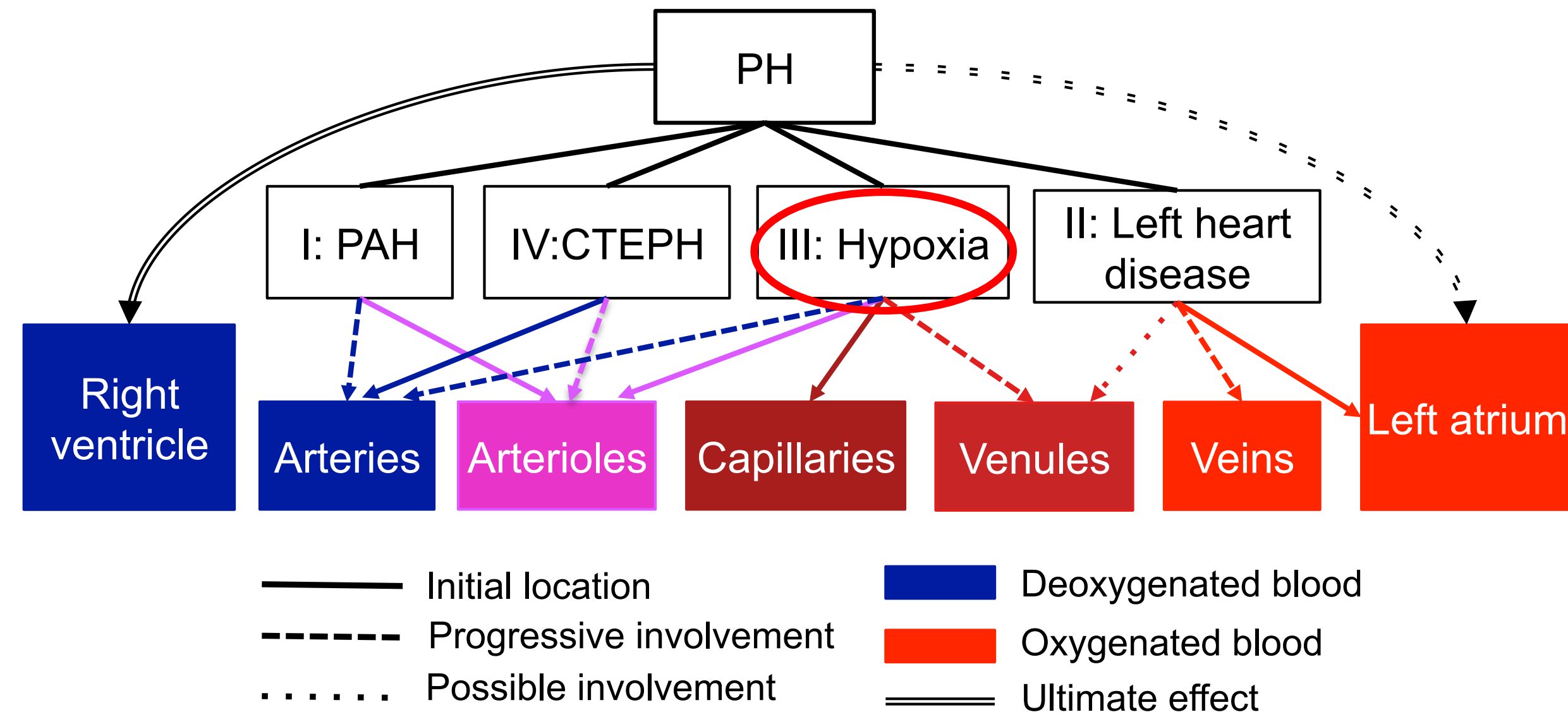


**Pulmonary Hypertension**

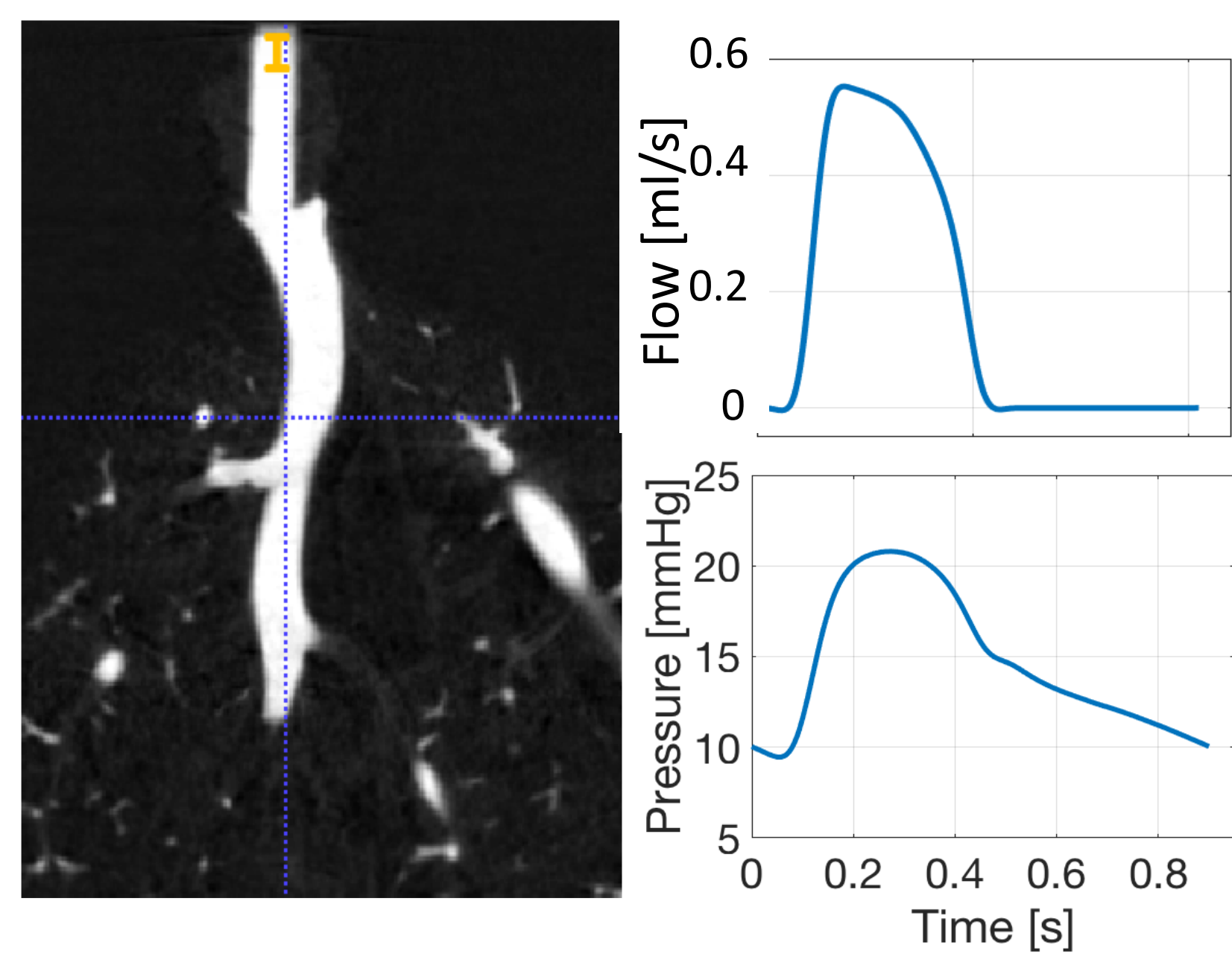


**Pulmonary Hypertension (PH)** is diagnosed when invasively measured mean blood pressure (BP) is above 25 mmHg in the large pulmonary arteries. Based on the pathophysiology, PH is further classified into four major groups:

- Group I:** Idiopathic pulmonary arterial hypertension (PAH) [Due to unknown cause]
- Group II:** PH due to left heart dysfunction
- Group III:** PH due to lung diseases including hypoxia (lack of O<sub>2</sub>)
- Group IV:** PH due to chronic thromboembolic disease (CTEPH)

PH is less prevalent but more fatal than the essential systemic hypertension, with median survival rate of 5-7 years only. It is incurable and the treatment strategies require frequent clinical visits for invasive pressure monitoring. Mechanical progression of the PAH involves vascular remodeling, including vessel stiffening and rarefaction, which typically starts in the vascular beds and then propagates towards the large vessels. The ultimate goal of this study is to develop a 1D FSI network model that uses non-invasive data from magnetic resonance imaging (MRI) and computed tomography (CT) to predict the pulmonary arterial BP and thereby minimize the number of invasive measurements. An important step towards reaching this goal is extracting geometric networks from the imaging data and determine how the vascular anatomy changes due to hypoxia induced PH.

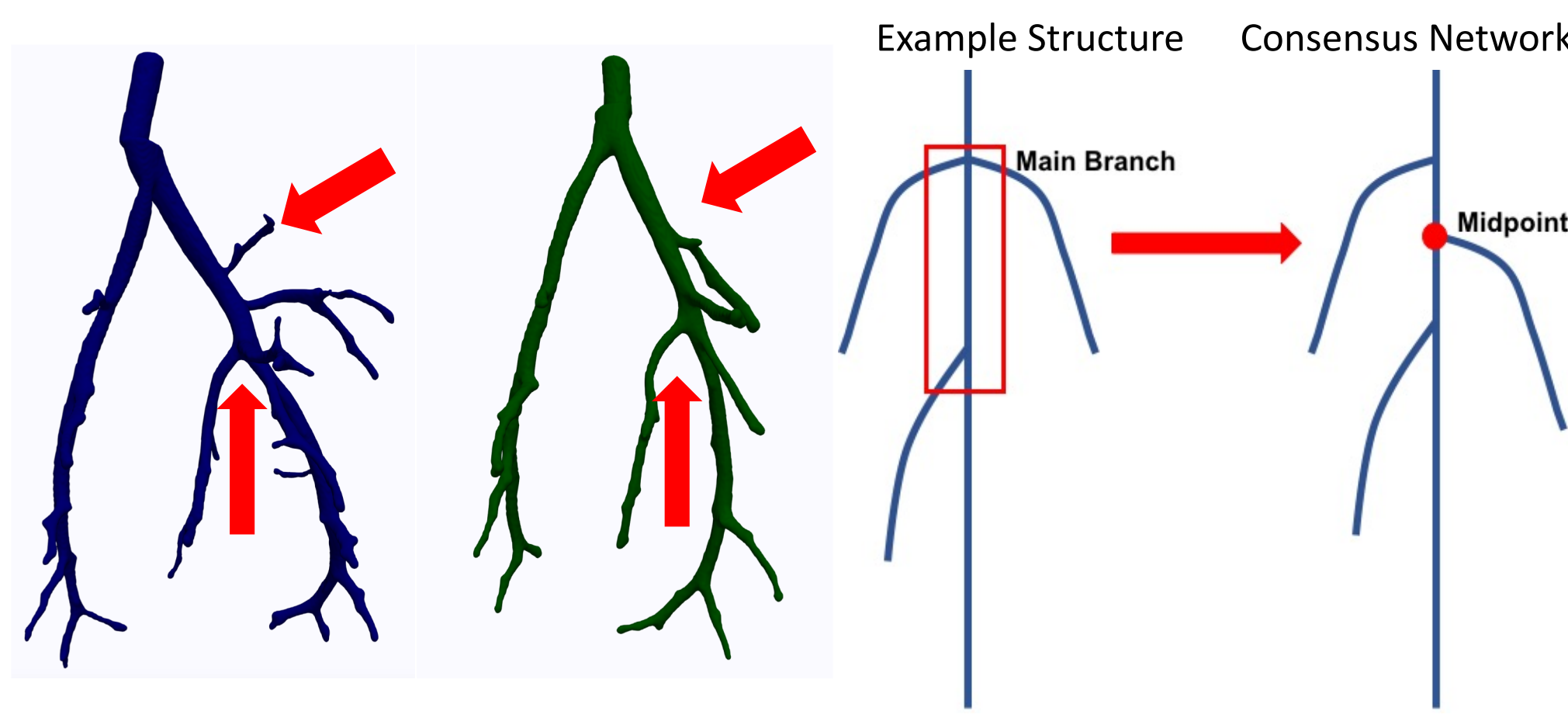
**Data**



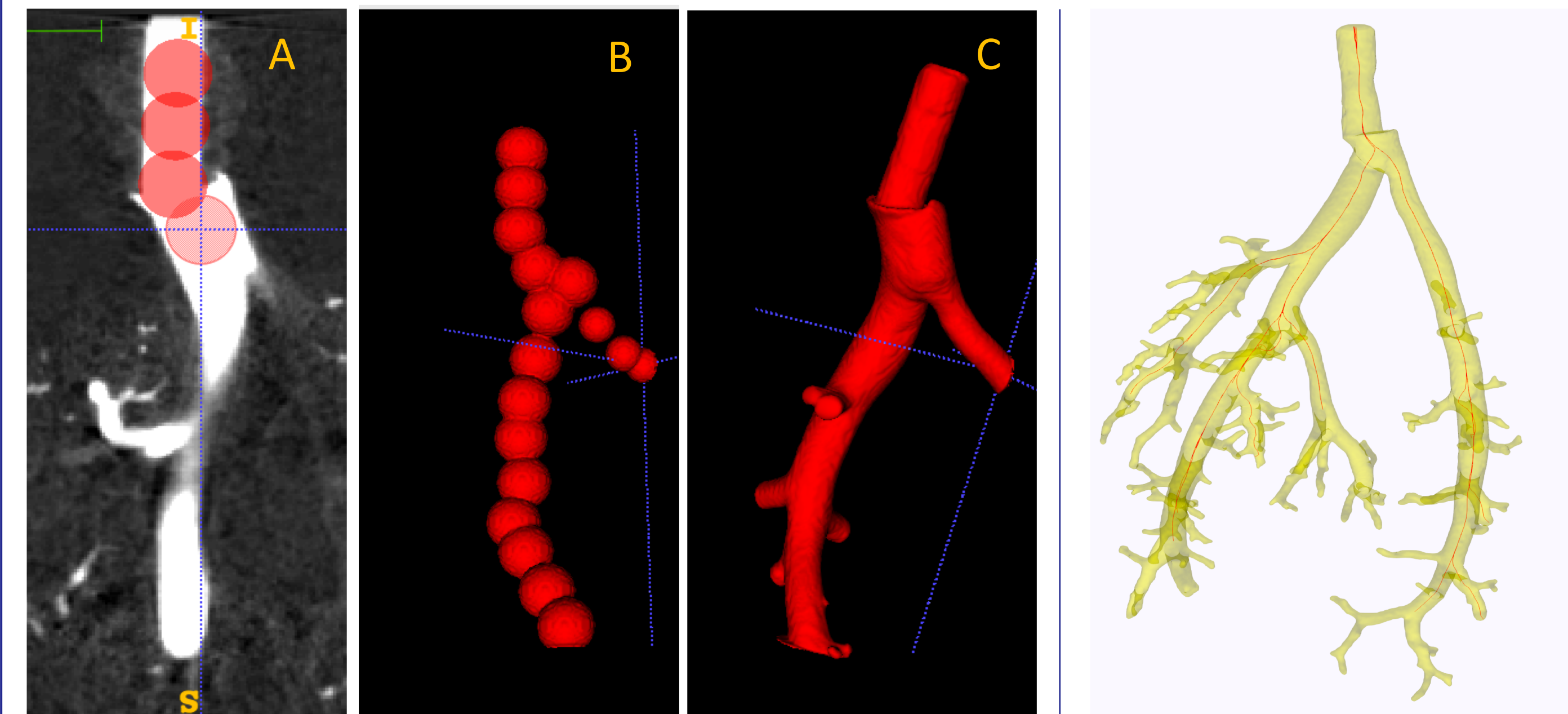
This study analyzes micro CT images from 3 healthy and 4 hypoxic mice, perfused at 4 pressure states [6.3, 7.4, 13.0, 17.2 mmHg]. In addition, we have simultaneous flow and BP measurements from the main pulmonary artery from 7 healthy and 4 hypoxic animal. Since the flow and BP measurements are from different animals, to conduct fluid dynamics simulations, we need to construct a consensus network.

**Consensus Network**

Imaging results revealed that the same large vessels can be identified in all animals, but their branching structures differ. To arrive at a consensus network, we map all vessels to the most prevalent bifurcating structure.



**Extracting Networks**



The networks needed for 1D fluid simulations consists of centerlines, radii and connectivity. To obtain these, we use the following software:

**ITK-Snap** is used to visualize and segment (in 3D) the DICOM images acquired from micro CT. A 3D structure is obtained using Active Contour Segmentation, which evolves manually placed “bubbles” along the vasculature. A smoothing factor is chosen by the user and the evolution is then run until a full network is captured.

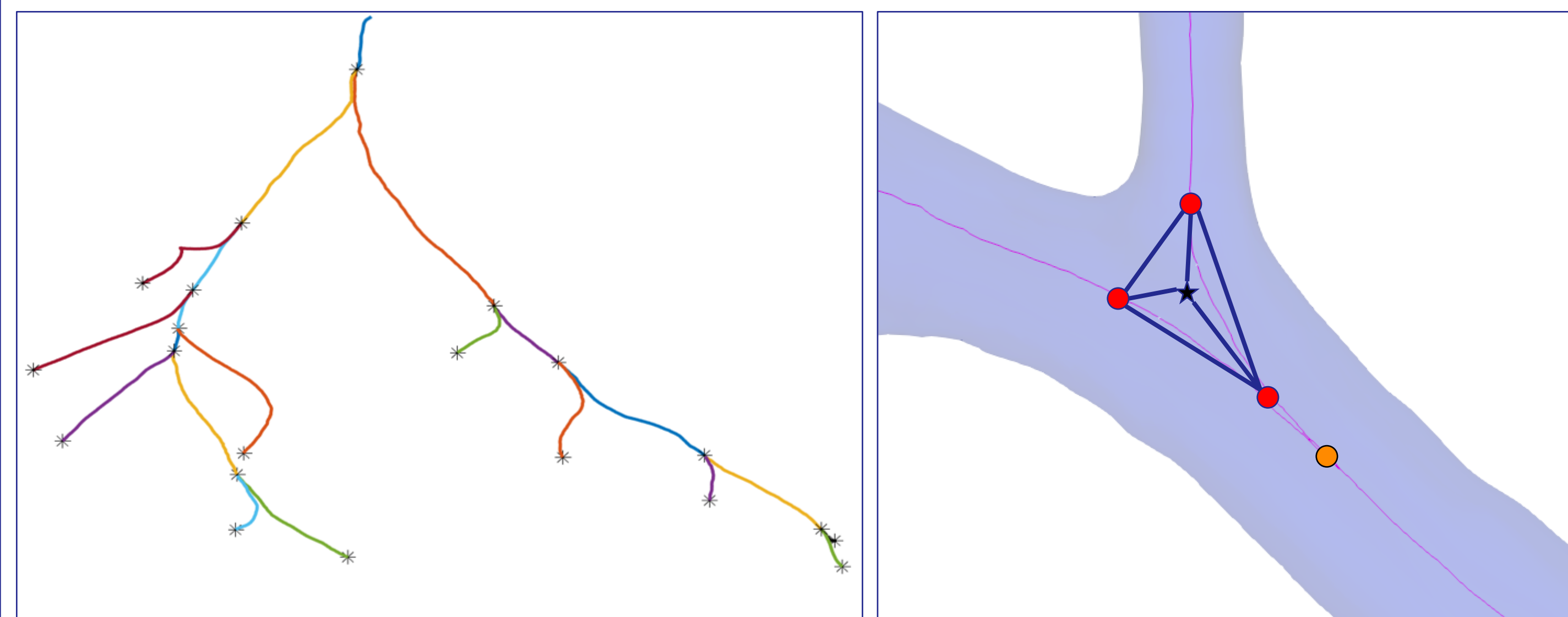
**VMTK** is used to extract centerline coordinates and radii in the segmented network. The user positions targets for source and endpoints and VMTK then places maximally inscribed spheres along the lumen of the vessel. Each sphere is connected through its center point via the minimization problem:

$$c(\tau) = \min_{\gamma \in \Omega} \int_{\gamma^{-1}(p_1)=0}^{\gamma^{-1}(p_2)=L} R[\gamma(\tau)]^{-1} d\tau$$

$c(\tau)$  is the centerline over the arc length  $\tau \in [0, L]$   
 $p_1$  and  $p_2$  are the points in the domain  $\Omega$   
 $\gamma$  is the path between the two points  
 $R$  is the radius of the maximally inscribed spheres located along the path

**Paraview** is used to change file formats and clip the network.  
**Matlab** is used to extract network connectivity, and assess uncertainty in both length and radii predictions.

**21 Vessel Network**

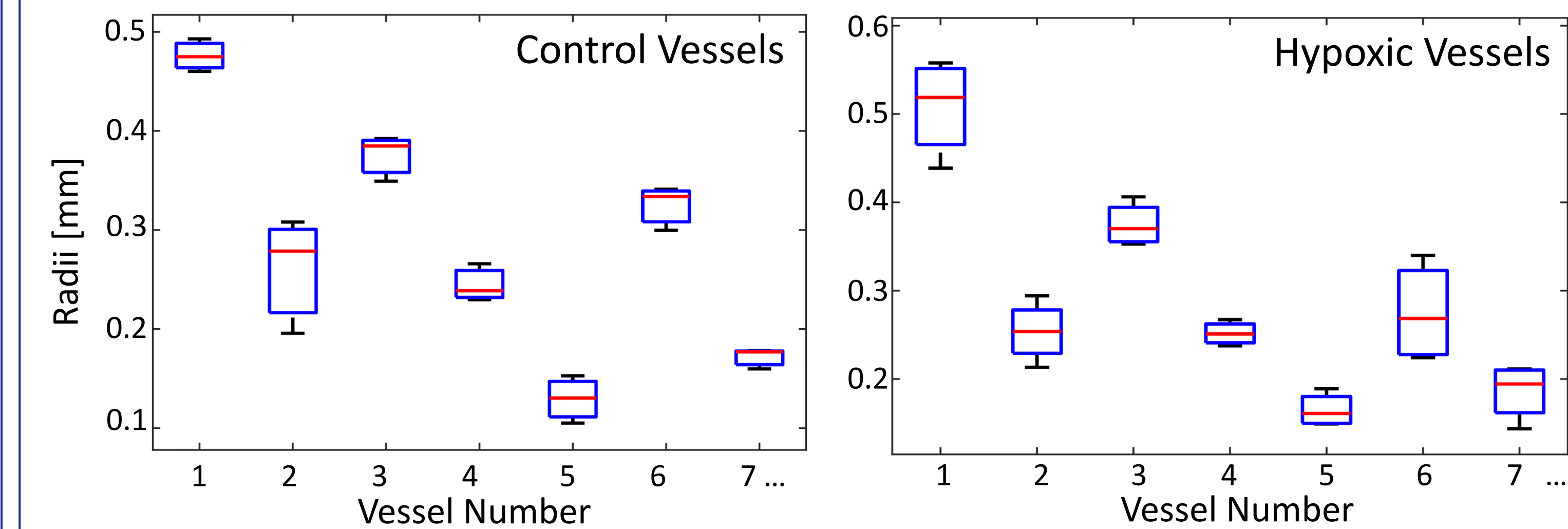
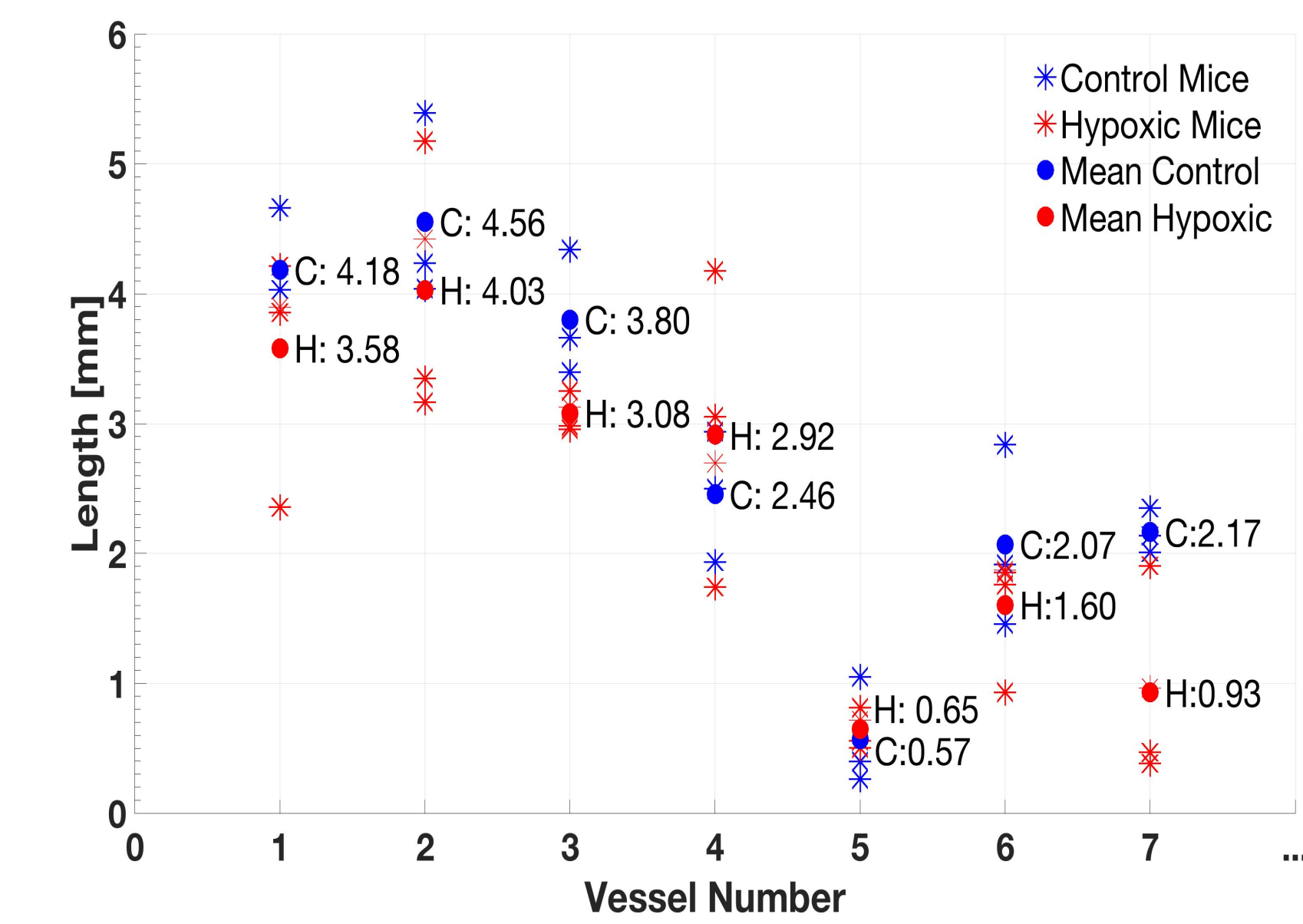


The first 21 vessels in each mouse (top left) were used to define a consensus network, in which flow and pressure can be predicted from solving a fluid dynamics model. To obtain vessel length (top right), we first segment the vessel based on bifurcation information from VMTK (red dots) and then compute the centroid (star) of the triangle seen above. The length of each vessel is then defined as the distance from centroid to centroid, and radii are taken between bifurcation points, which avoids the ostium region between vessels.

**Measurement Results**

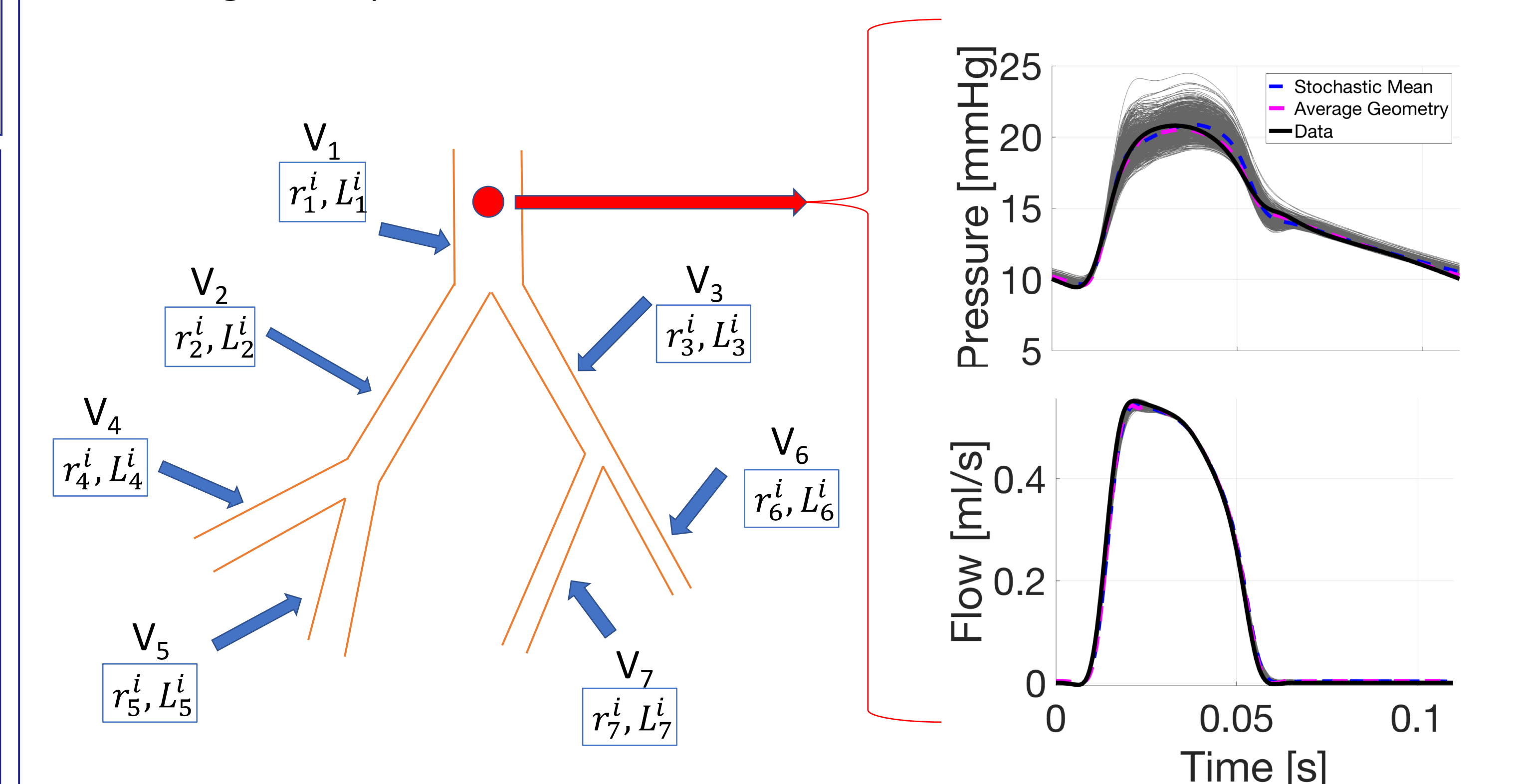
A standard distance formula (stated below) is used to find vessel lengths. Measurements were converted from pixels to mm using known diameter of cannula inserted in the main pulmonary artery (see, Vanderpool et al 2010 for experimental details).

$$L_i = \sum_i \sqrt{(\Delta x_i)^2 + (\Delta y_i)^2 + (\Delta z_i)^2}$$



**Fluid Dynamics Simulations**

Pressure and flow are predicted in the consensus network by solving the 1D Navier-Stokes equations. Accounting for the variability of radii and length measurements, both within each vessel and among different mice, gives us an idea of the uncertainty in the measurements. We choose network dimensions stochastically, and simulate pressure and flow through the network with the selected geometry. Future results will estimate parameters and compare estimates between control and hypoxic animals to understand how physiological changes, like vascular wall remodeling, affect prediction of the waveforms.



$$r_j^i \sim \text{Uni}(\tilde{r}_j, \sigma_{r_j}), L_j^i \sim \text{Uni}(\tilde{L}_j, \sigma_{L_j}) \quad i = 1, 2, \dots, 1000, j = 1, 2, \dots, 21$$

**Acknowledgements**

This work is supported by the National Science Foundation: NSF-1246991 (RTG) and NSF-1615820 (Research Award to Olufsen). ITK-Snap. Paraview. VMTK. L Antiga, D. A. Steinman, *IEEE Trans. Med. Imaging* 23(6):704–713, 2004. We want to thank Naomi Chesler, U Wisconsin, Madison and her group for providing data analyzed here.