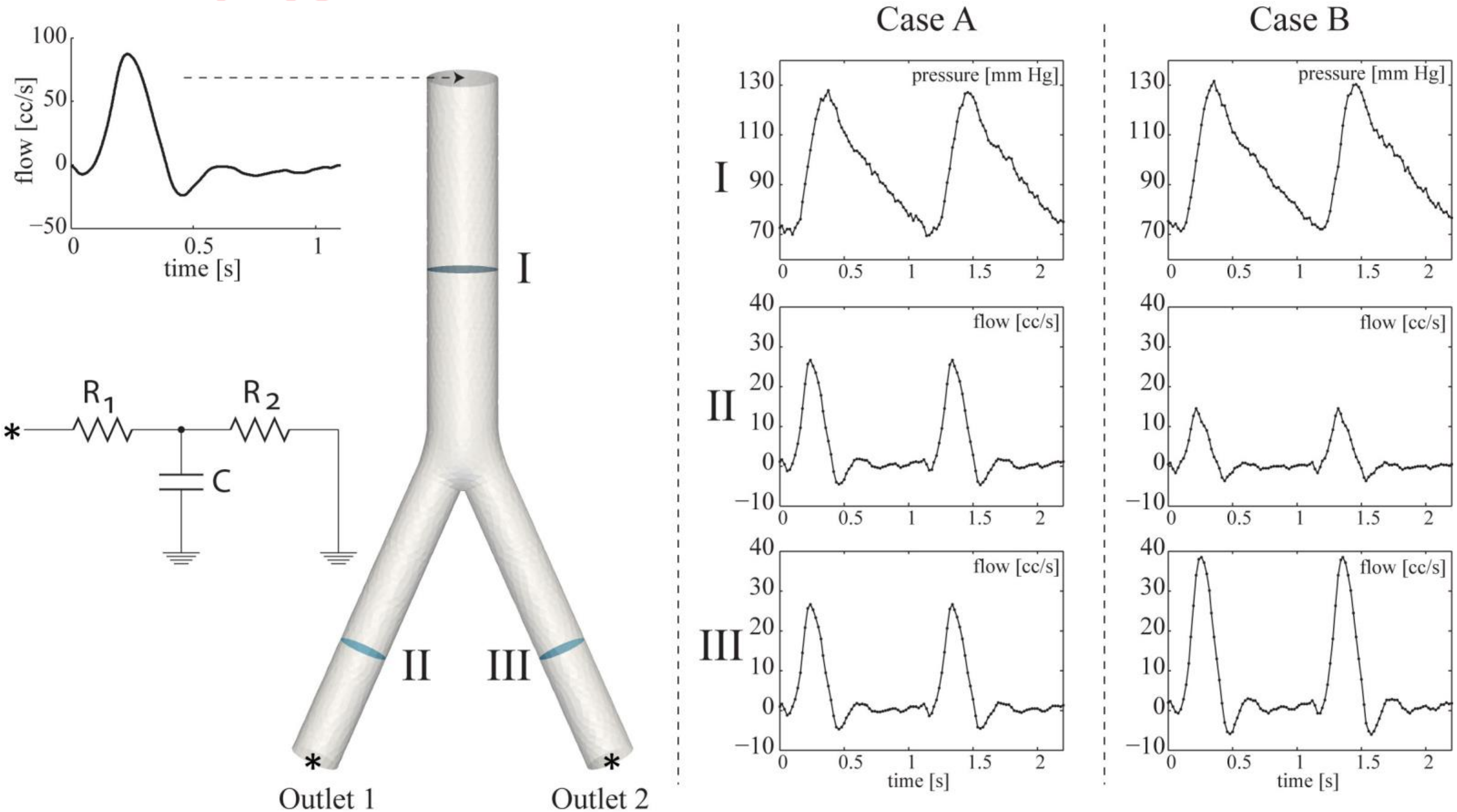
# Idealized Bifurcation

**Case A: symmetric distal beds**
**Case B: non-symmetric distal beds**




**Forward problem:**
Parameters values
assumed to be known

"synthetic data"
Pressure at I
Flows at II and II

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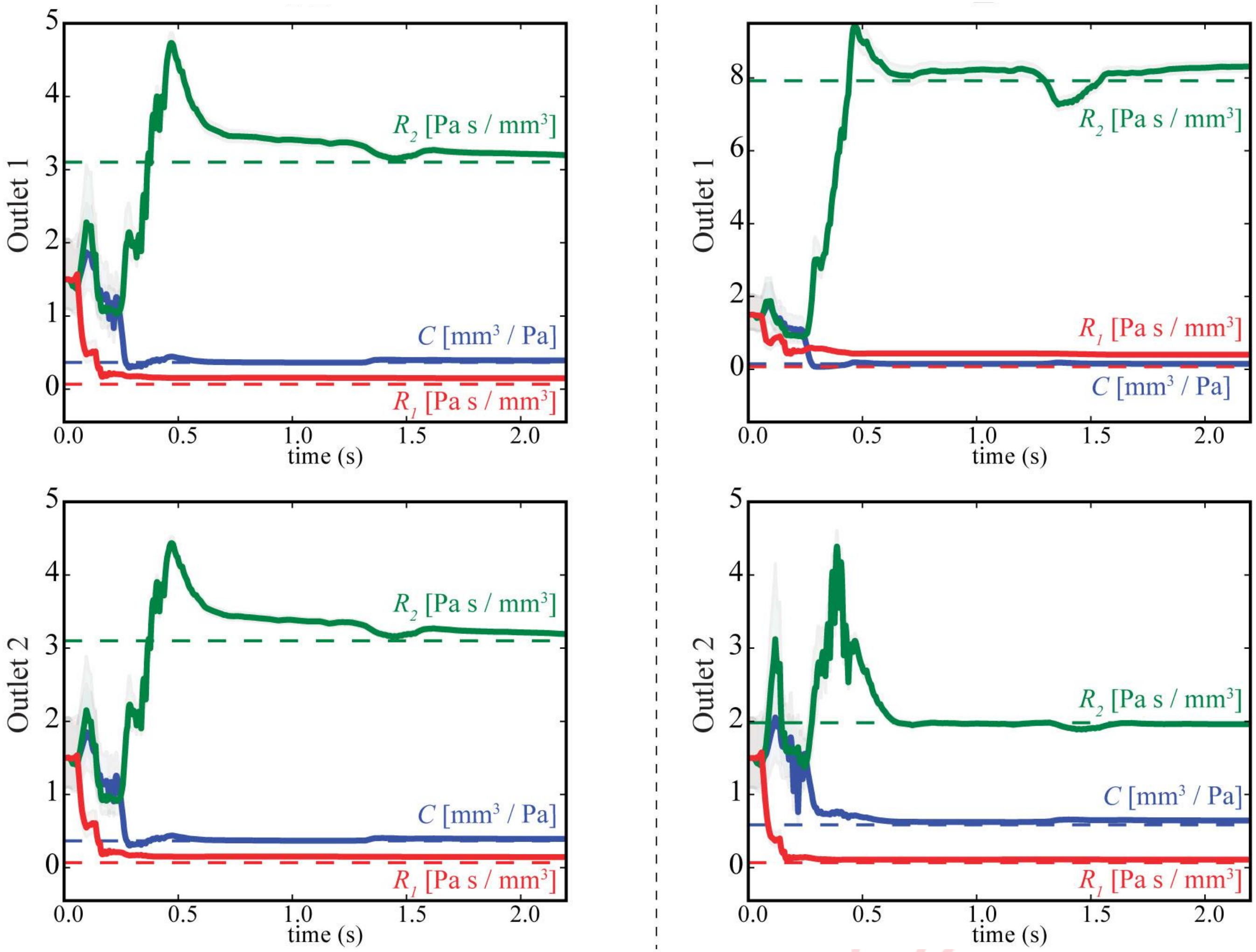
# Idealized Bifurcation (good initial guess for the state of P)

**A: symmetric distal beds** | **B: non-symmetric distal beds**




**Lesson:** If we have observations on Q & P, we can estimate any combination of the Windkessel parameters for multiple outlets

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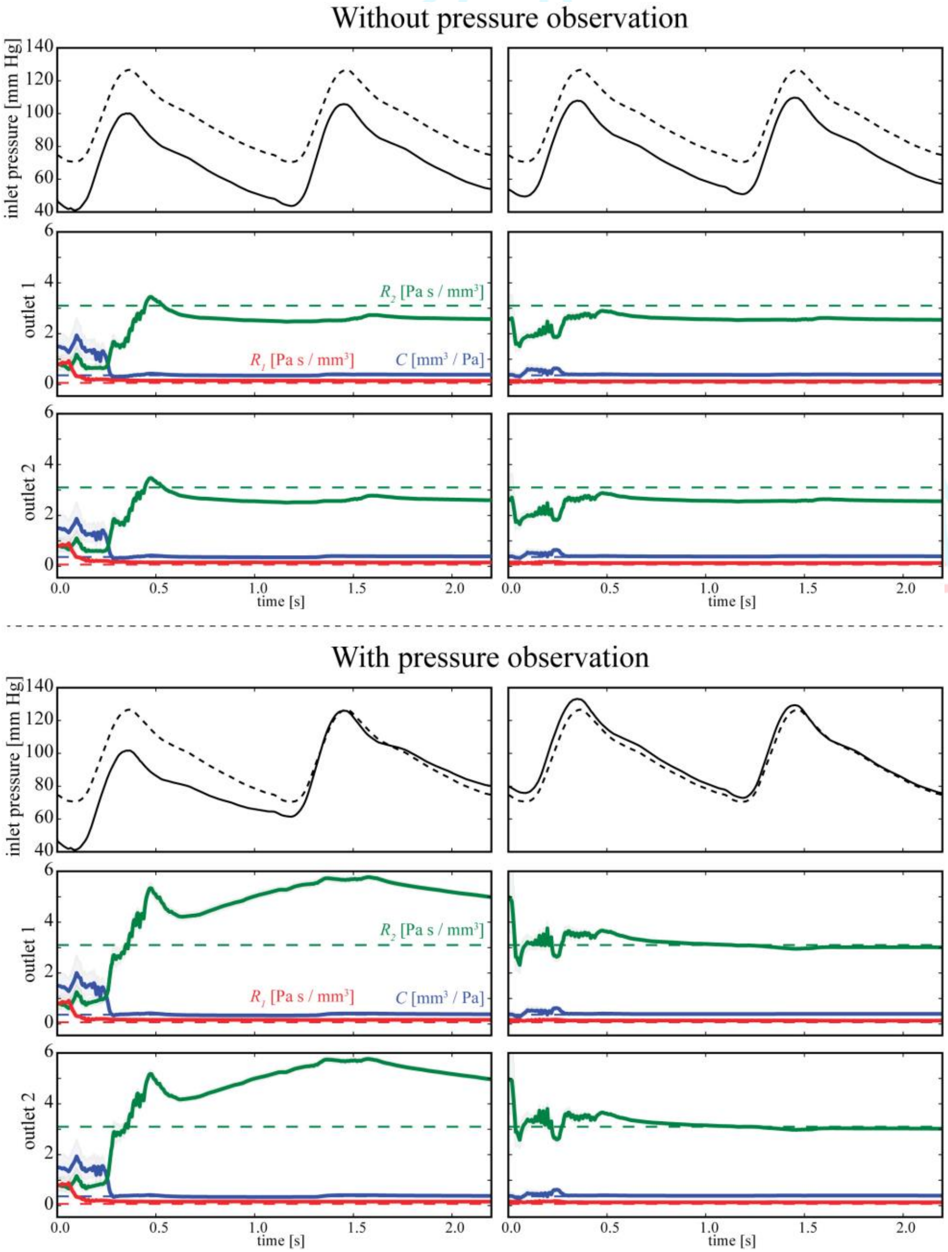
# Idealized Bifurcation (bad initial guess for the state of P)




**Lesson:** If no observation on P, and bad initial guess on state of P, the Windkessel parameters are <u>not identifiable</u>

**We need information on Pressure! (either as initial guess on the state, or a observation)**

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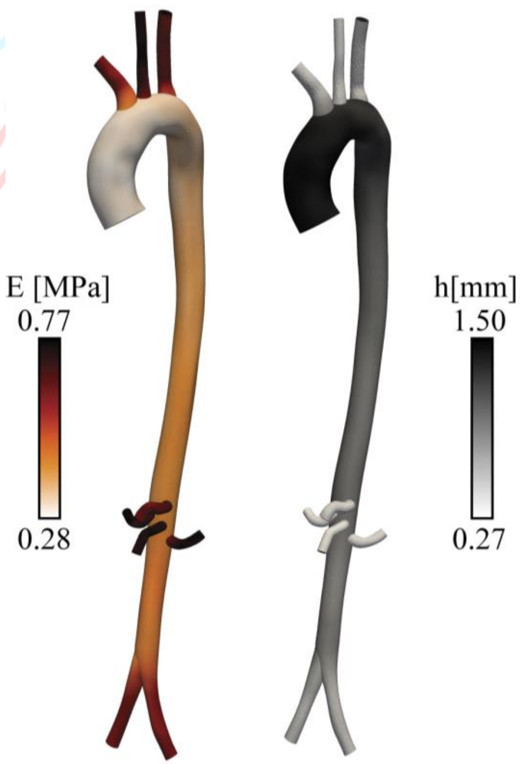
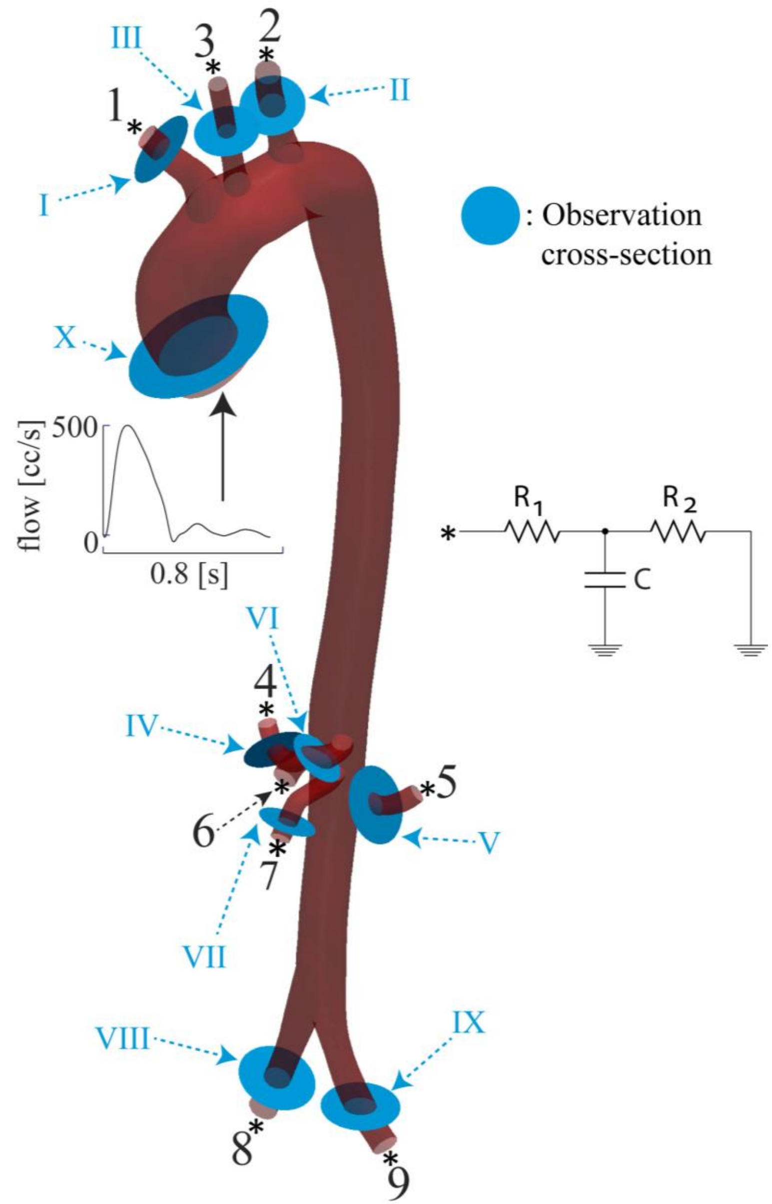
# Full patient-specific aorta (with synthetic data)

**Forward problem:**
Parameters values assumed to be known




| cross-section | case A (no P obs.) | case B (P obs. left carotid) | case C (P obs. all outlets) |
|---|---|---|---|
| I | Q | Q | P,Q |
| II | Q | Q | P,Q |
| III | Q | P,Q | P,Q |
| IV | Q | Q | P,Q |
| V | Q | Q | P,Q |
| VI | Q | Q | P,Q |
| VII | Q | Q | P,Q |
| VIII | Q | Q | P,Q |
| IX | Q | Q | P,Q |

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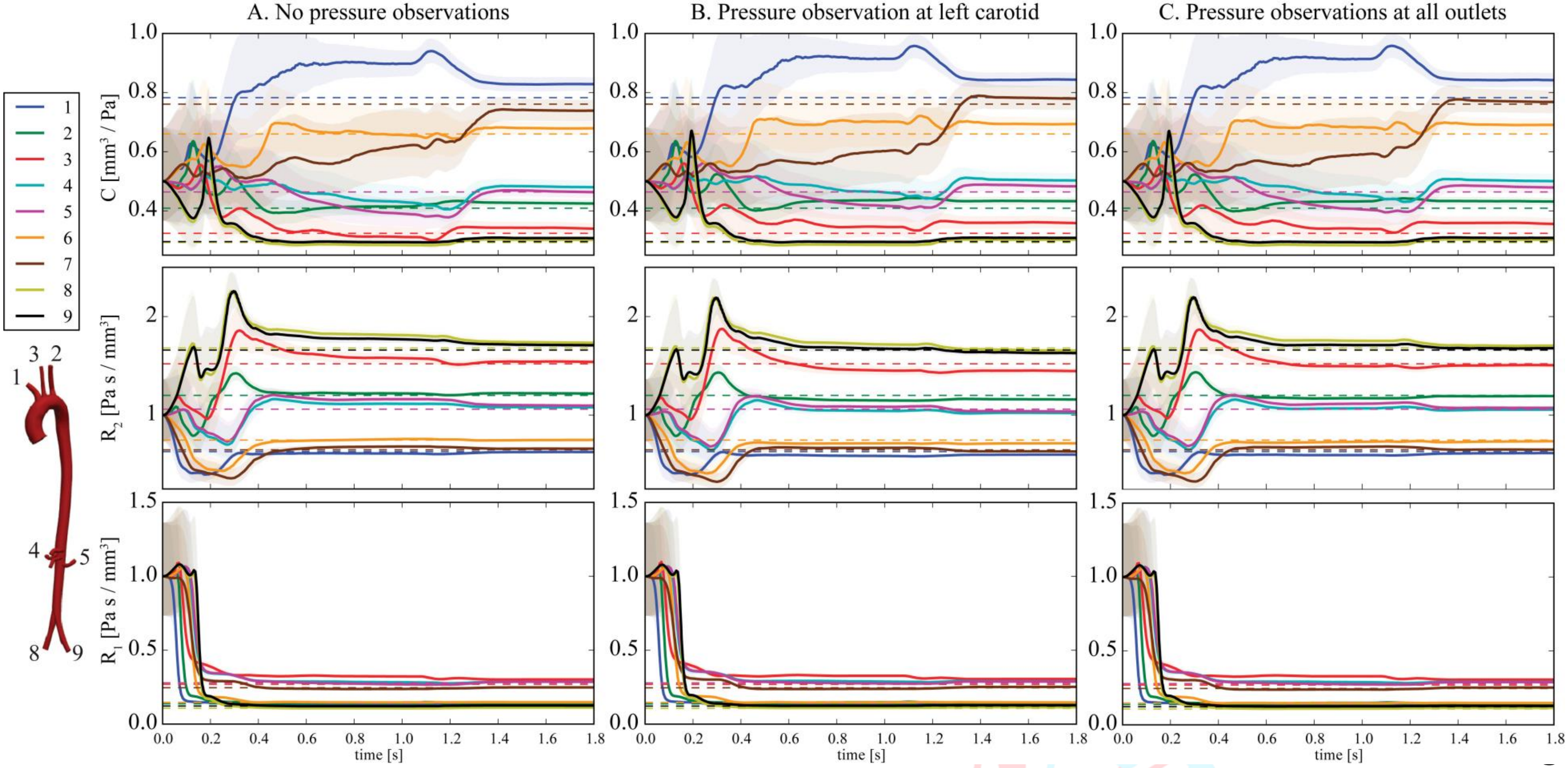
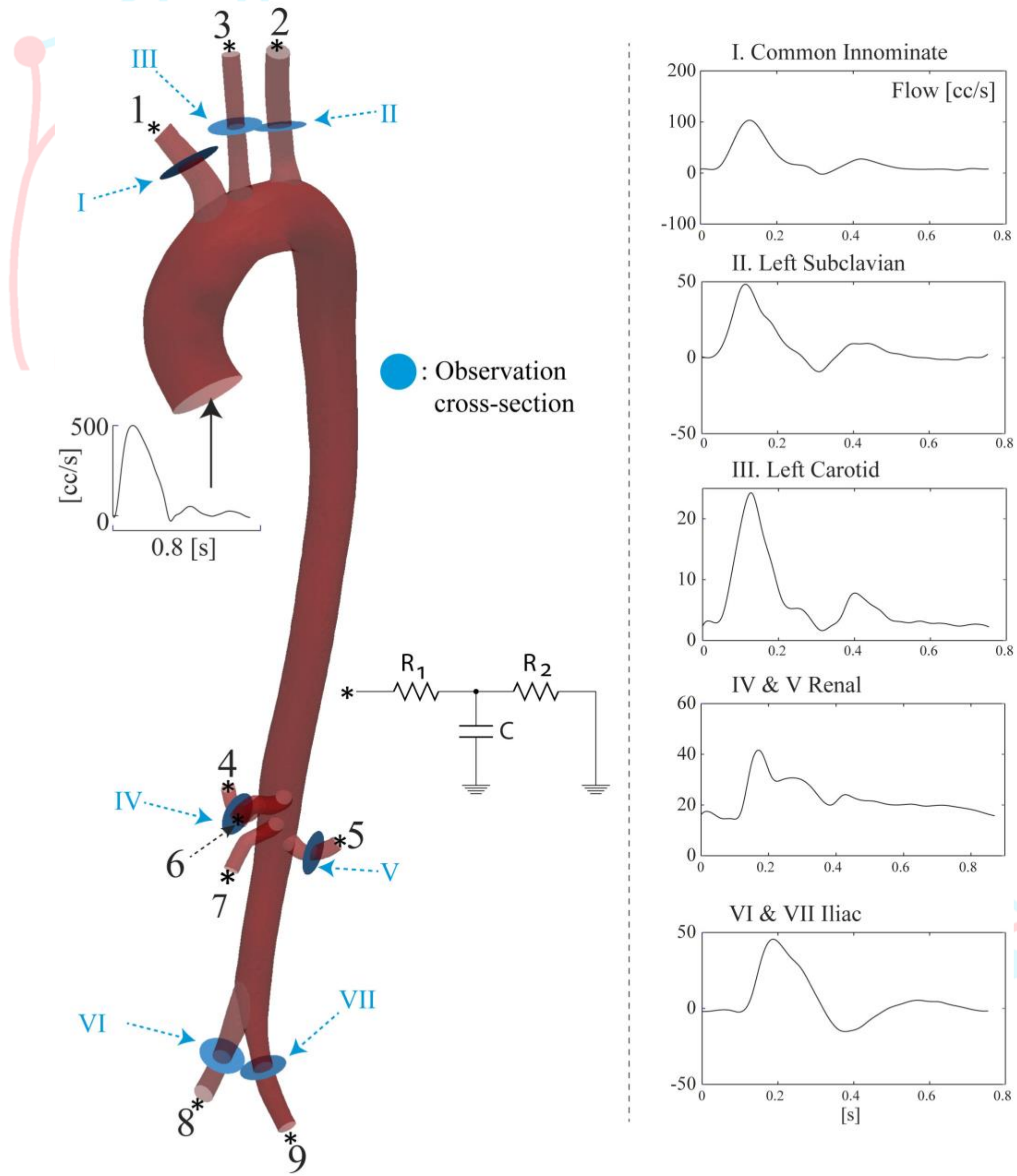
# Full patient-specific aorta (with synthetic data)




**Lesson:** surprisingly, even without an observation on pressure, things work if a good initial estimate on the pressure state is known (which of course means we know something about the pressure)

# Full patient-specific aorta (with real data)

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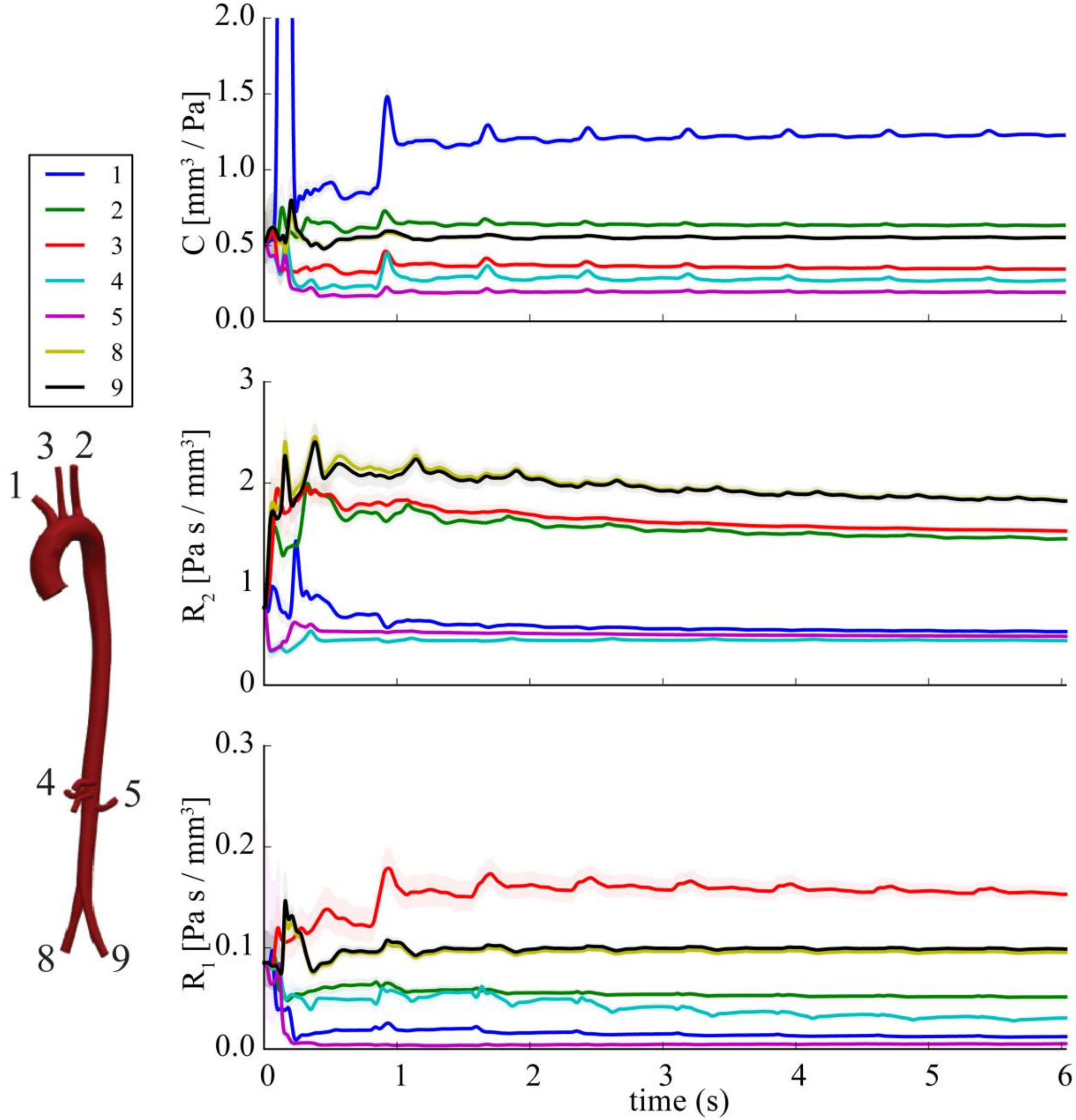
# Full patient-specific aorta (with real data)




**Lesson:** all parameters are identifiable: estimates on C, $R_1$ and $R_2$ remain constant after several cycles

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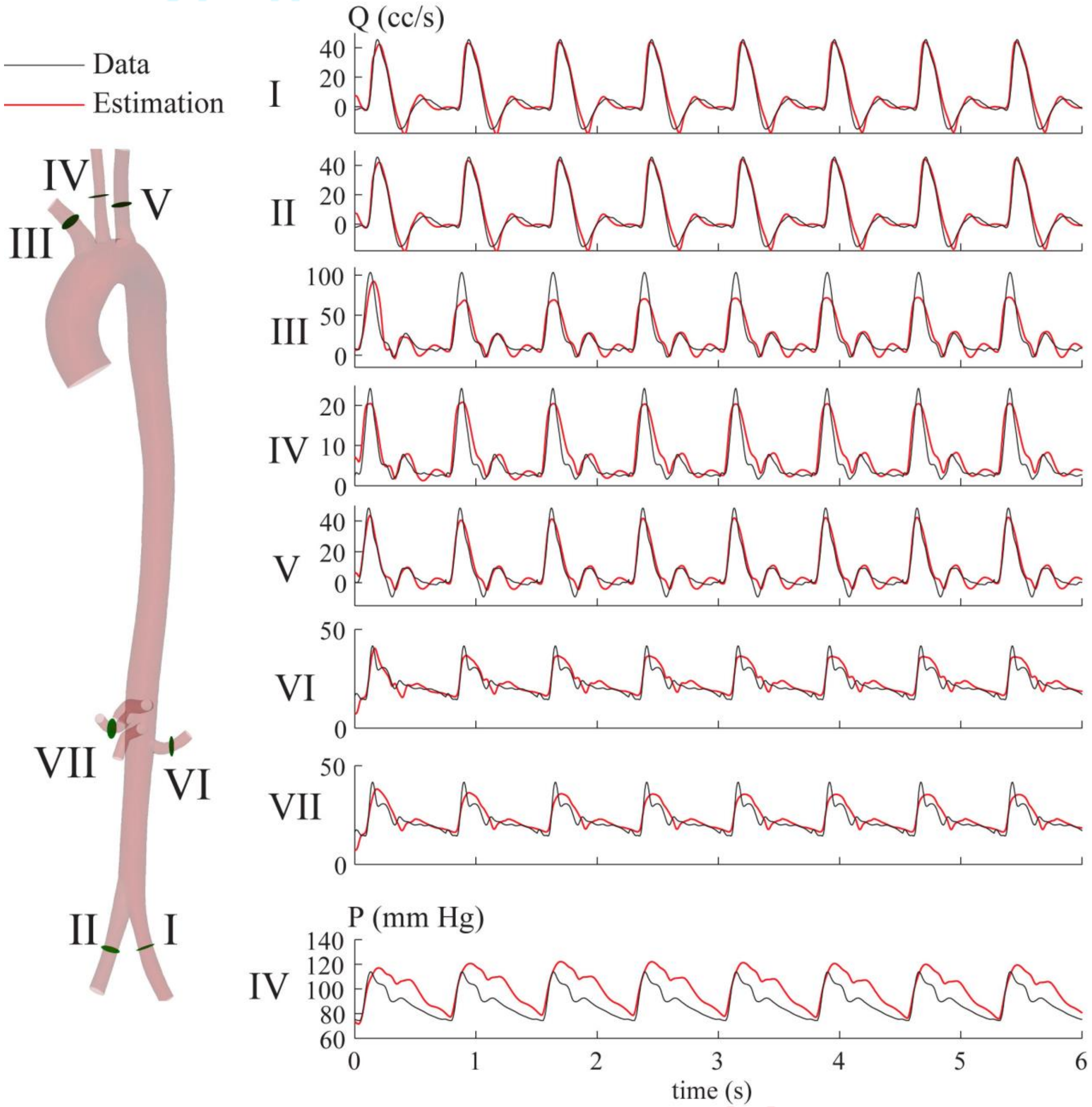
# Full patient-specific aorta (with real data)

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# Conclusions

- Computational for CV modeling usually rely on a large number of parameters
- Estimating these parameters is often the most time consuming and non-systematic task of the modeling process
- 1D techniques, combined with physics-based knowledge of the circulation can be used to quickly estimate the first round of material parameters for the 3D techniques
- Automatic techniques for efficient and automatic material & BC parameter estimation are important to drive both translational and fundamental hemodynamic simulation

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