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Towards a Multi-fidelity Hemodynamic Model Pipeline for the Analysis of Cardiovascular Flow Under Uncertainty

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Sandia National Laboratories

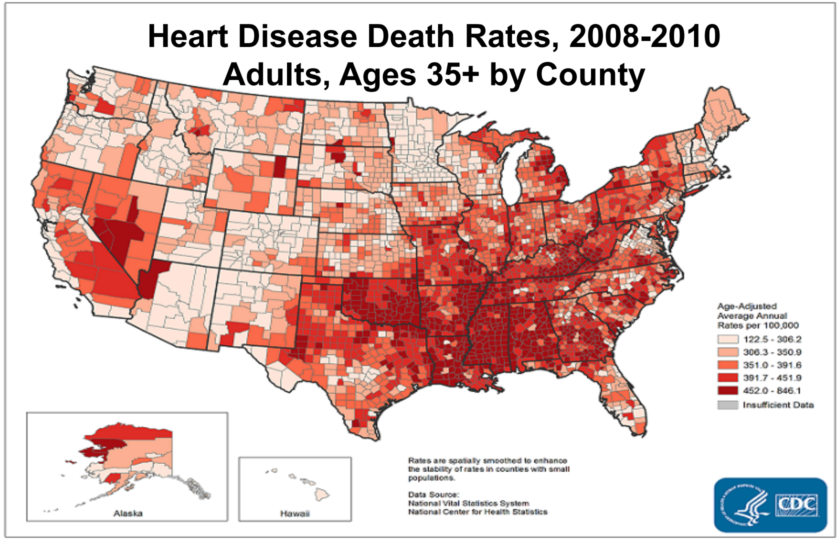
Outline

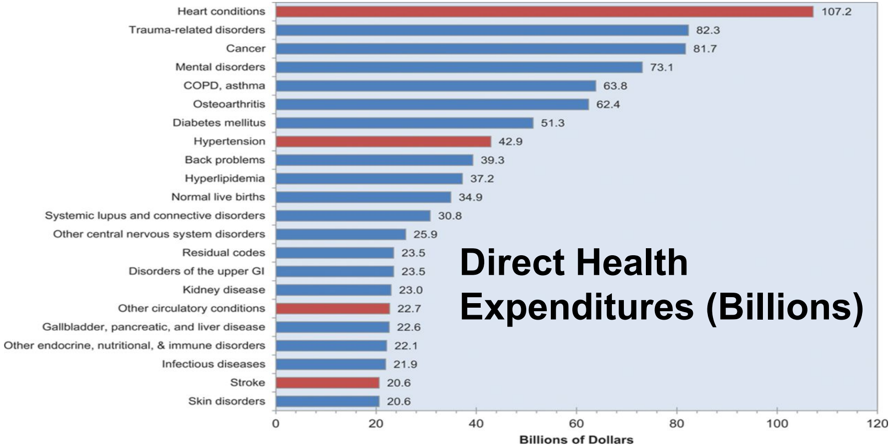
Problem Set-Up

OVERVIEW, MODELING, AND PATIENT-SPECIFIC PROBLEMS

Cardiovascular Disease

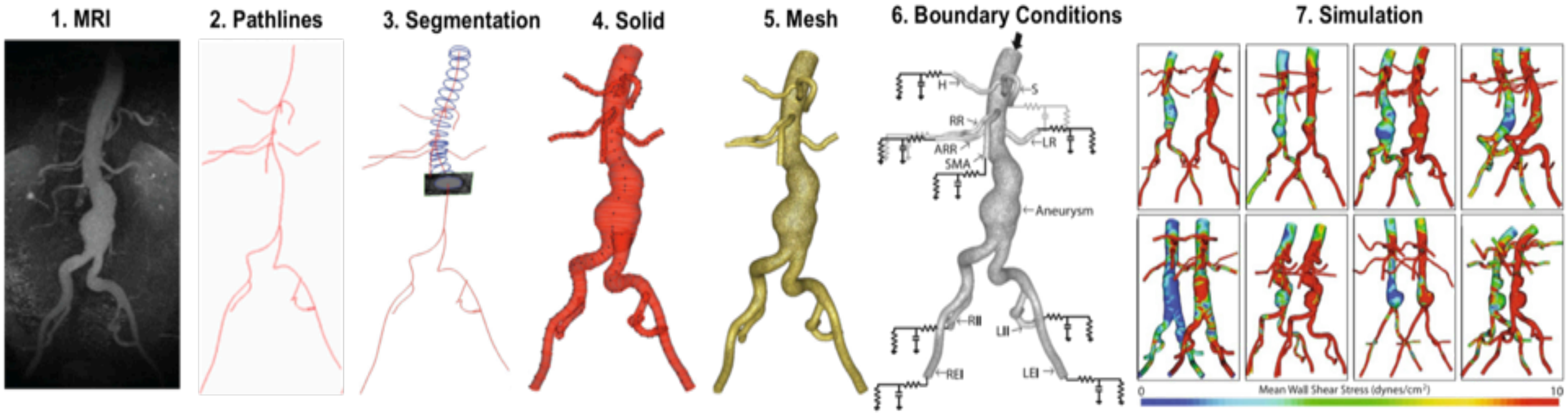
- Cardiovascular disease is the **leading case of death worldwide** (~17 million annual deaths).
- About **610,000 people** die of heart disease in the United States every year (**1 in every 4 deaths**).[1]
- Heart disease is the **leading cause** of death for both men and women in the United States.
- Heart disease costs the United States about **$500 billion** each year.[1]





[1]Centers for Disease Control and Prevention AHA 2014 Statistics Report, Circulation

Patient-Specific Modeling via SimVascular



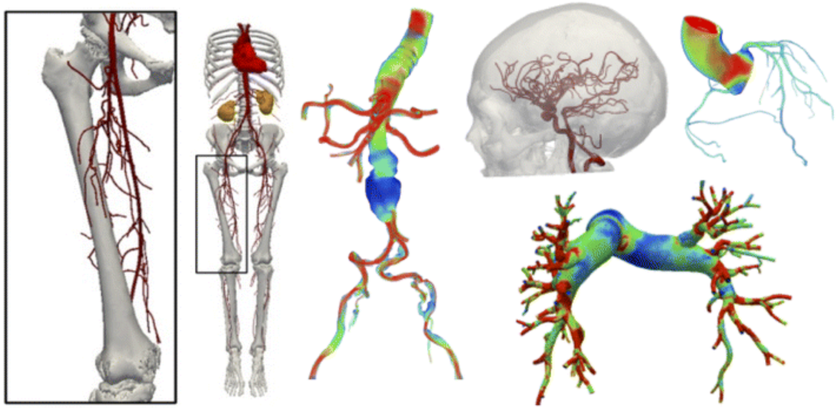
- Patient Specific data (CT scans, 4D-MRI, Angio data)
- Prescribe input flow or pressure waveform
- Prescribe boundary conditions (R, RCR, coupled LPN)
- Simulation (FSI and Rigid)

Uncertainty Quantification Overview

MOTIVATION AND METHODS

Clinical Motivation

- **Goal:** Hemodynamic models for diagnosis and treatment of cardiovascular disease and surgical planning in clinical setting.
- **Issue:** inability to account for uncertainties hinder clinical adoptions of computational methods
- **Solution:** transition to a stochastic framework
  - Modeling parameters defined as probability distributions
  - Employ varying-fidelity models to maintain reasonable computational cost

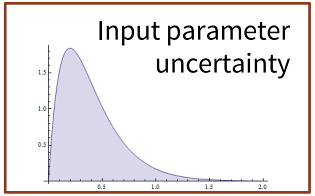


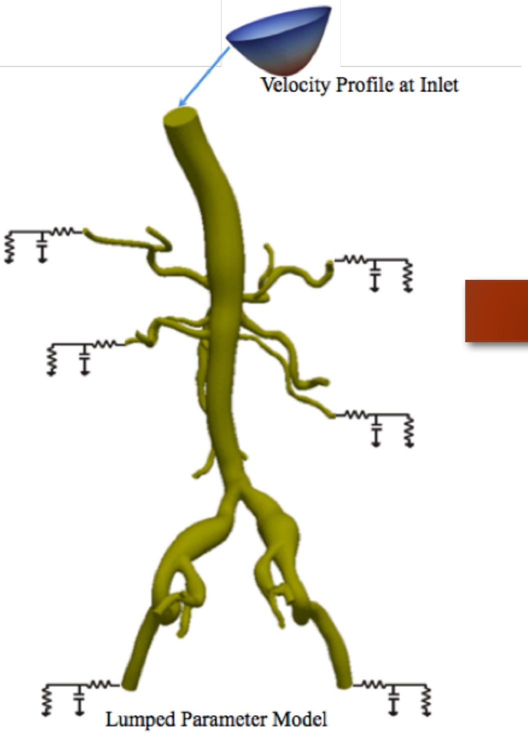
Sampling of models from OSMSC model repository

Sources of Uncertainty

Uncertain Inputs

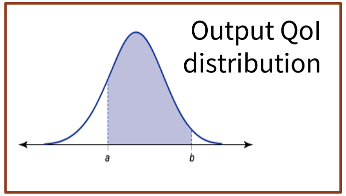
- Noise in image data
- Clinical data
- Boundary conditions
- Physiologic assumptions
- Material properties





Uncertain Outputs

- Wall shear stress
- Oscillatory shear index
- Cardiac work
- Oxygen delivery
- Pressure levels
- Flow rates
- Residence Time



Sankaran and Marsden, "A stochastic collocation method for uncertainty quantification and propagation in cardiovascular simulations," J. Biomech. Eng., 2011.

Approaches for Uncertainty Quantification

1. Monte Carlo
   - Random sample of input values ($\boldsymbol{x} \in \mathbb{R}^N$) with sample statistics as the moments for quantity of interest *f(x)*
2. Stratified Monte Carlo (Latin Hypercube)
   - Random sample from a stratified sample
3. Polynomial Chaos Expansion
   - Exponential convergence (in polynomial degree)
   - Express the uncertain output as

$$f(x) \cong \sum_{i=0}^{k} \alpha_i p_i(x)$$

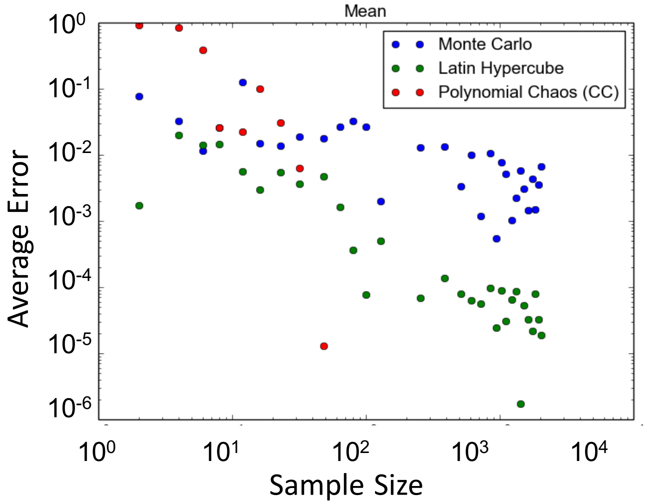
   - Moments then given by the coefficients of expansion

$$\mu_f = \alpha_0 \,, \qquad \sigma_f = \sum_{i=1}^{\infty} \alpha_i{}^2 \|p_i(x)\|_w^2$$

   - Coefficients from Galerkin projections (using numerical quadrature)

$$\langle f(x), p_i(x) \rangle = \langle \sum_j \alpha_j p_j(x), p_i(x) \rangle = \alpha_i \|p_i(x)\|^2 = \alpha_i$$

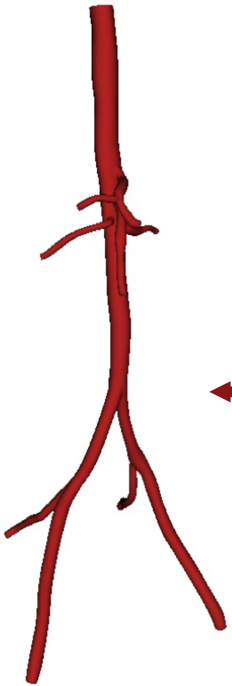
Mean of $\boldsymbol{f(x) = 5 + x + \cos(x)}$



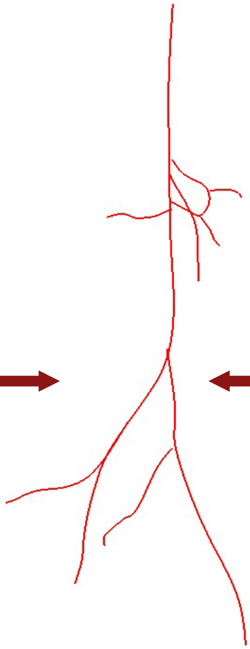
Polynomial Chaos method converges ***much*** *faster than LHC or MC*

Modeling Work To-Date

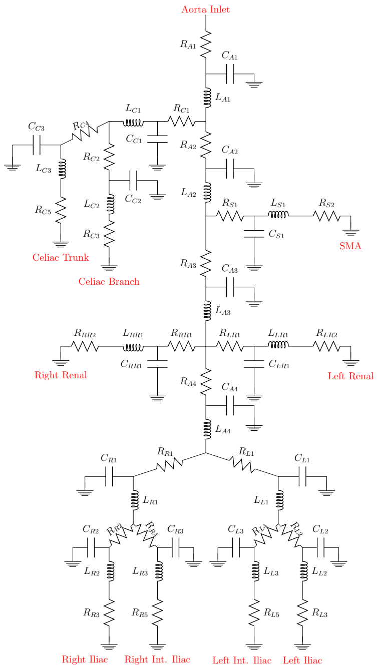
0D, 1D, AND 3D MODELING



3D Model



1D Model



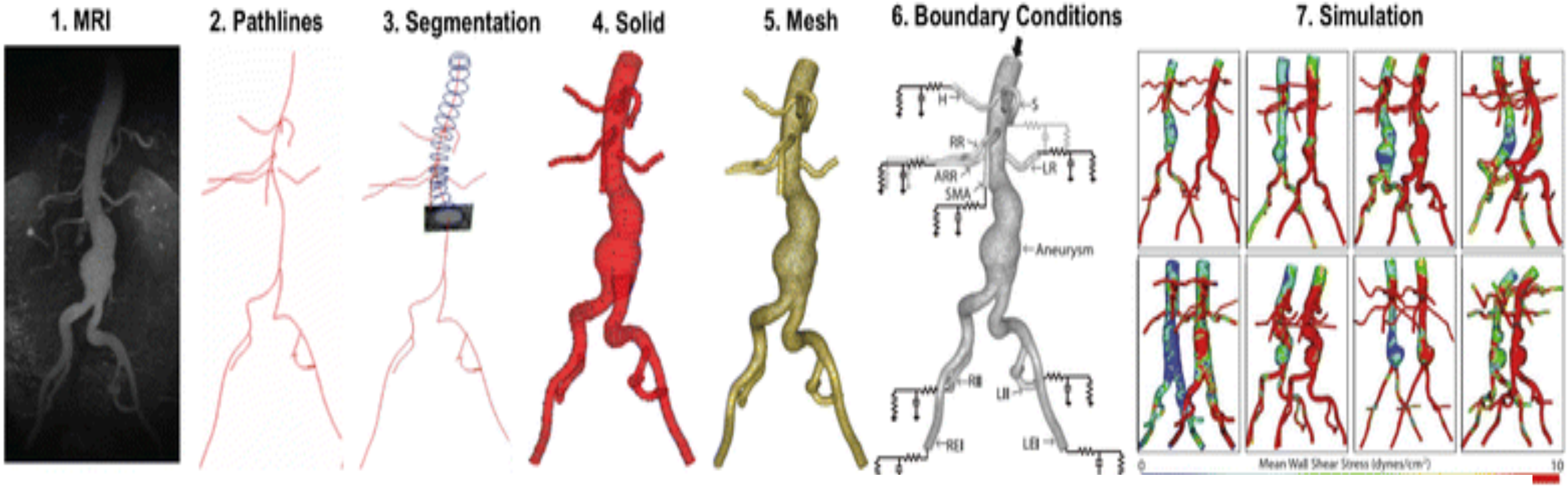
0D Model

3D SimVascular Model

MODELING AND FEM METHODOLOGY,
AORTA-ILIAC MODEL

Pipeline for Model Generation

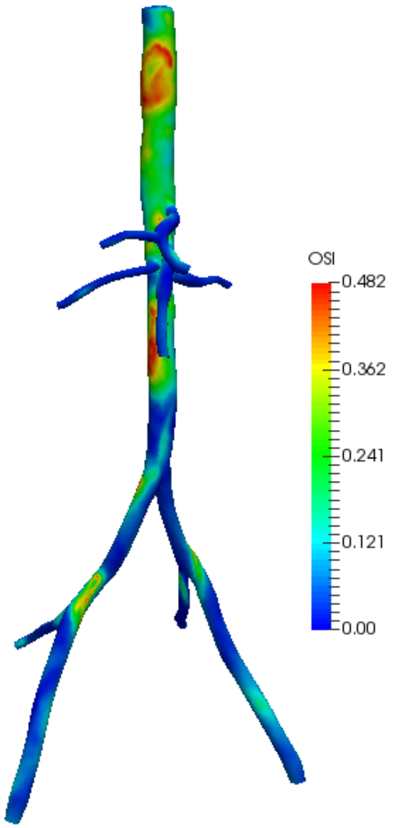
- 3D Formulation: anatomic model construction from medical image data, solution of the incompressible Navier-Stokes equations



SimVascular 3D formulation pipeline

SimVascular Flow Solver

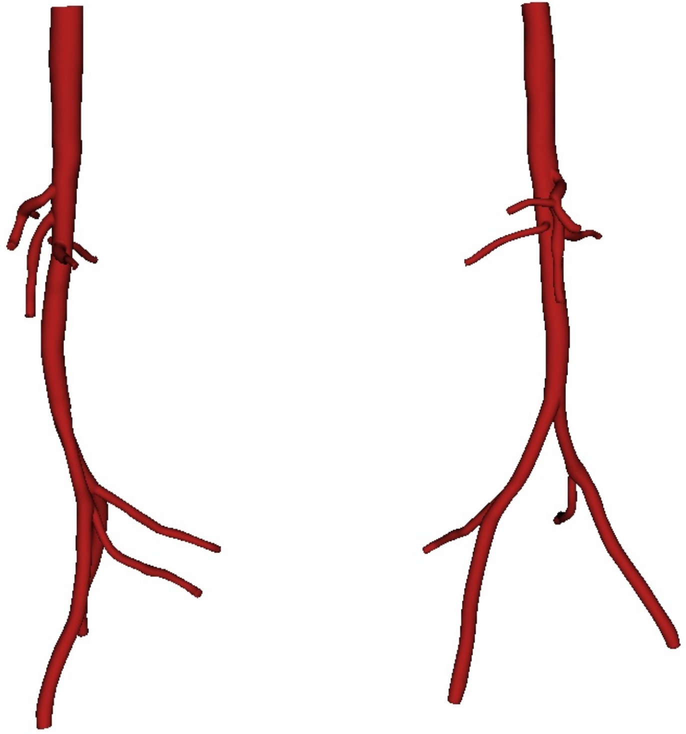
- Finite element method SUPG
- Implicit coupling to LPN BCs
- Backflow stabilization
- Fluid structure interaction with coupled momentum method (Figueroa and Taylor)[1]
- Variable wall material properties: thickness, elastic modulus
- Efficient linear solver with custom preconditioner



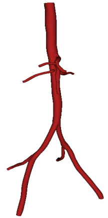
Figueroa, C., et al, A coupled momentum method for modeling blood flow in three-dimensional deformable arteries, *Computer Methods in Applied Mechanics and Engineering*, 195 (41), 2006, 5685-5706, http://dx.doi.org/10.1016/j.cma.2005.11.011.

Pipeline Comparison with Aorta-Iliac Model (OSMSC0006)

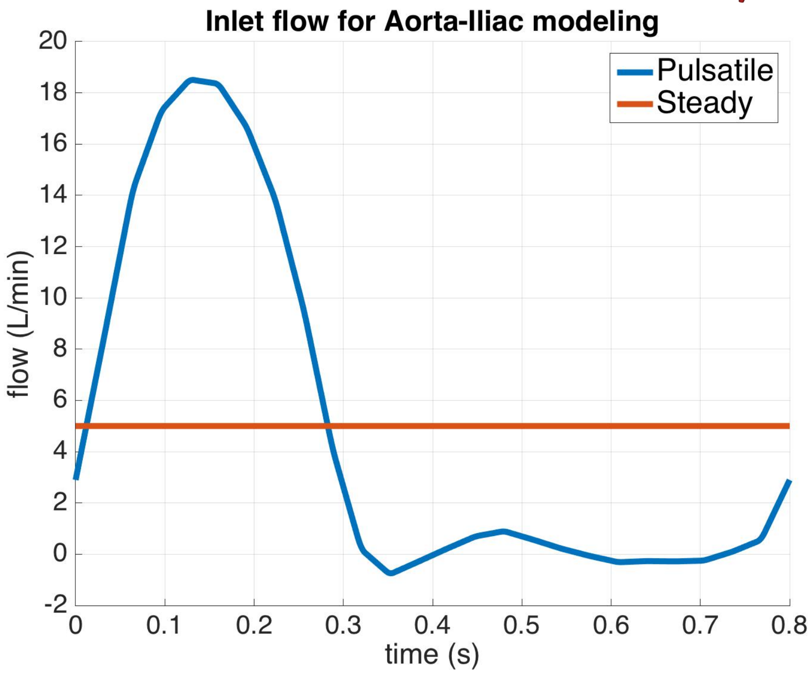
- **Goal**: confirm the validity of using 1D (generated from pipeline code) as a surrogate model
- **Output:** Comparison of flow and pressure waveforms from 3D Rigid, 3D FSI, and 1D solvers
- **Method:** Apply identical input waveforms and identical R and RCR boundary conditions.



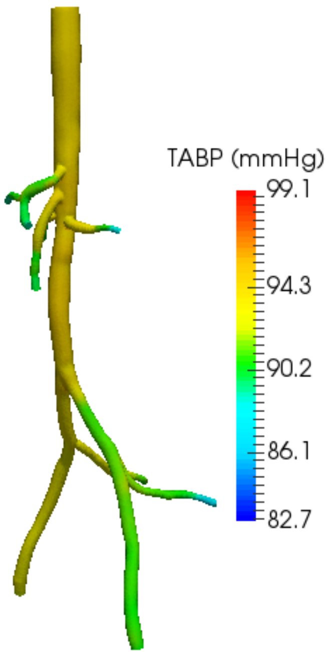
Modeling Parameters



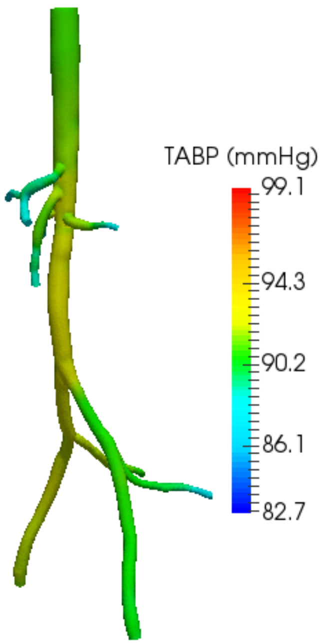
- **Inlet:** Prescribed waveform at aorta
  - Pulsatile and steady flow
  - Average flow = 5 L/min
  - Average blood pressure = 90 mmHg
  - Cardiac cycle = 0.8 s
- R and RCR BC at 9 outlets from tuning to above parameters
  - Resistances proportional to outlet area
  - Capacitances = $O(10^{-5})$ chosen to match target pressure waveform amplitude (120/80 mmHg)
  - Total resistance with R BC the same as with RCR BC



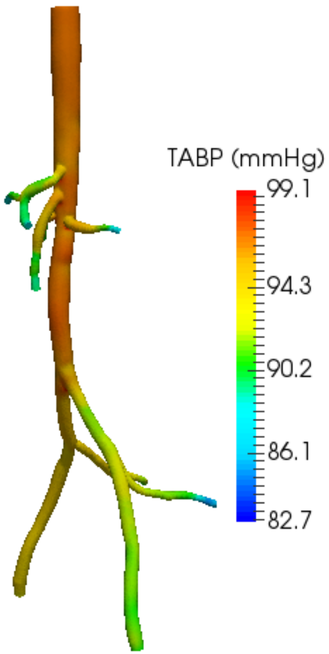
Aorta-Iliac with Pulsatile Flow: 3D TABP



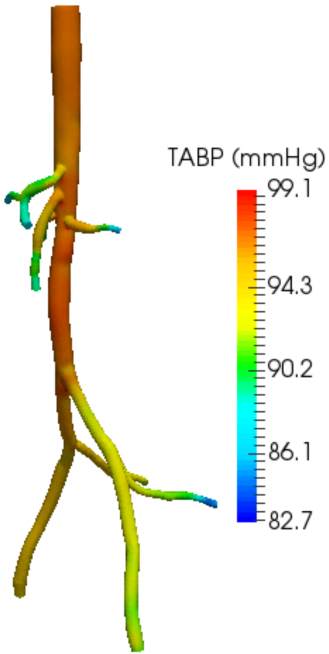
FSI Model: RCR



FSI Model: R

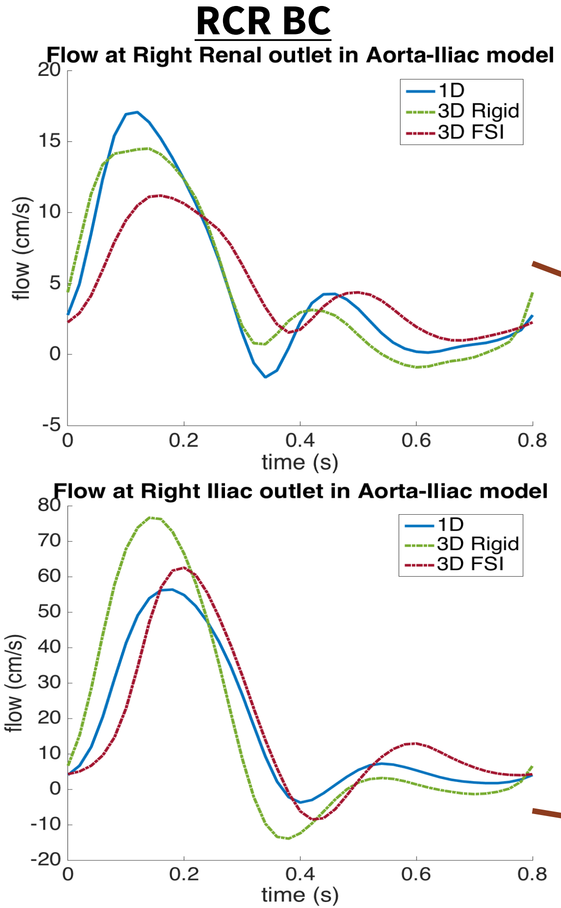


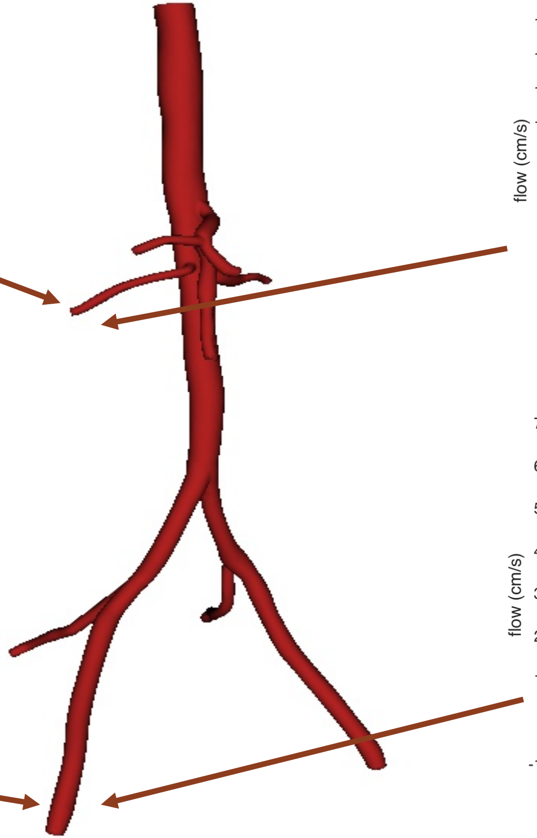
Rigid Model: RCR

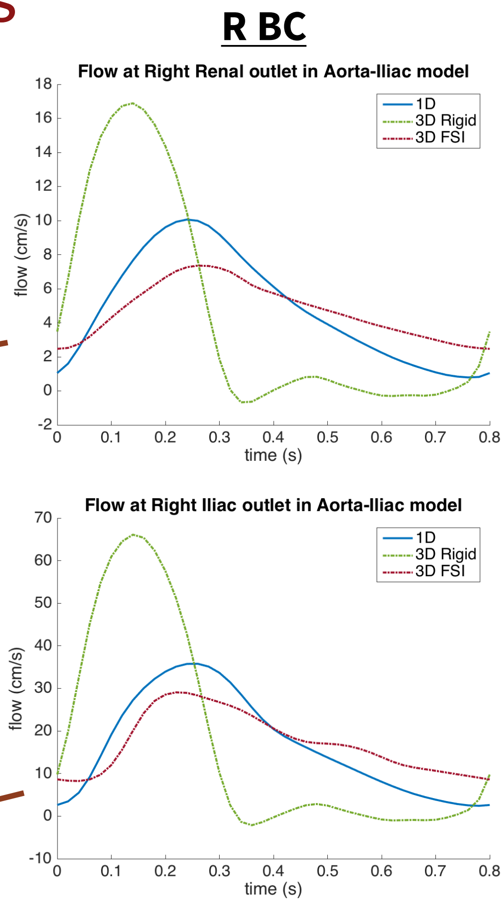


Rigid Model: R

Pulsatile Flow: Inlet and Outlet Flow plots



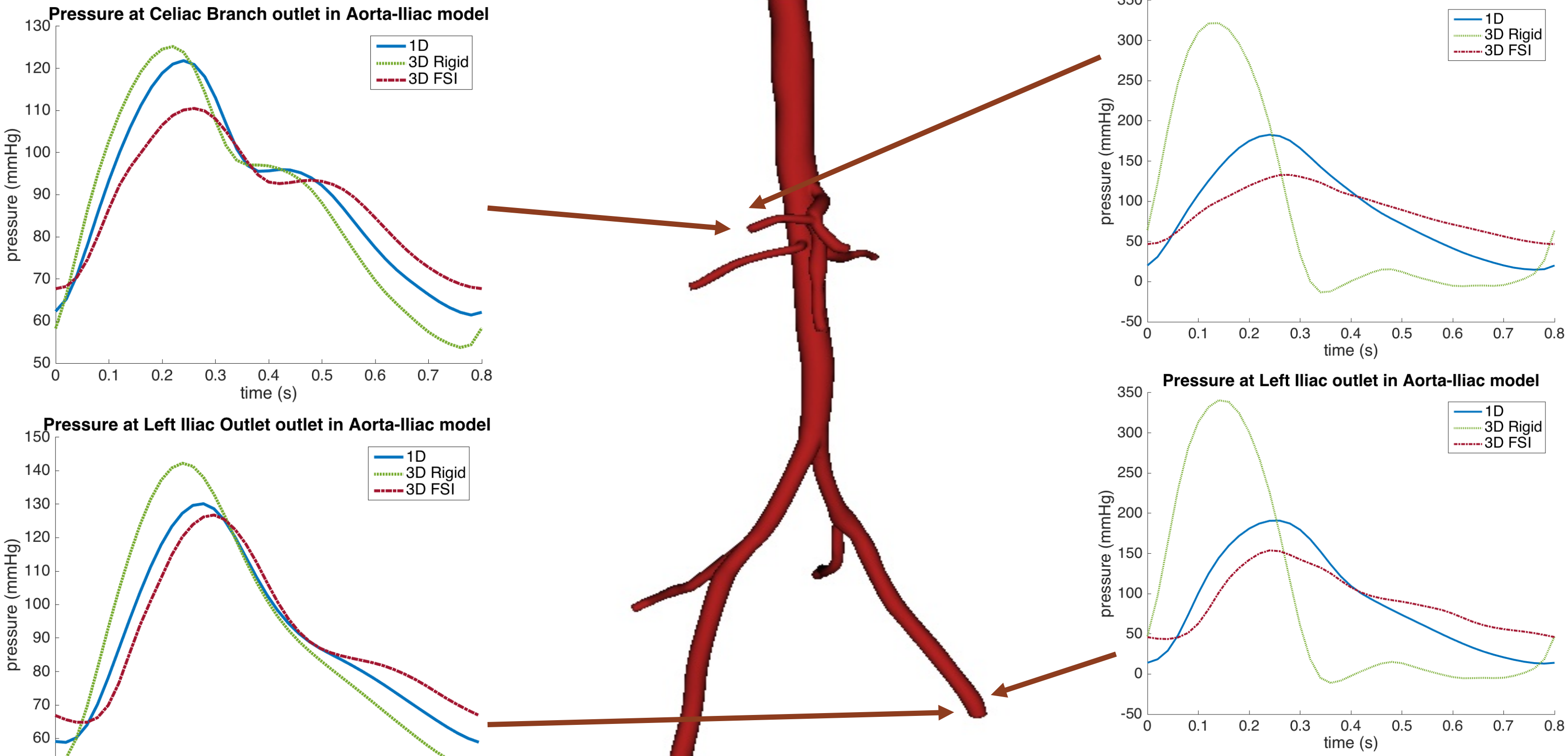




Pulsatile Flow: Inlet and Outlet Pressure plots

RCR BC

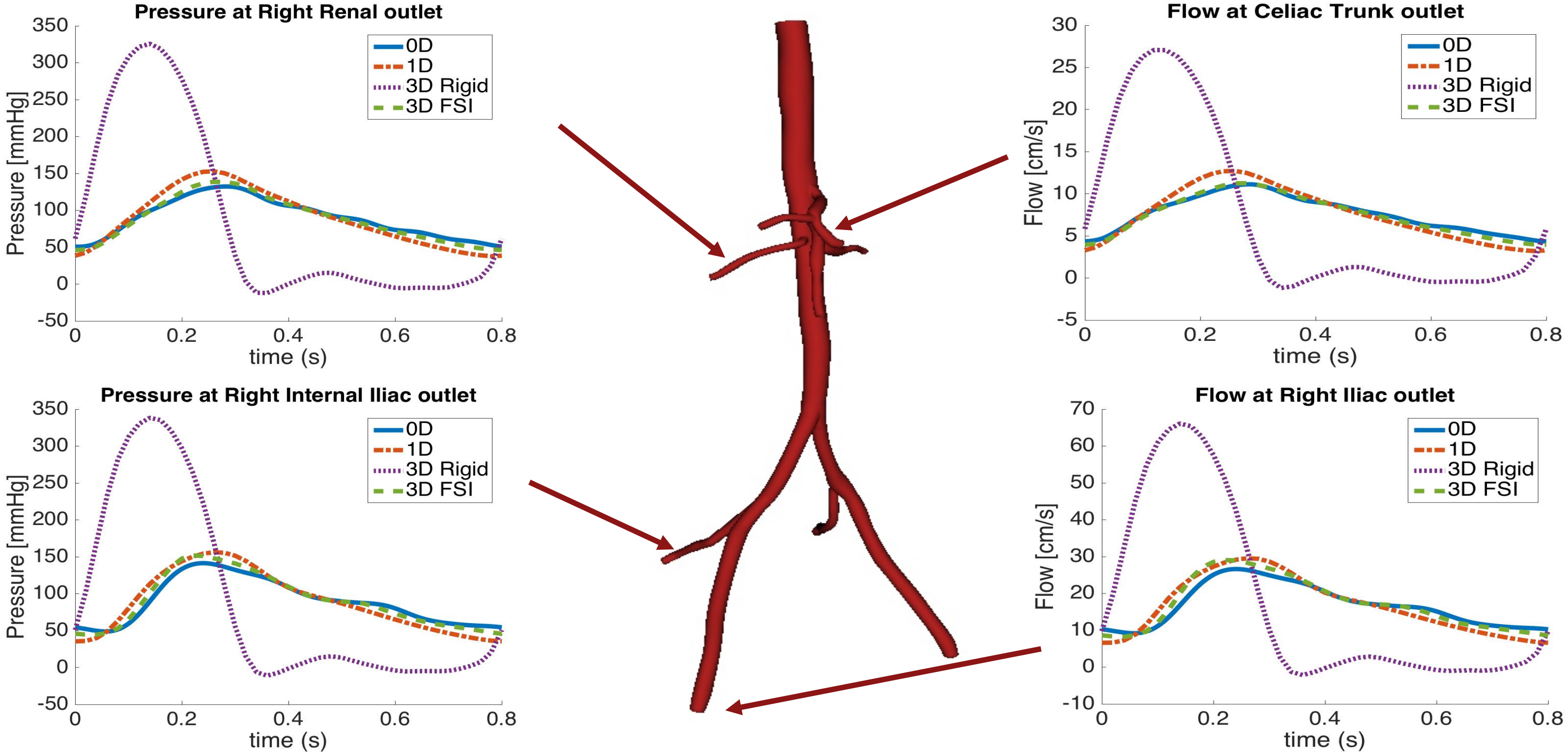
R BC



Aorto-femoral model (pulsatile flow and R boundary conditions)

Pressure Plots

Flow Plots



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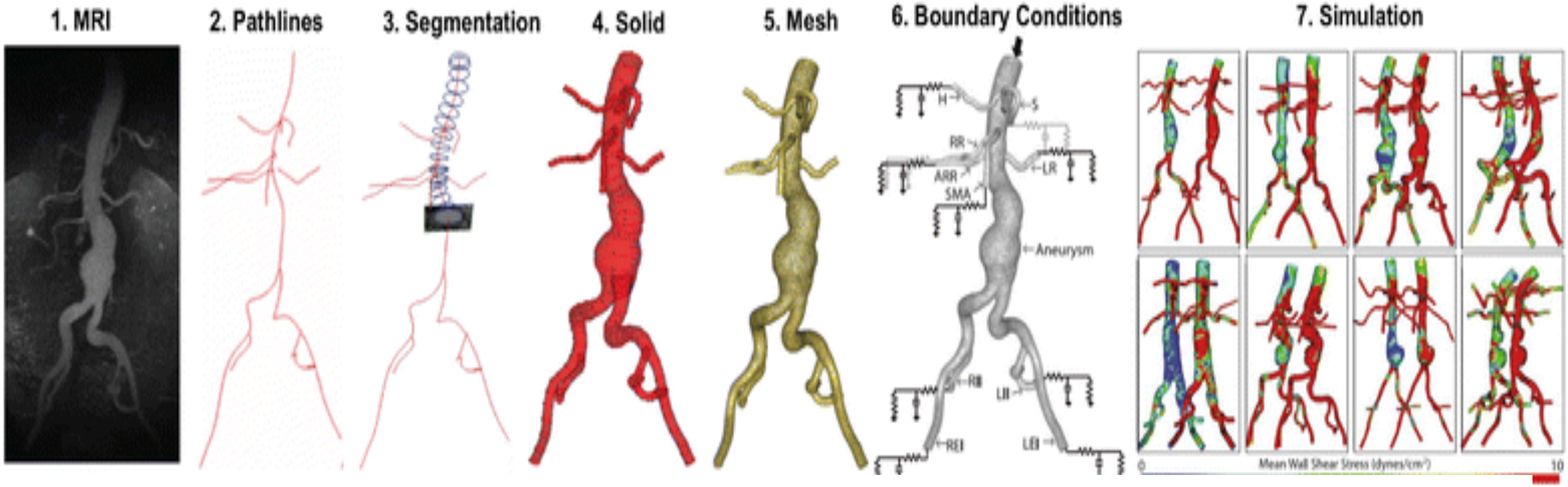
1D Model

METHODOLOGY, AORTA-ILIAC MODEL

Revisiting Pipeline for Model Generation

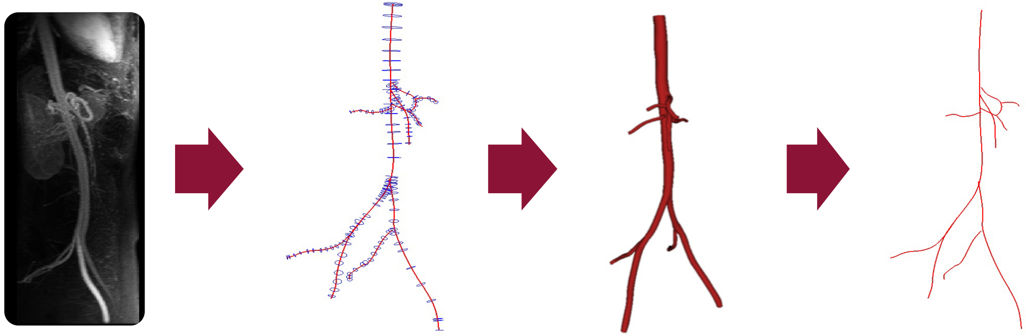
- 1D Formulation: generated from vessel centerline paths and segmentations created for 3D formulation



SimVascular 3D formulation pipeline

Automatic Pipeline Overview

- Why?
  - 1D solver as more computationally efficient method for UQ
- Pipeline: uses SimVascular segmentations to generate input file to 1D solver
  - Generates 1D geometry: centerline of the vessel, segments and joints
- 1D solver
  - Takes input file [~.in] generated bythe pipeline as input
  - Returns vtk or txt files (pressure, flow, resistance, area vs. time step)



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1D Formulation: Newtonian Method

- Start with 3D Navier-Stokes equations (***conservation of mass and momentum***) in a cylinder and integrate over a vessel cross section
- Use constitutive model to relate pressure to wall deformation (empirically derived ***material model***)
- Assumptions: flow in axial direction, no-slip condition at the wall, deformable walls, pressure uniform in cross sectional areas.

Hughes and Lubliner[1] Formulation with a Linear Constitutive Equation

$$\frac{\partial A}{\partial t} + \frac{\partial Q}{\partial z} = 0$$

Mass Equation

$$\frac{\partial Q}{\partial t} + \frac{\partial}{\partial z}\left(\frac{4}{3}\frac{Q^2}{A}\right) + \frac{A}{1.06}\frac{\partial p}{\partial z} = -0.32\pi\frac{Q}{A} + 0.04\frac{\partial^2 Q}{\partial z^2}$$

Momentum Equation

$$p - p_0 = \left(\frac{E h_0}{r_0}\right)\left(\sqrt{\frac{A}{A_0}} - 1\right)$$

Constitutive Equation

[1]T.J.R. Hughes and J. Lubliner, On the One-Dimensional Theory of Blood Flow in the Larger Vessels , *Mathematical Biosciences* , 18(1-2) (1973), 161-170.

0D Lumped Parameter Models

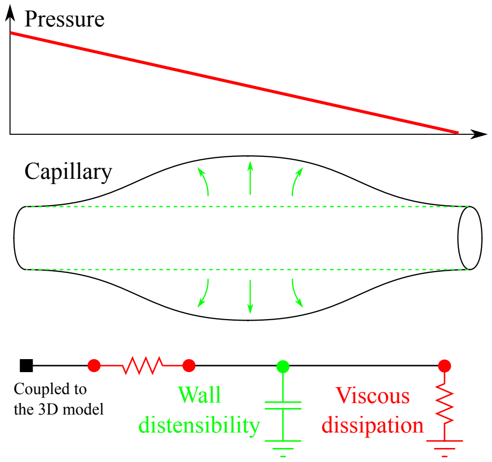
METHODOLOGY, WINDKESSEL MODEL, AORTA-ILIAC LPN

Lumped Parameter Models (Networks)

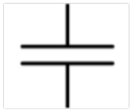
- Use as physiologic boundary conditions or stand-alone 0D models
- <u>Circuit Analogy:</u>

  Flow ⟷ Current

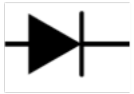
  Pressure Drop ⟷ Voltage



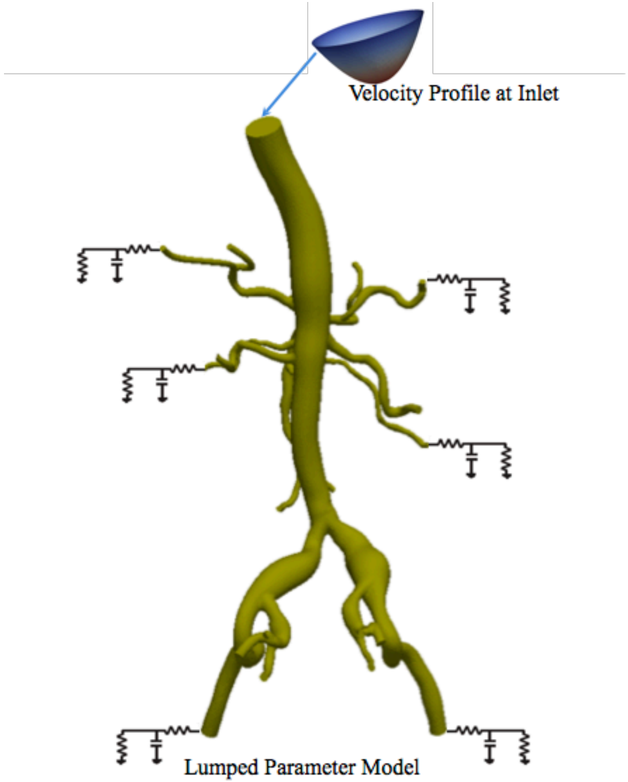
Resistor: $\Delta P = RQ$ 

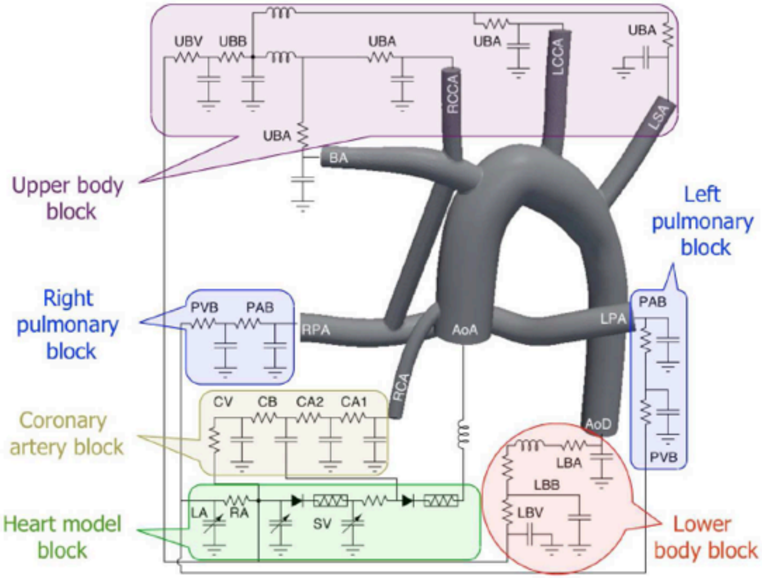
Capacitor: $Q = C\frac{dP}{dt}$ 

Inductor: $\Delta P = L\frac{dQ}{dt}$ 

Diode: $Q = \frac{|Q|+Q}{2}$ 

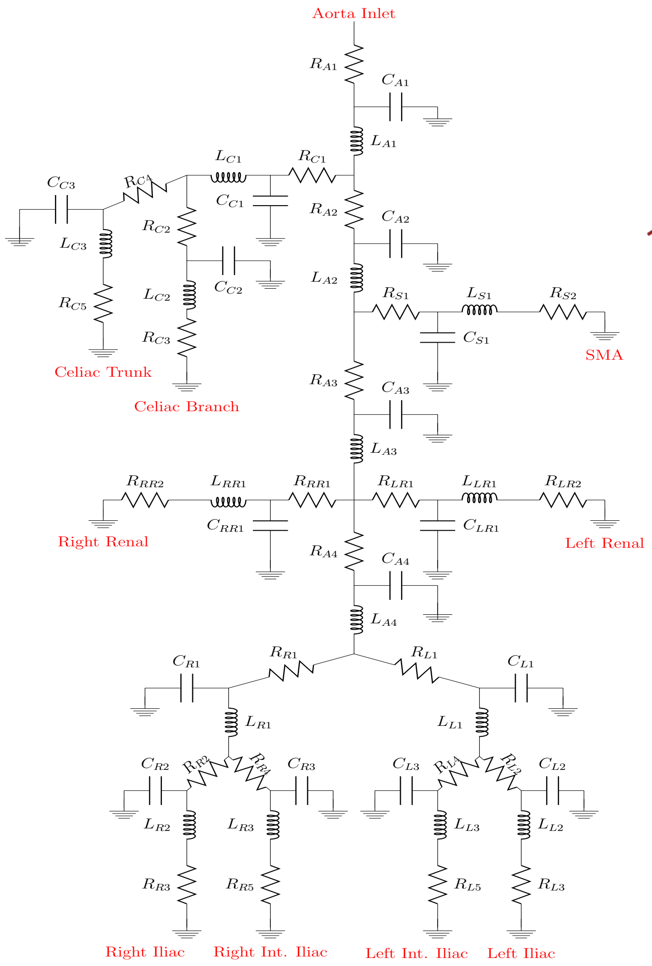
LPN as Boundary Conditions

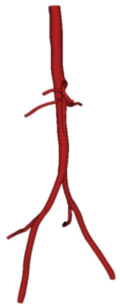




LPN as Standalone Model

- Simplified representation of the aorta model
  - Actual model as all 9 outlets, less spatial resolution
- Model parameter values assigned assuming a Poiseuille profile[1]:
  - $R = \frac{8\mu l}{\pi r^4}$
  - $C = \frac{3l\pi r^3}{2Eh}$
  - $L = \frac{l\rho}{\pi r^2}$
- Note: lengths and radii in formulas come from the 3D geometry





[1]Milišić V, Quarteroni A. Analysis of lumped parameter models for blood flow simulations and their relation with 1D models. *ESAIM: Mathematical Modelling and Numerical Analysis* 2004; 38(04):613–632.

Simplified 0D LPN

- Simplified model: Aorta and external iliac branches
- Physiologic input waveform Q(t)
- 6 BC parameters (left and right iliac RCR circuits)
- Solve a system of ODES for flows and pressures along model:

<u>System of ODES:</u>

$dQ_a = (1/L)*(P_C - P_a)$

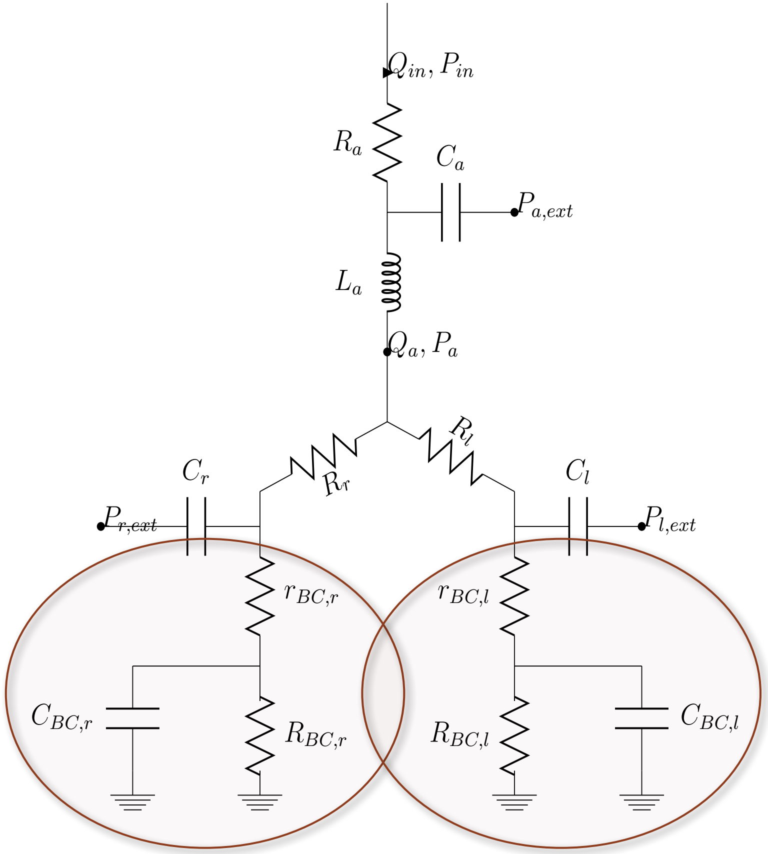
$dP_C = (1/C)*(Q_{in} - Q_a)$

$dP_{R1} = (P_a - P_{R1})/(R_{R1}*C_{R1}) - (P_{R1} - P_{R2})/(R_{R2}*C_{R1})$

$dP_{R2} = (P_{R1} - P_{R2})/(R_{R2}*C_{R2}) - (P_{R2})/(R_{R3}*C_{R2})$

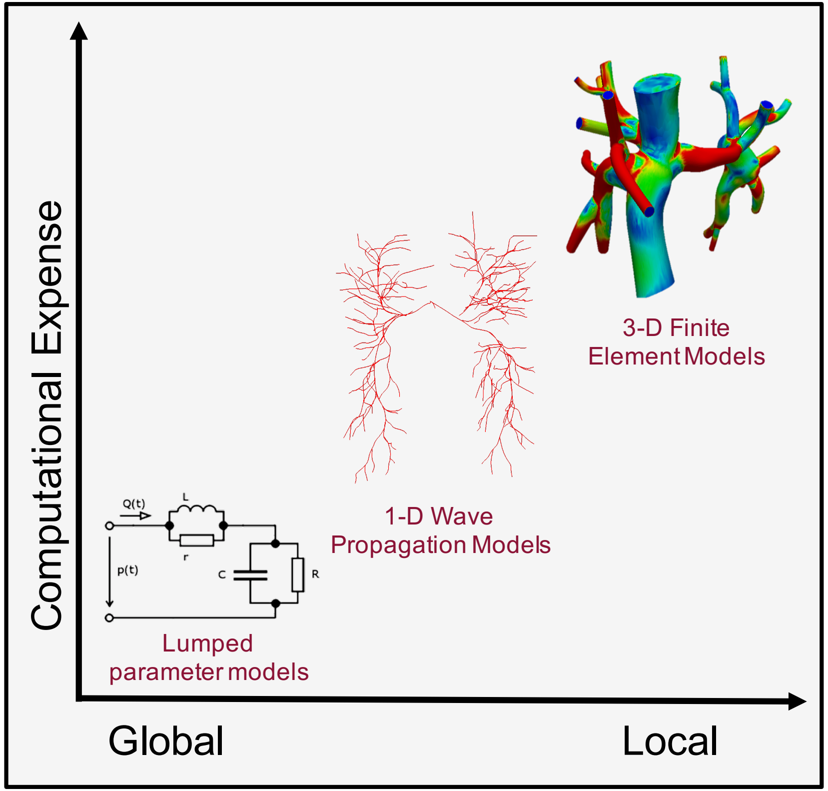
$dP_{L1} = (P_a - P_{L1})/(R_{L1}*C_{L1}) - (P_{L1} - P_{L2})/(R_{L2}*C_{L1})$

$dP_{L2} = (P_{L1} - P_{L2})/(R_{L2}*C_{L2}) - (P_{L2})/(R_{L3}*C_{L2})$

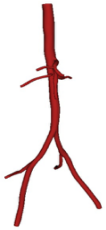


Uncertainty Quantification

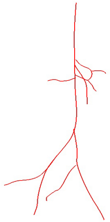
0D, 1D, AND 3D MODELING



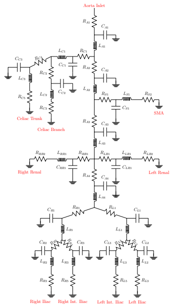
Aorta-Femoral Model



3D Model



1D Model



0D Model

9 Uncertain **Resistance BC Parameters** (Units [dyn•s/cm^5]):

1. Celiac Trunk[11 137.98, 20 684.83]
2. Celiac Branch [17 453.689, 32 413.99]
3. SMA [8258.12, 15 336.52]
4. Right Renal [17 453.76, 32 414.13]
5. Left Renal [14 407.74, 26 757.23]
6. Right Internal Iliac [14 407.04, 26 755.93]
7. Left Internal Iliac [11 137.80, 20 684.49]
8. Right Iliac [4925.42, 9147.22]
9. Left Iliac [4240.97, 7876.08]

Steady inlet flow (5 L/min = 83.33 mL/s)

20 **Quantity of Interests** (Steady state values)

1-18. Flows and Pressures at:

- Celiac Branch Outlet
- Celiac Trunk Outlet
- SMA Outlet
- Left Renal Outlet
- Right Renal Outlet
- Left Iliac Outlet
- Right Iliac Outlet
- Left Internal Iliac Outlet
- Right Internal Iliac Outlet

19-20. Min and Max WSS

Simulation and Cost Distribution of Fidelity Levels

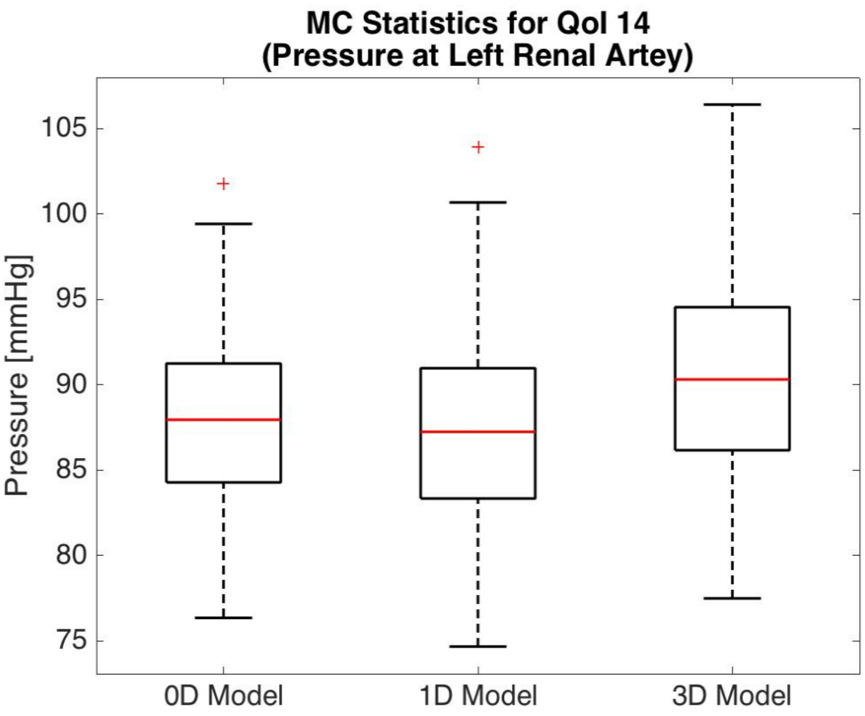
Solver	No. Simulations
3D	100
1D	2000
0D	10 000

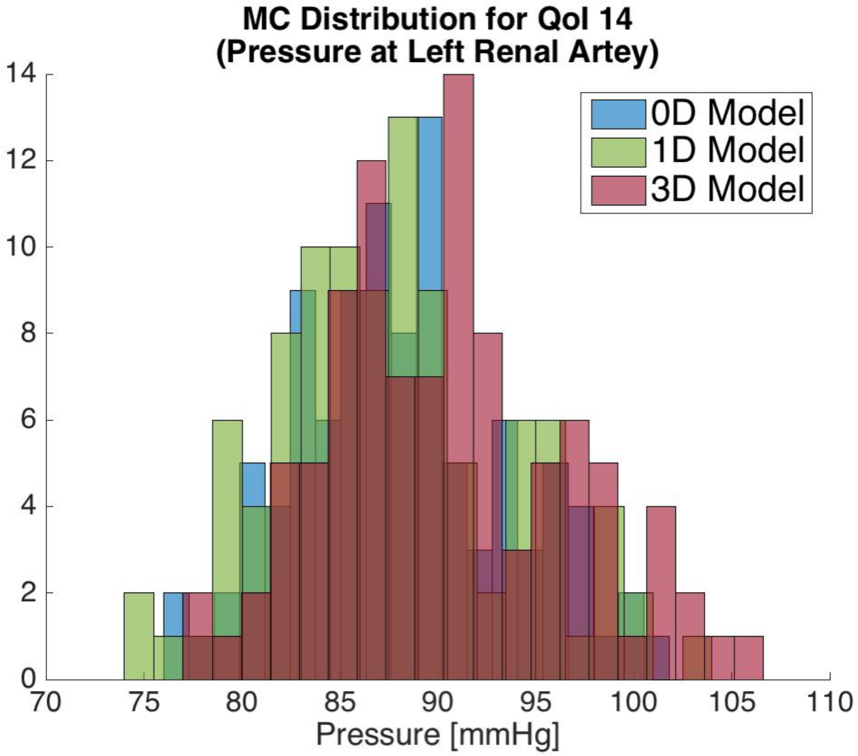
Table 1: Simulations of each fidelity

Solver	Cost (1 simulation)	Effective Cost (No. 3D Simulations)
3D	96 hr	1
1D	11.67 min	2E-3
0D	5 sec	1.45E-5

Table 2: Cost of each varying fidelity solver

Comparison of UQ on each fidelity level individually





Multi-Level Multi-Fidelity Approach

- **Monte Carlo** approaches reliably converge to the true value for any quantity of interest
  - **ISSUE:** Large number of simulations ➔ untenable for our application
- Multi-level and multi-fidelity approaches aim to reduce variance as obtained when using the same number of simulations with Monte Carlo

Seven methods compared:

1. Monte Carlo (MC)
2. Multi-Fidelity: 3D and 1D models (MFA)
3. Multi-Fidelity: 3D and 0D models (MFB)
4. Multi-Level: 3D and 1D models (MLA)
5. Multi-Level: 3D and 0D models (MLB)
6. Multi-Level: 3D, 1D, and 0D models (MLC)
7. Multi-Level Multi-Fidelity approach (MLMF)

Multi-Level Multi-Fidelity Overview

- Multi-Fidelity
  - Control Variate approach utilizing **two** models
  - Relies on correlation between the models
- Multi-Level
  - Low-Fidelity + (High Fidelity – Low Fidelity)
  - Relies on variance decay of the difference term
  - Can use **multiple** levels (> 2)
- Multi-Level/Multi-Fidelity
  - Combines the two approaches
  - Can use **multiple** levels (> 2)

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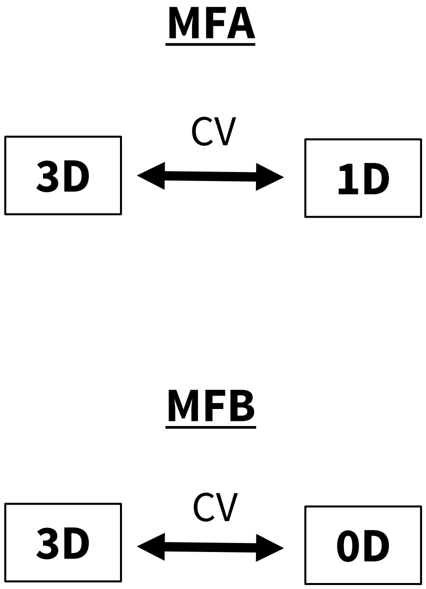

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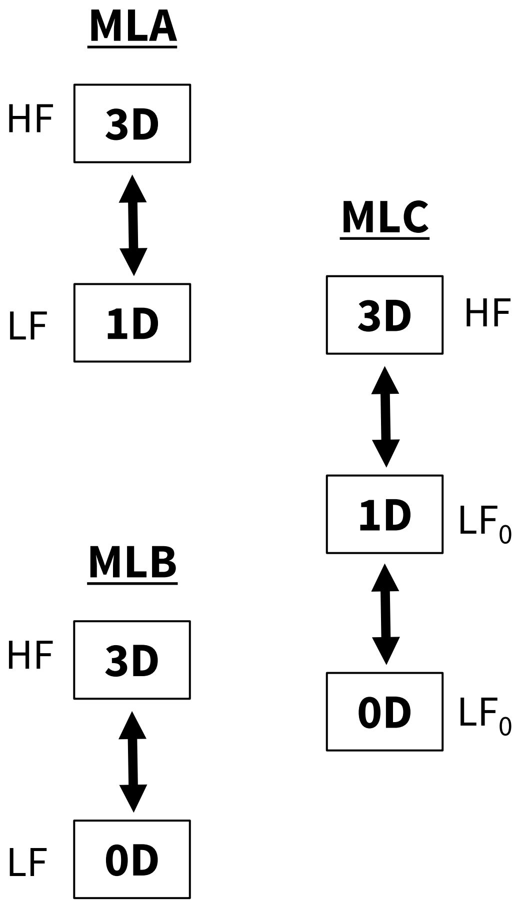
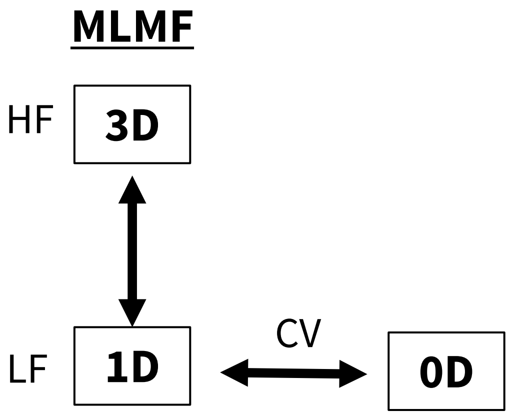
  - Can use **multiple** levels (> 2)
- Multi-Level/Multi-Fidelity
  - Combines the two approaches
  - Can use **multiple** levels (> 2)

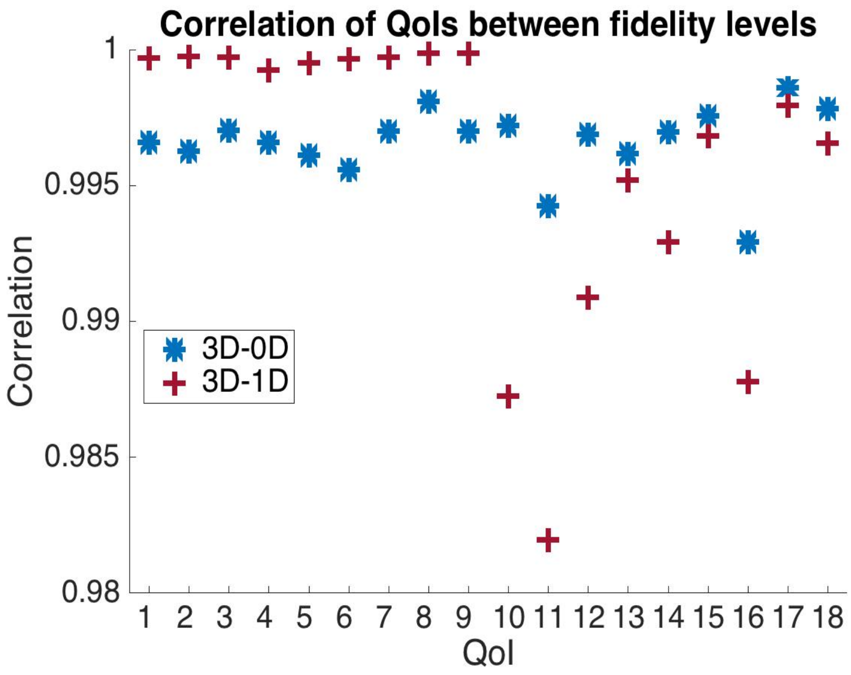


Multi-Level Multi-Fidelity Overview

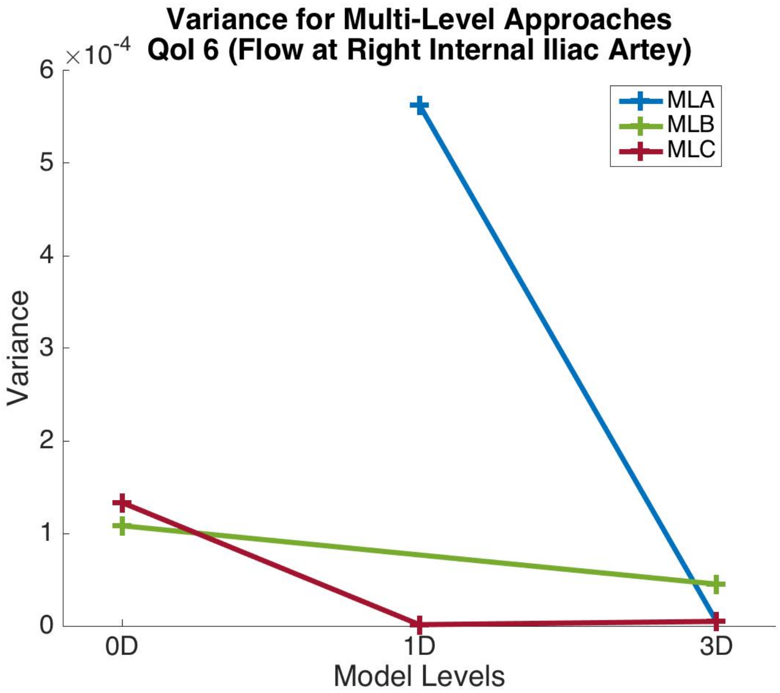
- Multi-Fidelity
  - Control Variate approach utilizing **two** models
  - Relies on correlation between the models
- Multi-Level
  - Low-Fidelity + (High Fidelity – Low Fidelity)
  - Relies on variance decay of the difference term
  - Can use **multiple** levels (> 2)
- Multi-Level/Multi-Fidelity
  - Combines the two approaches
  - Can use **multiple** levels (> 2)



MF: Correlation



ML: Variance Decay



Multi-Level/Multi-Fidelity Expected Value and Variance

Method	Expected Value	Estimator Variance
MC	$\hat{Q}^{MC}_{N_{3D}} = \frac{1}{N_{3D}} \sum_{i=1}^{N_{3D}} Q^{(i)}$	$\frac{\mathbb{V}ar\left(Q\right)}{N_{3D}}$
MFA	$\hat{Q}^{MFA}_{N_{3D}} = \hat{Q}^{MC,3D}_{N_{3D}} + \alpha_{3D,1D}\left(\hat{Q}^{MC,1D}_{N_{3D}} - \mathbb{E}\left[Q^{MC,1D}_{N_{1D}}\right]\right)$	$\mathbb{V}ar\left(\hat{Q}^{MC}_{N_{3D}}\right)\left(1 - \frac{r_{3D,1D}}{1+r_{3D,1D}}\rho^2_{3D,1D}\right)$
MFB	$\hat{Q}^{MFA}_{N_{3D}} = \hat{Q}^{MC,3D}_{N_{3D}} + \alpha_{3D,0D}\left(\hat{Q}^{MC,0D}_{N_{3D}} - \mathbb{E}\left[Q^{MC,0D}_{N_{0D}}\right]\right)$	$\mathbb{V}ar\left(\hat{Q}^{MC}_{N_{3D}}\right)\left(1 - \frac{r_{3D,0D}}{1+r_{3D,0D}}\rho^2_{3D,0D}\right)$
MLA	$\hat{Q}^{MLA}_{N_{3D}} = \hat{Q}^{MC,1D}_{N_{1D}-N_{3D}} + \hat{Y}^{3D,1D}_{N_{3D}}$	$\frac{\mathbb{V}ar(Q^{1D}_{N_{1D}-N_{3D}})}{N_{1D}-N_{3D}} + \frac{\mathbb{V}ar(Y^{3D,1D}_{N_{3D}})}{N_{3D}}$
MLB	$\hat{Q}^{MLB}_{N_{3D}} = \hat{Q}^{MC,0D}_{N_{0D}-N_{3D}} + \hat{Y}^{3D,0D}_{N_{3D}}$	$\frac{\mathbb{V}ar(Q^{0D}_{N_{0D}-N_{3D}})}{N_{0D}-N_{3D}} + \frac{\mathbb{V}ar(Y^{3D,0D}_{N_{3D}})}{N_{3D}}$
MLC	$\hat{Q}^{MLC}_{N_{3D}} = \hat{Q}^{MC,0D}_{N_{0D}-N_{1D}} + \hat{Y}^{1D,0D}_{N_{1D}-N_{3D}} + \hat{Y}^{3D,1D}_{N_{3D}}$	$\frac{\mathbb{V}ar(Q^{0D}_{N_{0D}-N_{1D}})}{N_{0D}-N_{1D}} + \frac{\mathbb{V}ar(Y^{1D,0D}_{N_{1D}-N_{3D}})}{N_{1D}-N_{3D}} + \frac{\mathbb{V}ar(Y^{3D,1D}_{N_{3D}})}{N_{3D}}$
MLMF	$\hat{Q}^{MLMF}_{N_{3D}} = \hat{Q}^{1D}_{N_{1D}-N_{3D}} + \alpha_{1D,0D}\left(\hat{Q}^{0D}_{N_{1D}-N_{3D}} - \hat{Q}^{0D}_{N_{0D}-N_{3D}}\right) + \hat{Y}^{3D,1D}_{N_{3D}}$	$\frac{\mathbb{V}ar(Q^{1D}_{N_{1D}-N_{3D}})}{N_{1D}-N_{3D}}\left(1 - \frac{r_{1D,0D}}{1+r_{1D,0D}}\rho^2_{r_{1D,0D}}\right) + \frac{\mathbb{V}ar(Y^{3D,1D}_{N_{3D}})}{N_{3D}}$

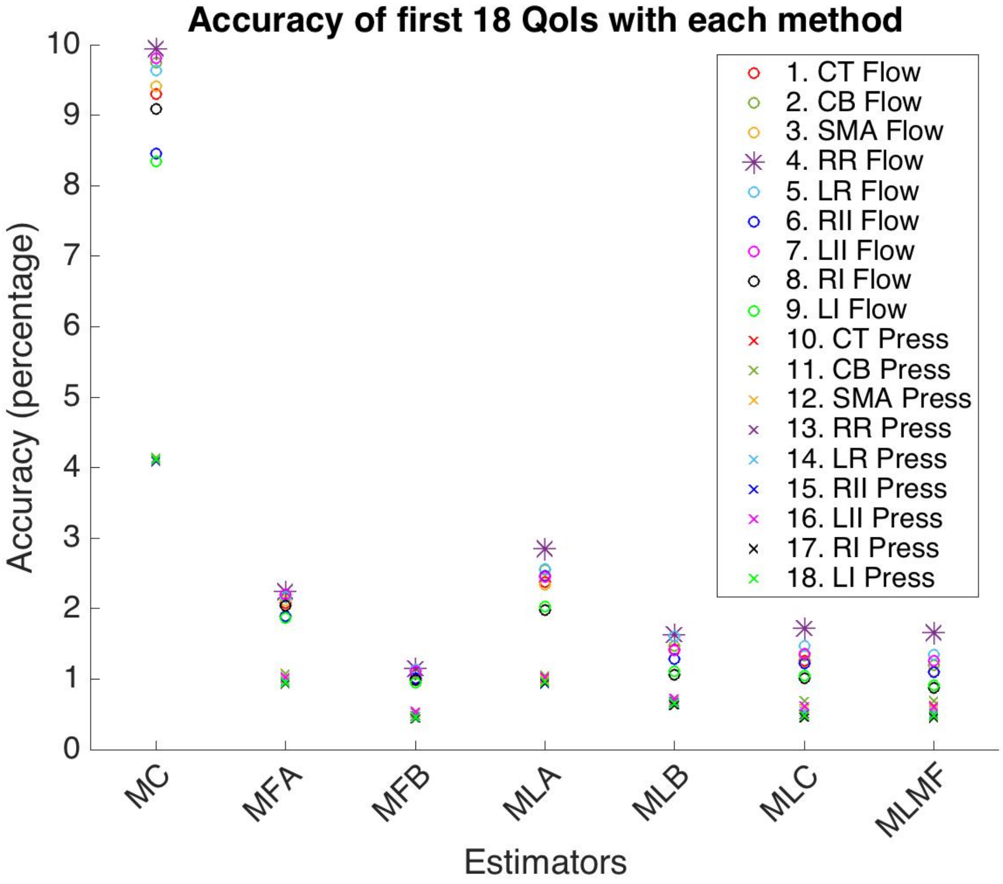
Table 3: Expected values and variances of the Monte Carlo, Multi-Fidelity, Multi-Level and Multi-Level/Multi-Fidelity estimators with $Y^{3D,1D}_{N_{3D}} = \left(Q^{3D}_{N_{3D}} - Q^{1D}_{N_{3D}}\right) Y^{3D,0D}_{N_{3D}} = \left(Q^{3D}_{N_{3D}} - Q^{0D}_{N_{3D}}\right), Y^{1D,0D}_{N_{0D}-N_{1D}} = \left(Q^{1D}_{N_{0D}-N_{1D}} - Q^{0D}_{N_{0D}-N_{1D}}\right)$

Cost Comparison – non-optimized allocation

Method	Effective Cost (3D Simulations)	No. 3D Simulations	No. 1D Simulations	No. 0D Simulations
MC	100	100	–	–
MFA	104.4192	100	2 000	–
MFB	100.1578	100	–	10 000
MLA	104.4192	100	2 000	–
MLB	100.1578	100	–	10 000
MLC	104.5754	100	2 000	9 900
MLMF	104.5754	100	2 000	9 900

Table 4: Cost of each method (QoI: flow at right renal artery)

Accuracy for Quantities of Interest



Flow at the right renal artery is above 1% accuracy with all estimators

Extrapolation – optimized allocation for 1% Accuracy

Method	Effective Cost (3D Simulations)	No. 3D Simulations	No. 1D Simulations	No. 0D Simulations
MC	9 885	9 885	–	–
MFA	56	21	15 681	–
MFB	39	36	–	154 880
MLA	305	212	41 990	–
MLB	156	150	–	342 060
MLC	165	156	1 324	351 940
MLMF	165	156	1 249	362 590

Table 5: Extrapolation for 1% Accuracy (QoI: flow at right renal artery)

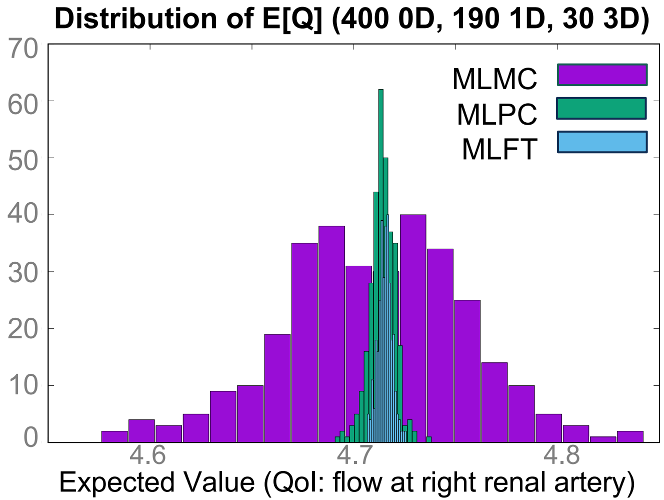
Conclusion

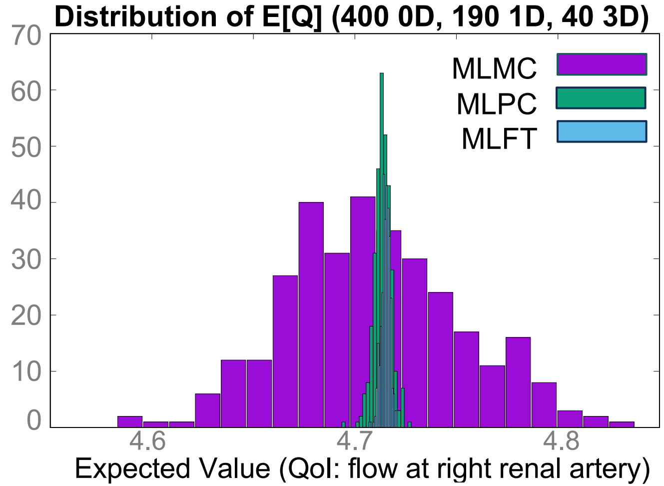
- In summary, the work to date has moved towards the implementation of multi-fidelity uncertainty quantification approach for our cardiovascular applications.
  - Framework to use 3D model geometry to generate 1D and 0D models
  - UQ **individually** on three fidelity levels for the same aorto-femoral model
  - UQ on three fidelity levels using **multi-fidelity approach**
  - Extrapolation to optimize distribution of model simulations for a target accuracy of a given QoI
- The initial results of the MLMF exploration are **promising for optimization of these schemes** on the aorta-femoral model, as well as on similar cardiovascular models.

Next Steps

- Modeling:
  - Additional Geometries (more complex/diseased)
  - Additional QoI (WSS, OSI)
  - Uncertain Parameters (material properties, inflow waveforms, boundary conditions)
  - Mesh refinement/coarsening
- Uncertainty Quantification:
  - Approaches specific to the regularity, sparsity, and rank of the problem
  - Exploit the underlying model structure and accelerate convergence
  - Preliminary results are promising for successful acceleration in low-dimensional cases
- Integration with Sandia National Lab's DAKOTA toolkit

Long-term Goal: *Uncertainty quantification will ultimately enhance the results of our computational modeling so these results are increasingly clinically relevant.*





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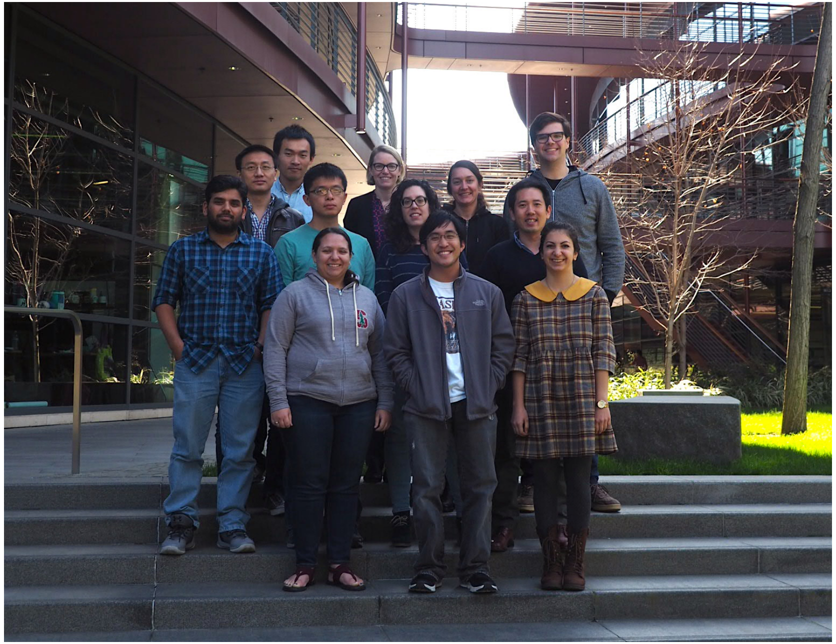

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