History of Vascular Modelling

William Harvey – discovery of the circulation
1628

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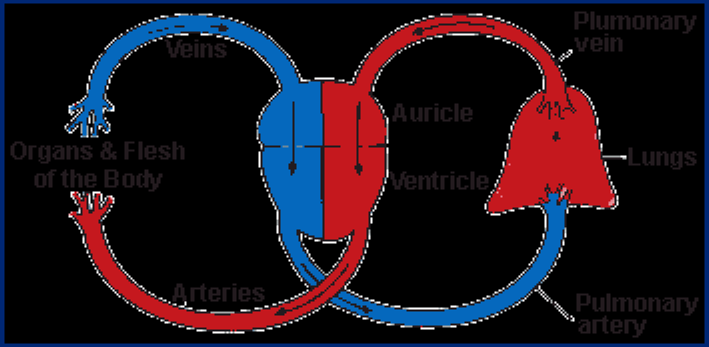
William Harvey (1578-1657)



Since all things, both argument and ocular demonstration, show that the blood passes through the lungs and heart by the force of the ventricles, and is sent for distribution to all parts of the body, where it makes its way into the veins and porosites of the flesh, and then flows by the veins from the circumference on every side to the centre, from the lesser to the greater veins, and is by them finally discharged into the vena cava and right auricle of the heart, and this in such a quantity or in such a flux and reflux thither by the arteries, hither by the veins, as cannot possibly be supplied by the ingesta, and is much greater than can be required for mere purposes of nutrition; it is absolutely necessary to conclude that the blood in the animal body is impelled in a circle, and is in a state of ceaseless motion. (1628)

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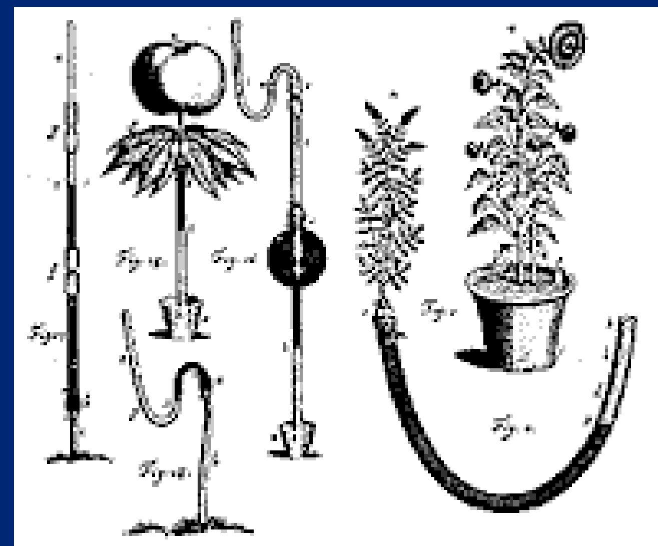
History of Vascular Modelling

Stephen Hales
1677 – 1761



Vegetable staticks 1733

- blood pressure measurements
- flow resistance occurs mainly in the microcirculation
- effects of elasticity of the arteries

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History of Vascular Modelling

Development of fluid dynamics

- Euler
- Daniel Bernoulli (Professor of Anatomy)
- Poiseuille (Physician)

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History of Vascular Modelling

Thomas Young
1773 –1829

Thomas Young (1773-1829)

Developed the theory of wave propagation in elastic tubes

` … the enquiry, in what manner, and in what degree, the circulation of the blood depends on the muscular and elastic powers of the heart and of the arteries, supposing the nature of those powers be known, must become simply a question belonging to the most refined departments of the theory of hydraulics.'   1809

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History of Vascular Modelling

Flow profile and the link with atherosclerosis

- Wormersley 1955 – velocity profile and viscosity
- Caro, Fitz-Gerald & Schroter 1971 – correlation between low wall shear stress and fatty streaks
- Fry 1973 – transport of lipoproteins through the arterial wall

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Modelling pulse propagation in the systemic & pulmonary circulation

Nicholas Hill, Mathematics & Statistics, University of Glasgow
Gareth Vaughan, Mathematics & Statistics, University of Glasgow

Mette Olufsen, Mathematics, North Carolina State University, U.S.A.

Martin Johnson, Scottish Pulmonary Vascular Unit, Western Infirmary, Glasgow
Christopher Sainsbury, BHF Glasgow Cardiovascular Research Centre, University of Glasgow

N.A.Hill@maths.gla.ac.uk *Xi'an, 6 April, 2011*

Acknowledgements: Professor Charles Peskin, Courant Institute, New York University & EPSRC.

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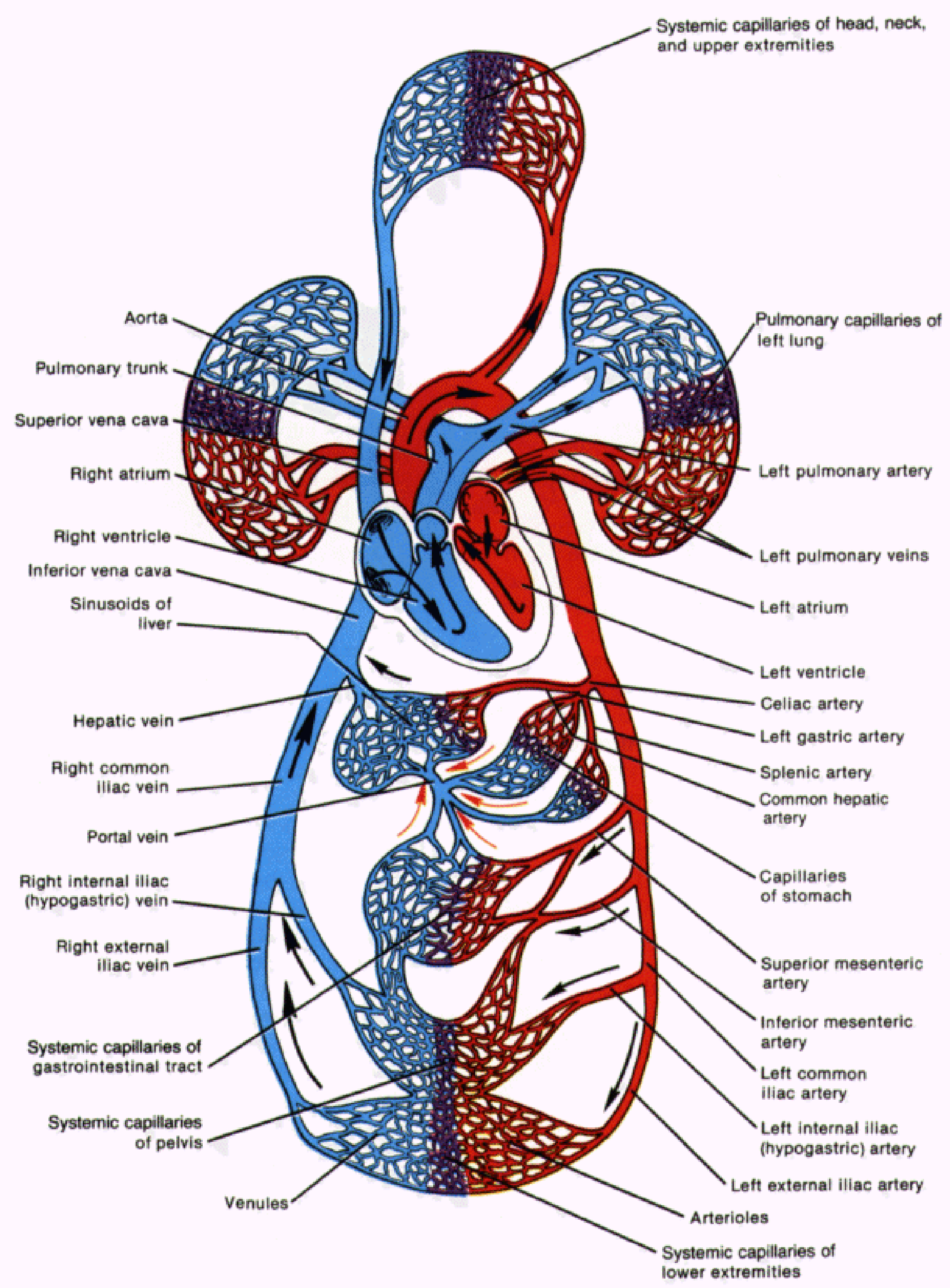

The Cardiovascular System:

- Systemic circulation:
  - Systemic arteries
  - Systemic veins
- Pulmonary circulation:
  - Pulmonary arteries
  - Pulmonary veins
- Left and right heart:
  - Atrium
  - Ventricle

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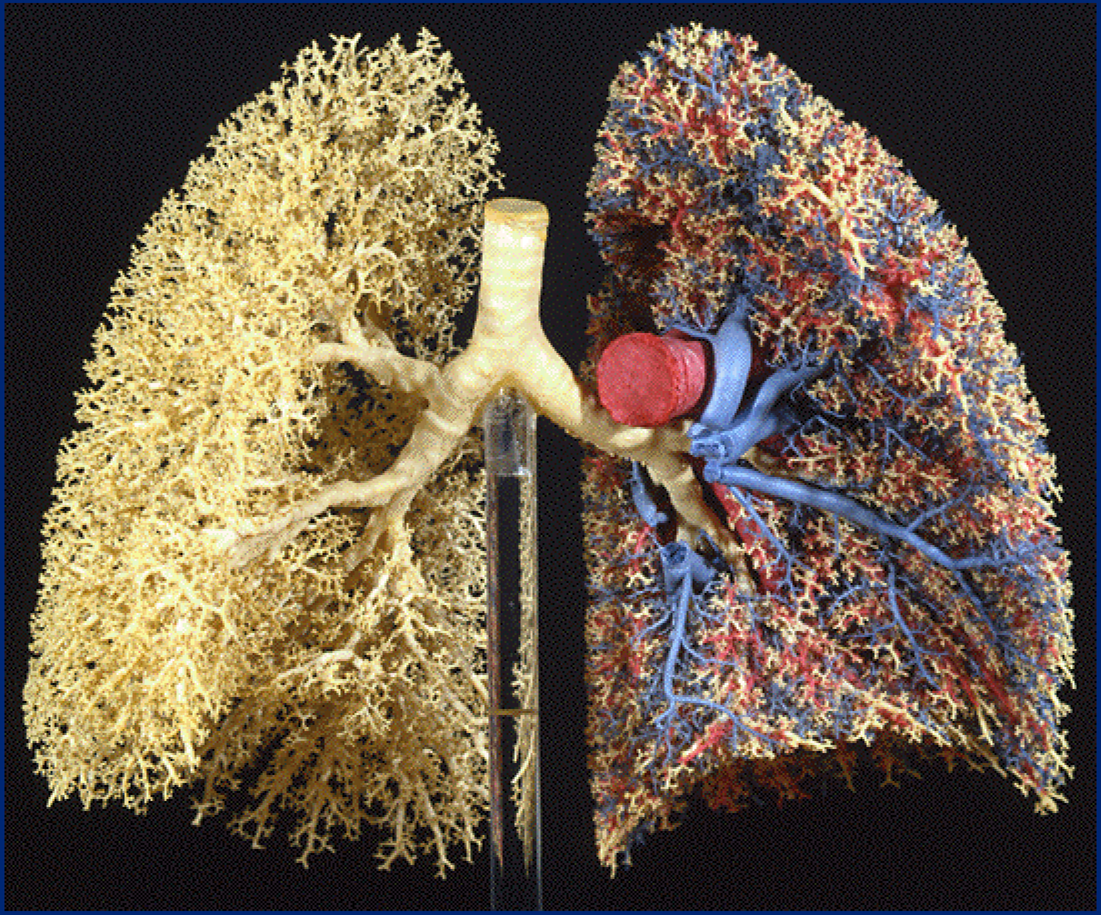
Pulmonary Circulation

Right Ventricle ✹ Pulmonary Artery ✹ Capillary Blood Vessels ✹ Pulmonary Veins ✹ Left Atrium



- Pulmonary capillary blood volume 150 ml
- Blood-Gas exchange area 70 m^2
- Average capillary radius 4 μm

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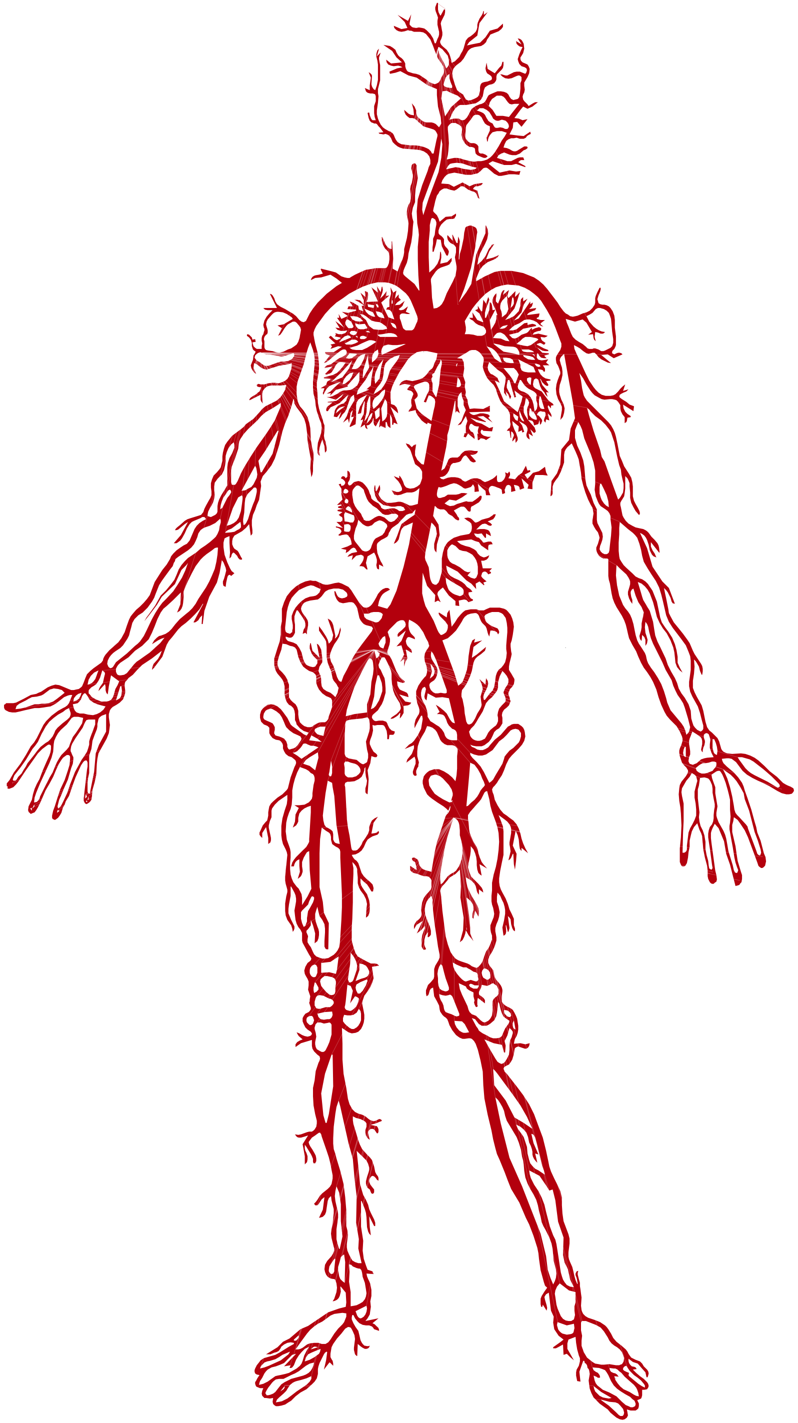

Systemic arteries:

- Consist of
  - Large arteries (cm)
  - Small arteries (mm)
  - Arterioles (100 μm)
  - Capillaries (50 μm)
- Pressure drop across resistance arteries

Pulmonary vasculature:

- Consists of
  - Pulmonary arteries (mm)
  - Pulmonary Capillaries (4 μm)
- Pressurised venous system

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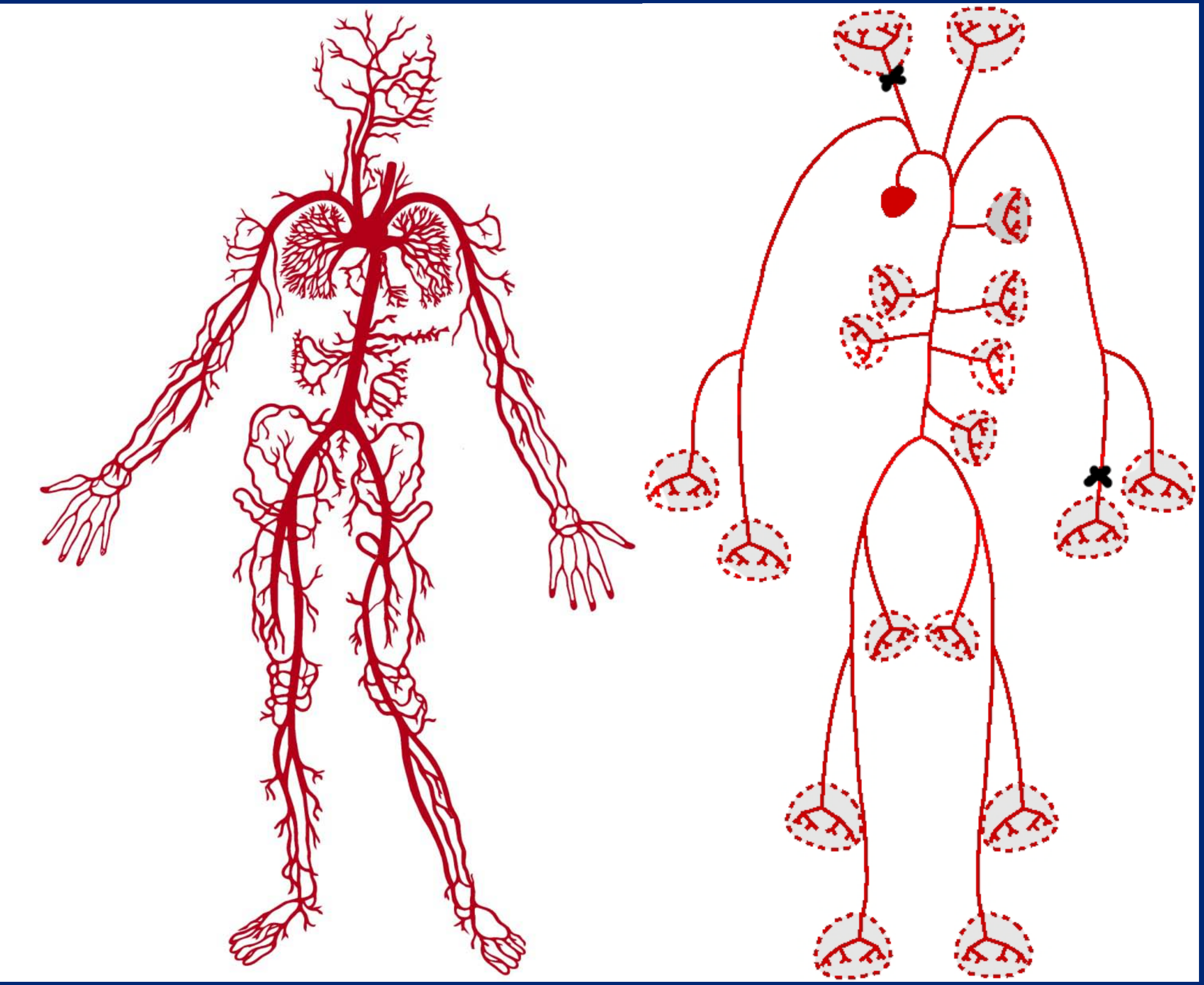
Systemic Artery Model



- 1-D cross-sectional average
- Large systemic arteries – tapered vessels
- Structured tree vascular beds

Olufsen, M.S. et al., Numerical Simulation and Experimental Validation of Blood Flow in Arteries with Structured-Tree Outflow Conditions, *Annals of Biomedical Engineering*, **28**, 1281-1299, 2000.

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Mathematical Model

- 1D fluid dynamics model for wave-propagation in the large arteries – nonlinear, moving walls, flat velocity profile with a boundary layer, solved numerically.
- Smaller arteries modelled as a structured tree using linearised equations that allow mathematical analysis.
- Use fast recursive algorithms.
- New algorithm to calculate pressure and flow within structured tree.

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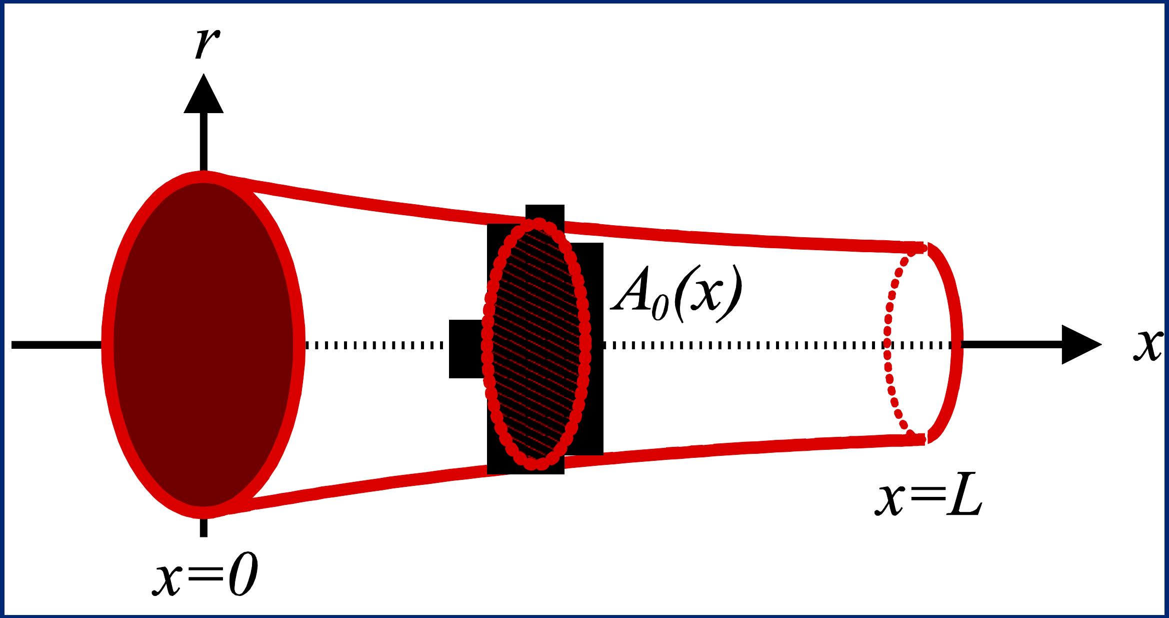
The large arteries



Flow Equations for Large Arteries

- Continuity equation -

$$\frac{\partial q}{\partial x} + \frac{\partial A}{\partial t} = 0 \tag{1}$$

- Momentum equation -

$$\frac{\partial q}{\partial t} + \frac{\partial}{\partial x}\left(\frac{q^2}{A}\right) + \frac{A}{\rho}\frac{\partial p}{\partial x} = \frac{2\pi\nu R}{\delta}\frac{q}{A} \tag{2}$$

- State equation -

$$p(x,t) - p_0 = \frac{4}{3}\frac{Eh}{r_0}\left(1 - \sqrt{\frac{A_0}{A}}\right) \tag{3}$$

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Equations for Flow in the Structured Tree

From linearised 1D axisymmetric N-S equations, and Fourier expansions for u, p and q, we get,

the momentum equation,

$$\boxed{i\omega Q = -\frac{A_0}{\rho}\frac{\partial P}{\partial x}(1 - F_J)} \qquad (4)$$

- where $F_J = \frac{2J_1(w_0)}{w_0 J_0(w_0)}$

and the continuity equation,

$$\boxed{i\omega CP + \frac{\partial Q}{\partial x} = 0} \qquad (5)$$

for the small vessels.

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Impedance Relation

- solving (4) and (5) gives,

$$Q(x,\omega) = a\cos(\omega x/c) + b\sin(\omega x/c)$$

$$P(x,\omega) = i\sqrt{\frac{\rho}{CA_0(1-F_J)}}(-a\cos(\omega x/c) + b\sin(\omega x/c))$$

$$\Rightarrow \boxed{Z(x,\omega) = \frac{P(x,\omega)}{Q(x,\omega)} = \frac{ig^{-1}(b\cos(\omega x/c) - a\sin(\omega x/c))}{a\cos(\omega x/c) + b\sin(\omega x/c)}}$$

- with wave propagation velocity $c = \sqrt{\frac{A_0(1-F_J)}{\rho C}}$

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Recursion for the Impedance

- Assuming we know the impedance $Z(x,\omega)$ at the end of a vessel, we can find the impedance at the root of the vessel. So we have
$$Z(0,\omega) = f(Z(L,\omega))$$
- a bifurcation condition,
$$\frac{1}{Z_P} = \frac{1}{Z_{d_1}} + \frac{1}{Z_{d_2}}$$
- and terminal conditions Z_{term}, r_{min}
- So we can find the impedance at the root of the structured tree.

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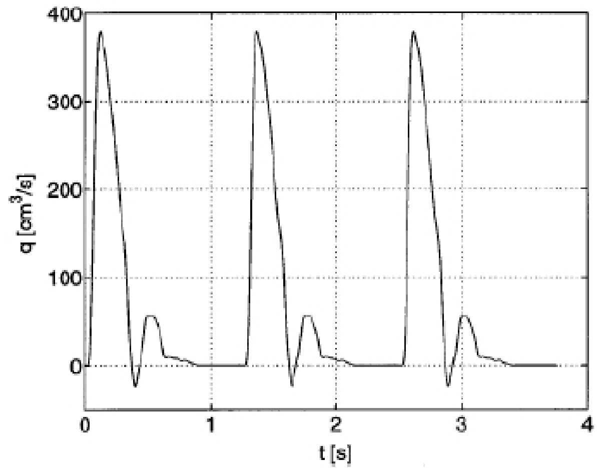
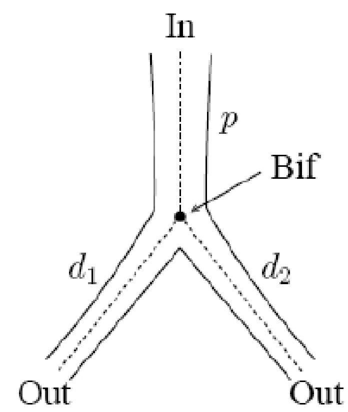
Flow measurements using MRI





- Inflow - Periodic waveform.
- Conserved flow, $q_p = q_{d_1} + q_{d_2}$.
- Continuous pressure, $p_p = p_{d_1} = p_{d_2}$.

Pulmonary Arterial System Data

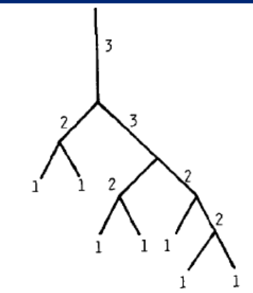


FIGURE 1

Strahler orders in a dichotomously branching system (see text).

Integrated Data for the Total Pulmonary Arterial System

Order	Number of branches	Diameter (mm)	Length (mm)	End branches	Capillary bed (%)
17	1.000	30.000	90.50	3.000×10^8	1.000×10^2
16	3.000	14.830	32.00	1.000×10^8	3.333×10
15	8.000	8.060	10.90	3.021×10^7	1.007×10
14	2.000×10	5.820	20.70	1.376×10^7	4.588
13	6.600×10	3.650	17.90	3.983×10^6	1.328
12	2.030×10^2	2.090	10.50	1.159×10^6	3.863×10^{-1}
11	6.750×10^2	1.330	6.60	3.470×10^5	1.157×10^{-1}
10	2.290×10^3	0.850	4.69	8.916×10^4	2.972×10^{-2}
9	5.861×10^3	0.525	3.16	4.805×10^4	1.602×10^{-2}
8	1.756×10^4	0.351	2.10	1.604×10^4	5.437×10^{-3}
7	5.255×10^4	0.224	1.38	5.358×10^3	1.786×10^{-3}
6	1.574×10^5	0.138	0.91	1.787×10^3	5.957×10^{-4}
5	4.713×10^5	0.086	0.65	5.975×10^2	1.992×10^{-4}
4	1.411×10^6	0.054	0.44	1.995×10^2	6.650×10^{-5}
3	4.226×10^6	0.034	0.29	6.664×10	2.221×10^{-5}
2	1.266×10^7	0.021	0.20	2.370×10	7.900×10^{-6}
1	3.000×10^8	0.013	0.13	1.000	3.333×10^{-7}

Capillary bed (%) is the calculated percent of the total capillary bed supplied by one branch of a given order.

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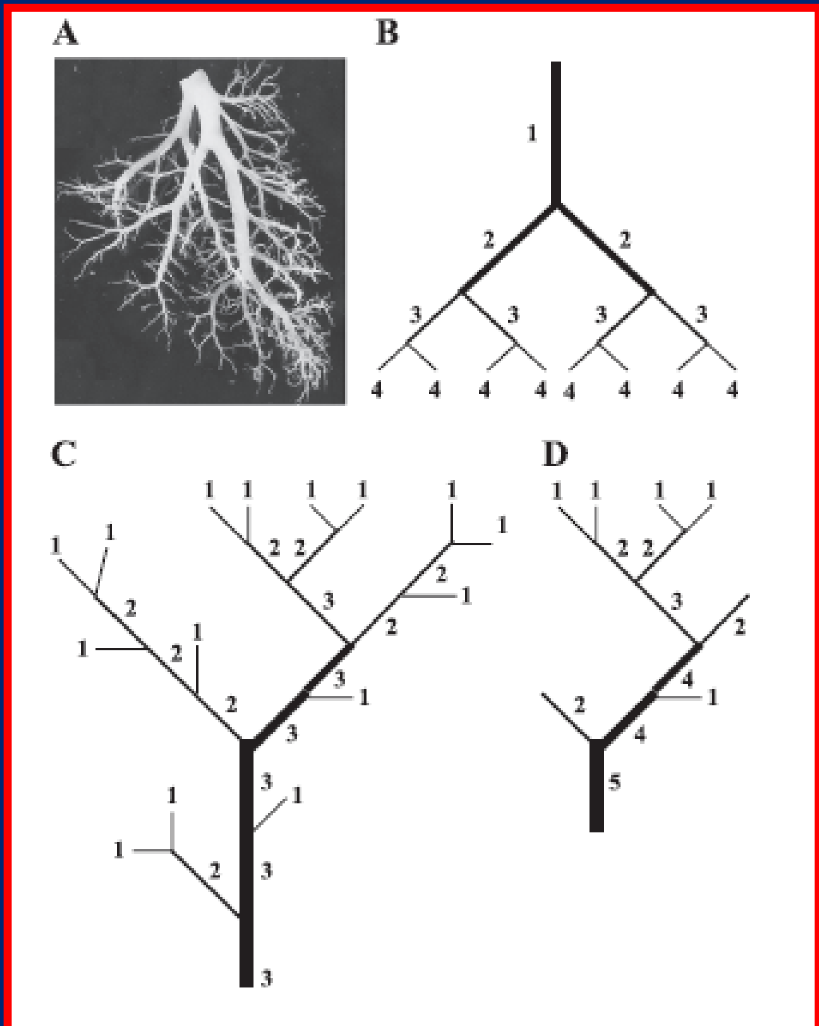
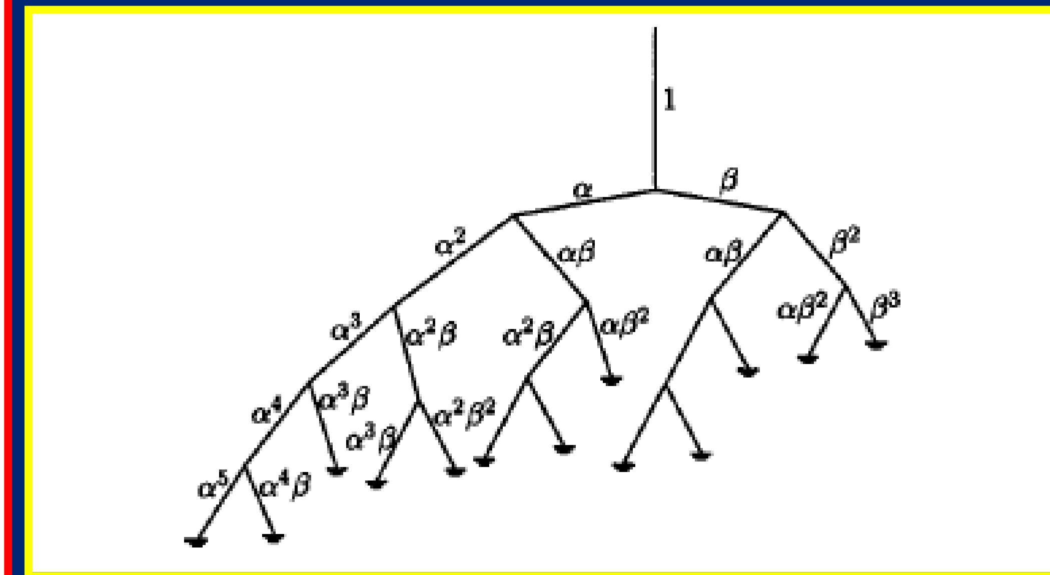
The Pulmonary Arterial Tree





The asymmetric structured tree model.

For any vessel $r = \alpha^i \beta^j r_0$

& $r_{\text{daughter1}} = \alpha r_{\text{parent}}$ and $r_{\text{daughter2}} = \beta r_{\text{parent}}$

Cast of the pulmonary arteries and branch classification schemes.

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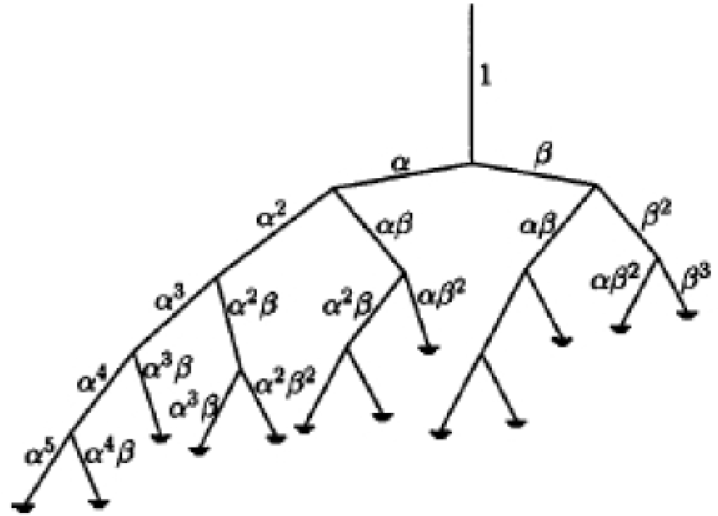
Structured Tree



- Provides outflow condition to model for large arteries.
- Structured tree of elastic vessels.
- Scaling relations $r_{d_1} = \alpha r_p, \quad r_{d_2} = \beta r_p$.

Parameters determining parent/daughter radius ratios

Area ratio is $\eta = (r_{\mathrm{d1}}^2 + r_{\mathrm{d2}}^2) / r_{\mathrm{pa}}^2 = 1.16 \,\&\, 1.08$

Radius exponent ξ

is given by $r_{\mathrm{pa}}^{\xi} = r_{\mathrm{d1}}^{\xi} + r_{\mathrm{d2}}^{\xi}, \xi = 2.7$

$\alpha = r_{\mathrm{d1}} / r_{\mathrm{pa}}$ and $\beta = r_{\mathrm{d2}} / r_{\mathrm{pa}}$

Radius ratio is $\gamma = \alpha / \beta$

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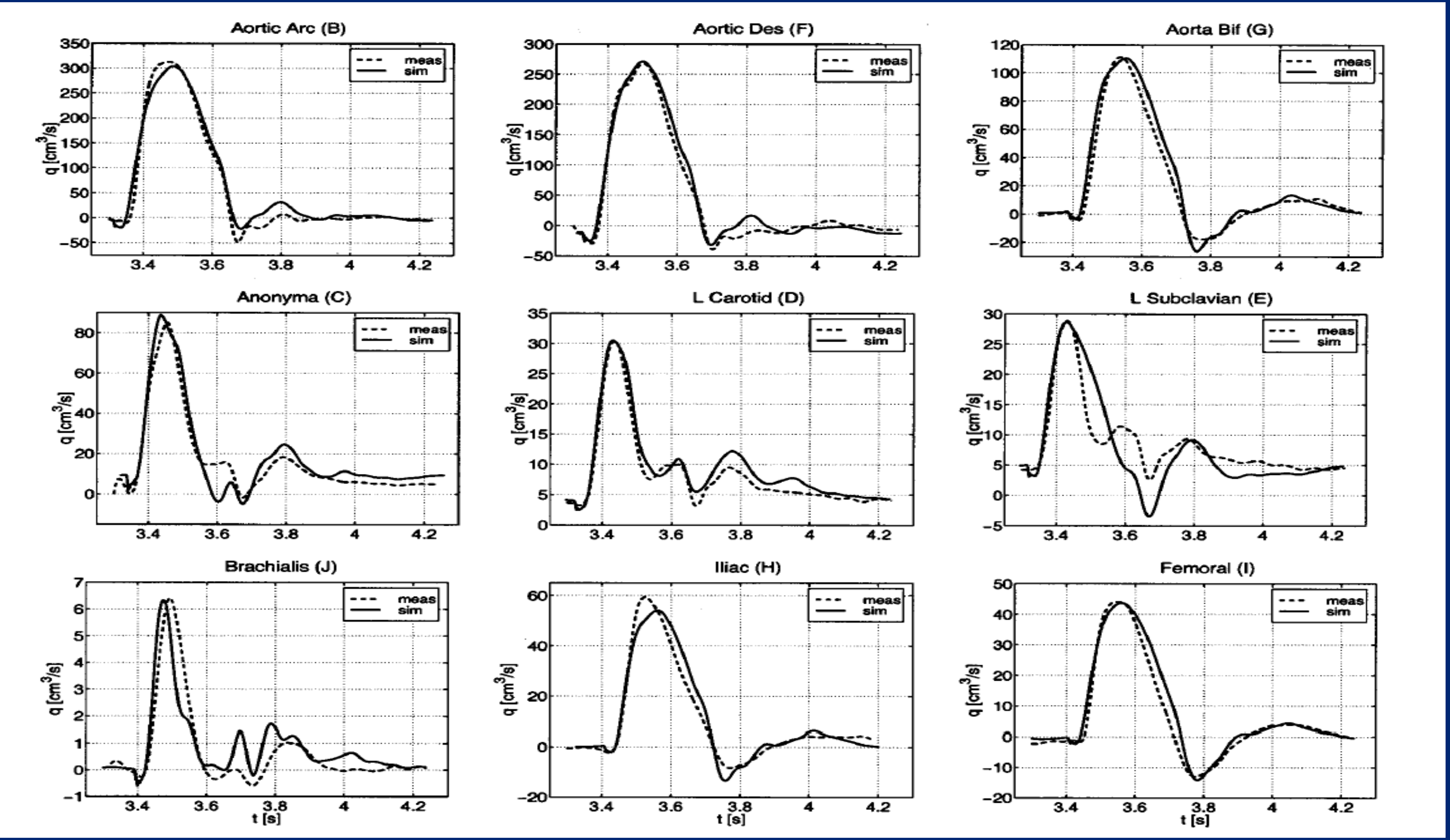
Results for systemic arteries: simulated versus measured flow rates



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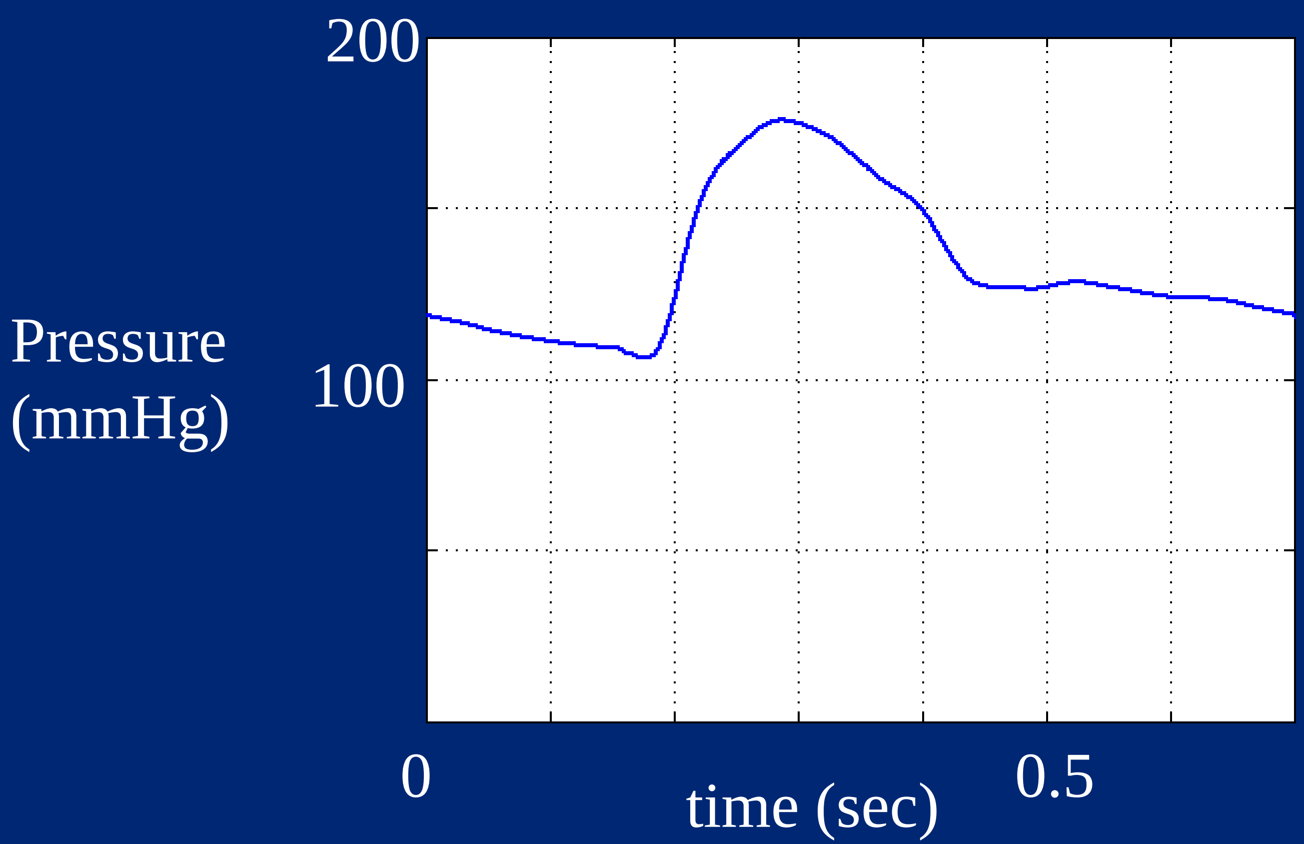
1. Pressure Results – systemic arteries



Pressure pulse for successive generations in the femoral artery vascular bed

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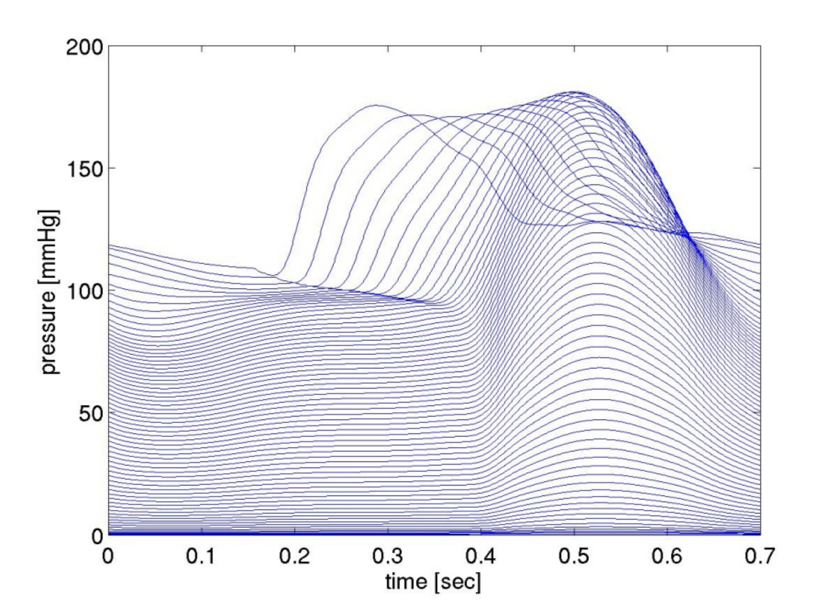
Femoral Artery Vascular Bed



- Pressure pulse for successive generations.
- Note propagation of the pressure wave.
- Pressure decreases and becomes steadier in the smaller vessels.
- Pressures depend on length to radius ratios and area ratios, but do not depend strongly on the number of generations.

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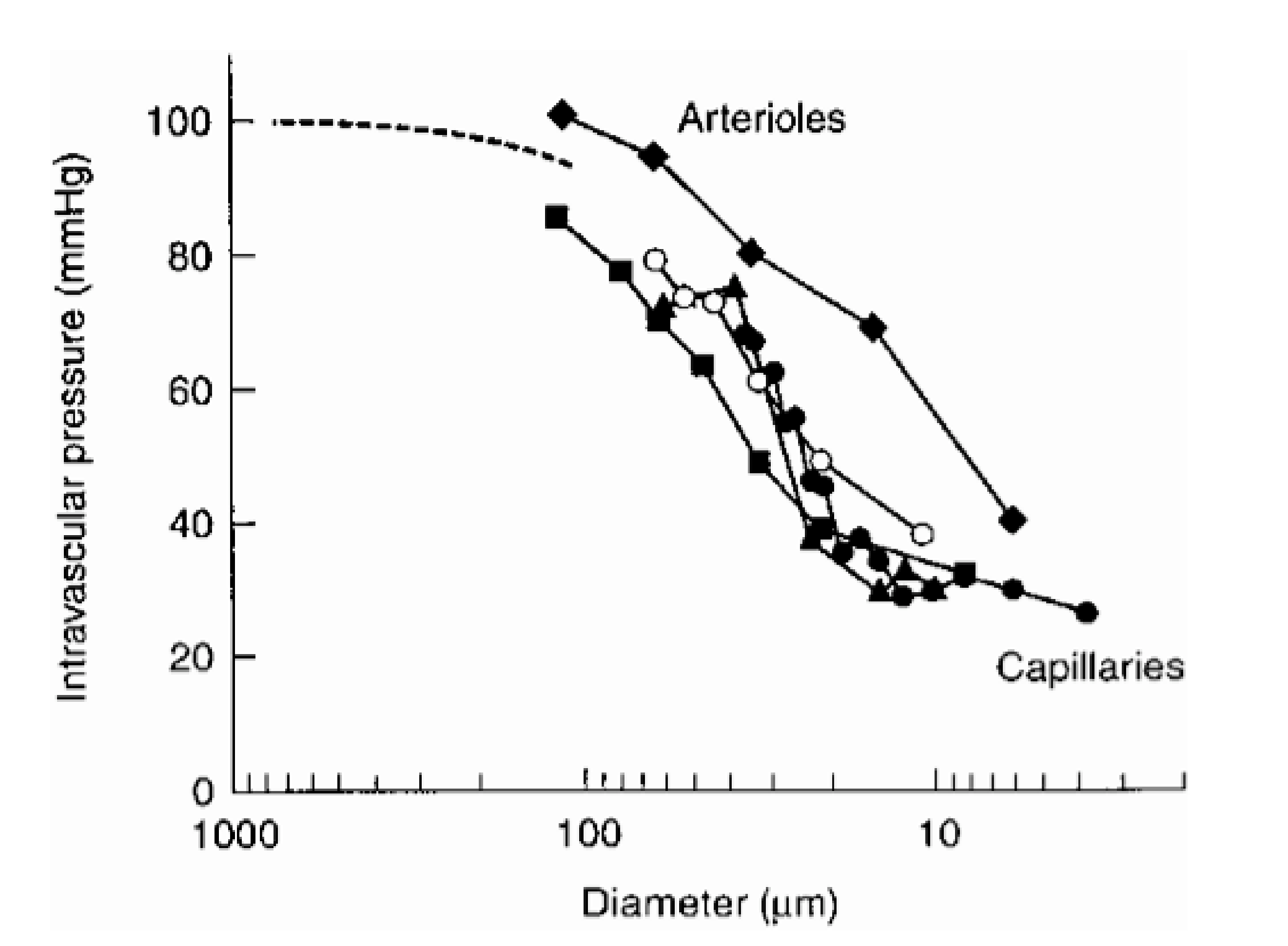
Intravascular pressure as a function of vessel diameter



(Levy 2001)

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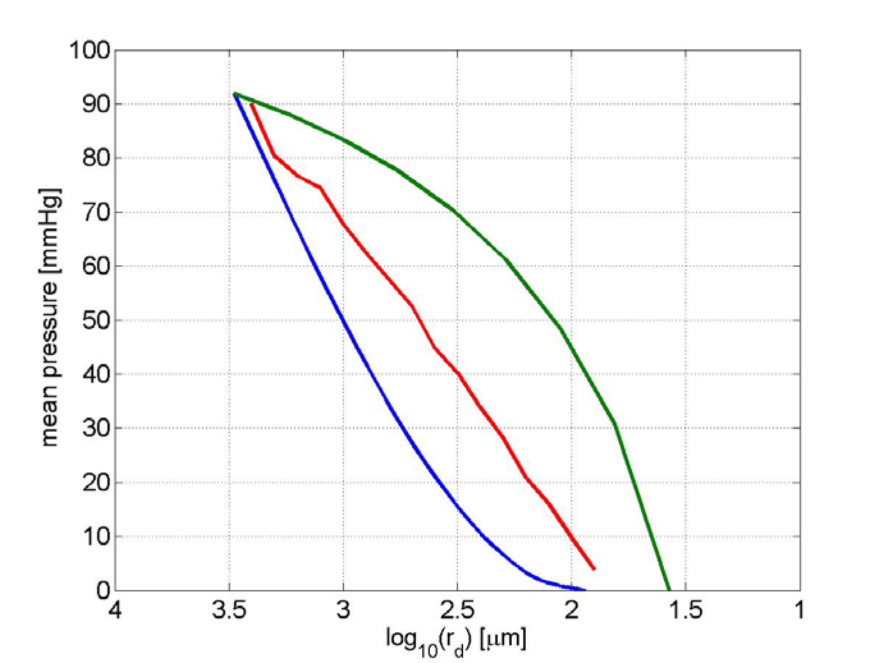
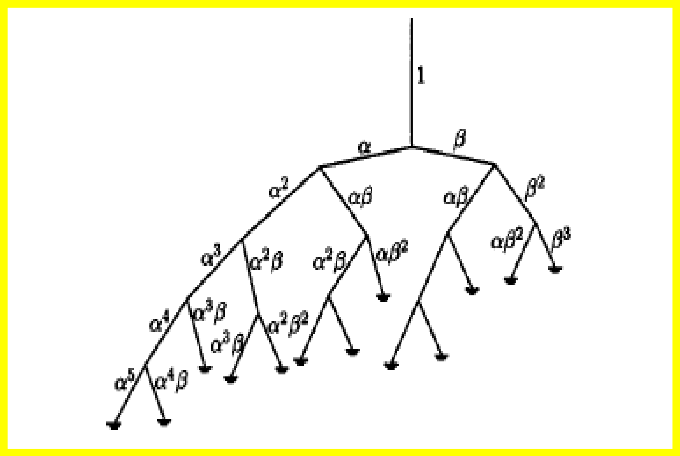
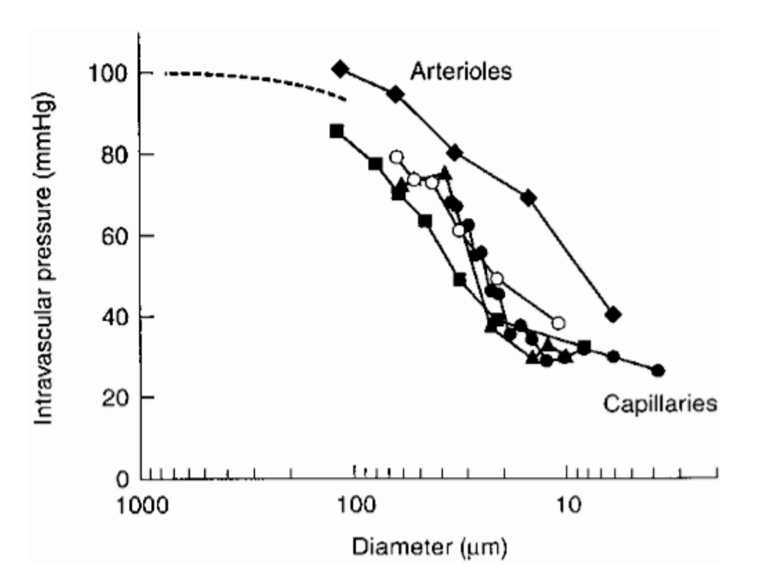
Mean pressure v. vessel radius





Shows extremes & mean for branches in the femoral structured tree.

Mean pressure > 50 $\log_{10}(r)$.



2. Pulmonary arteries & veins

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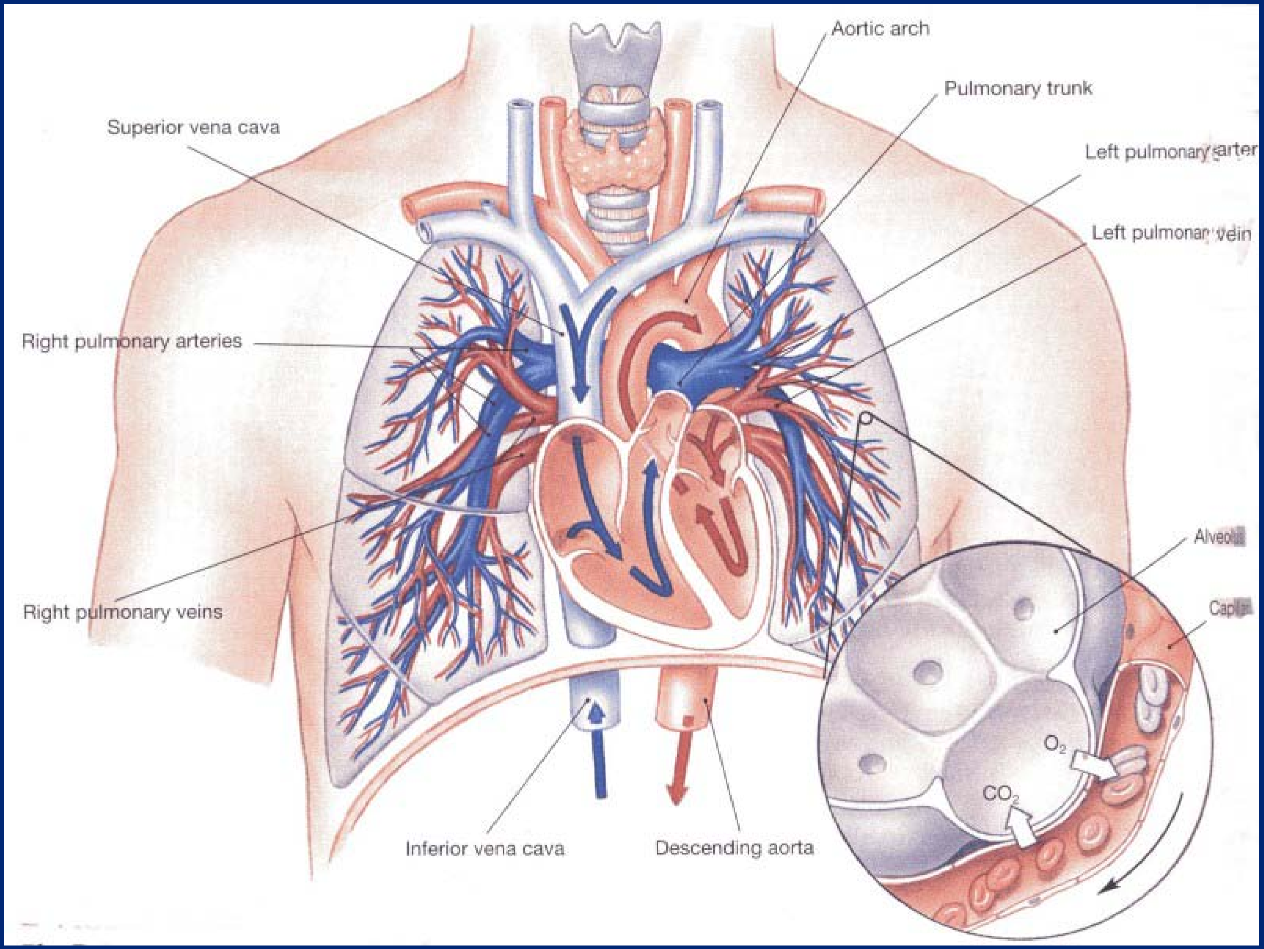
The Large Pulmonary Arteries



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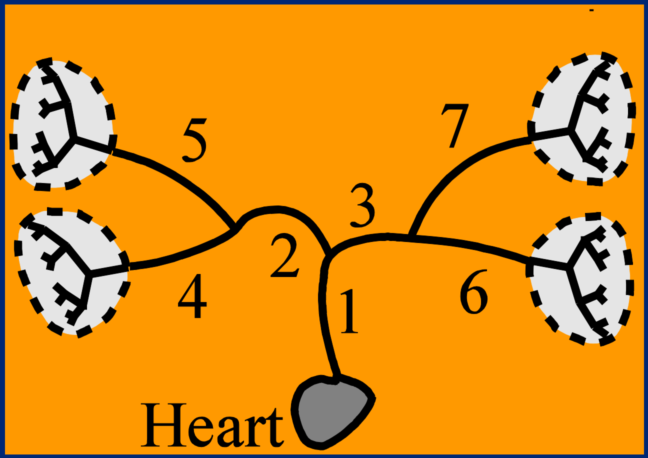
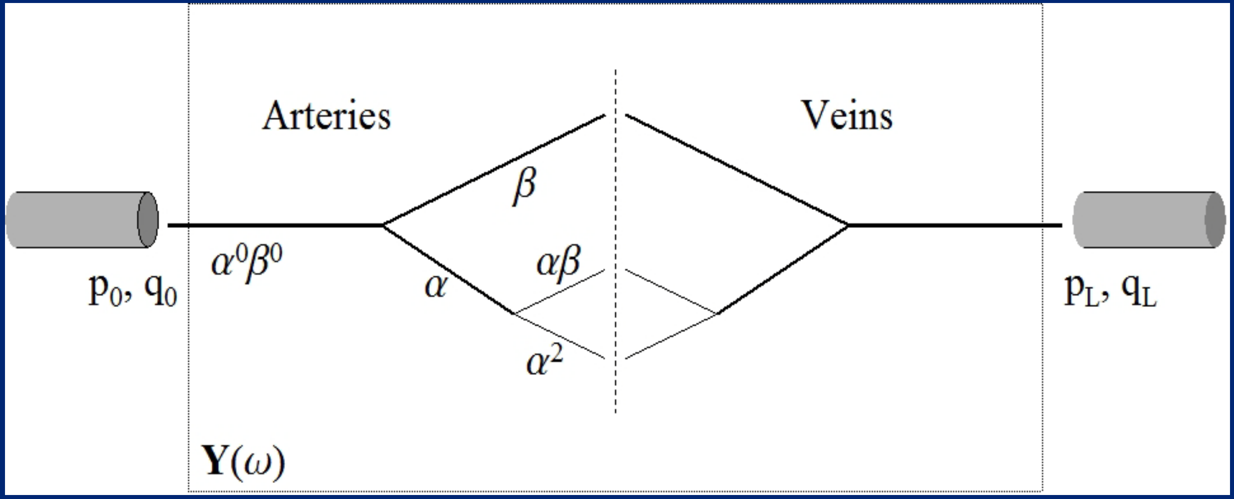
A model for pulmonary circulation



Sketch of main vessels with 4 vascular beds



Need to link arteries and veins

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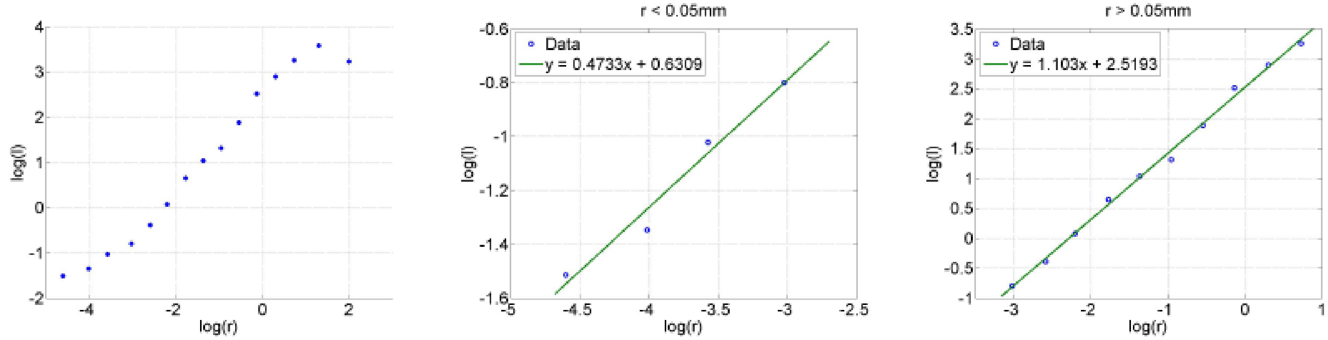
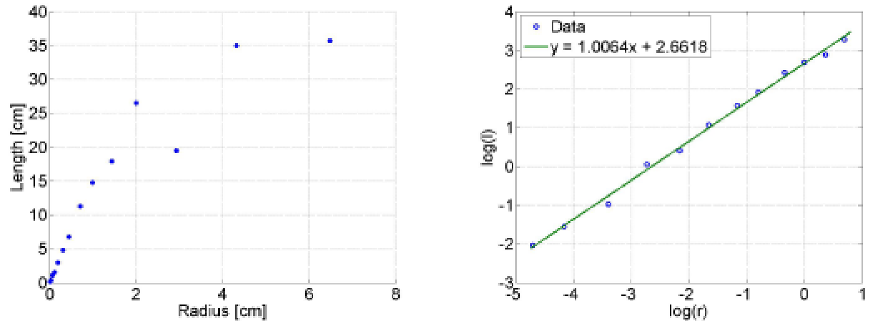
Physical Properties of the Pulmonary Circulation

- Arteries

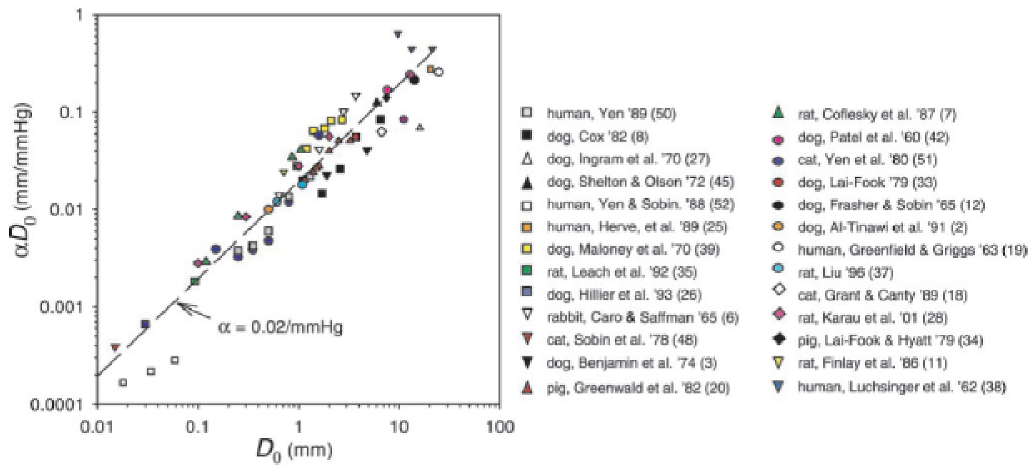


- Veins

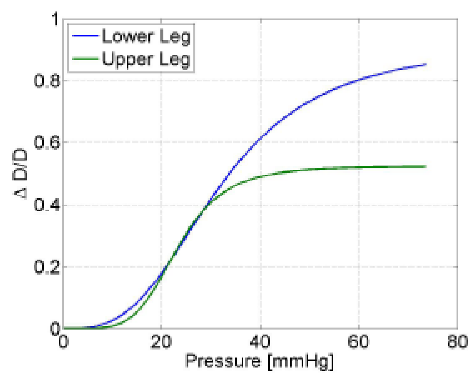


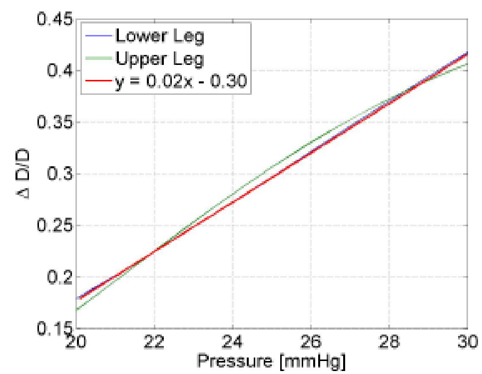
Elastic Properties of the Pulmonary Circulation

- Arteries

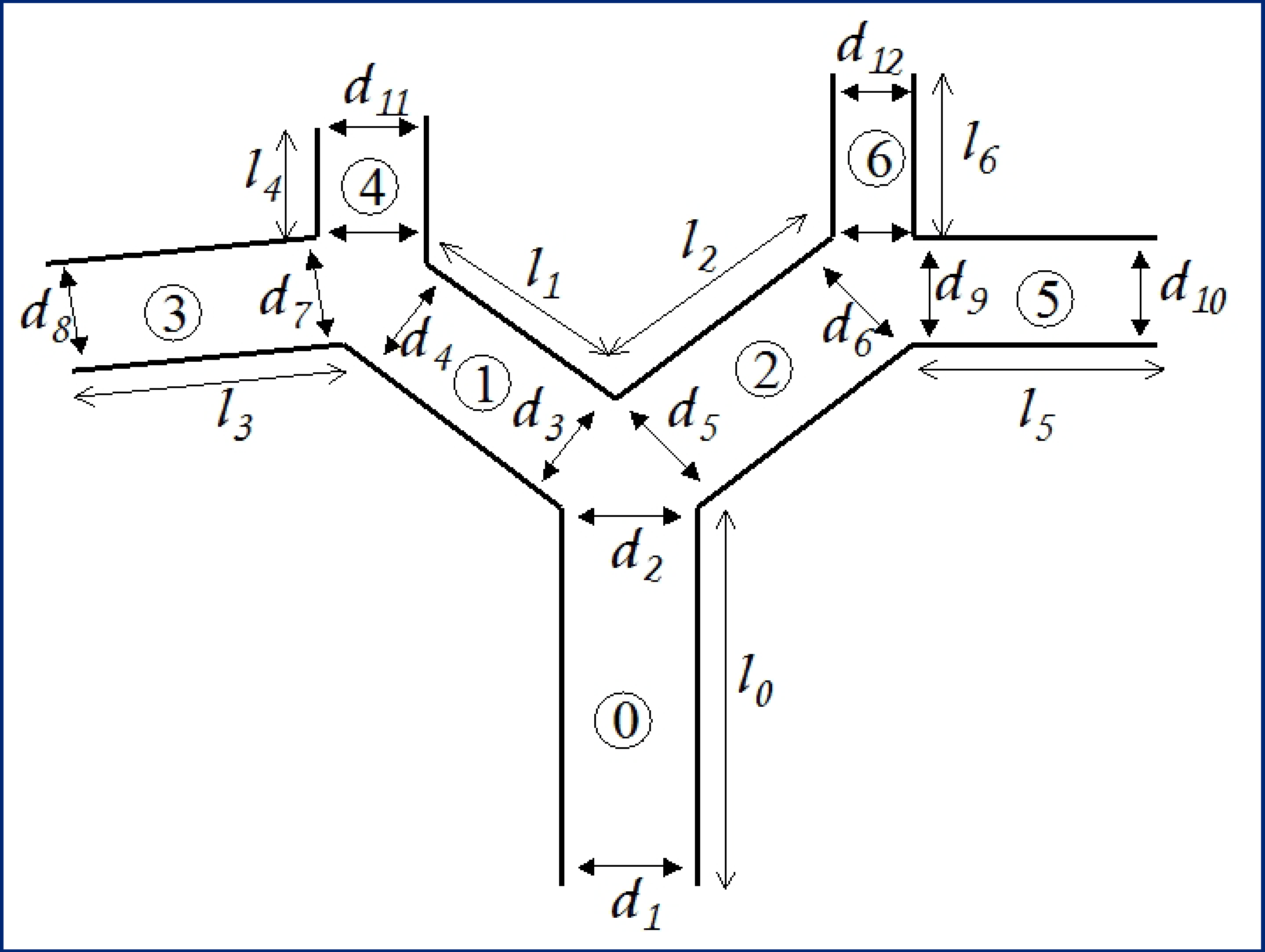


- Veins





Measurements of large pulmonary arteries



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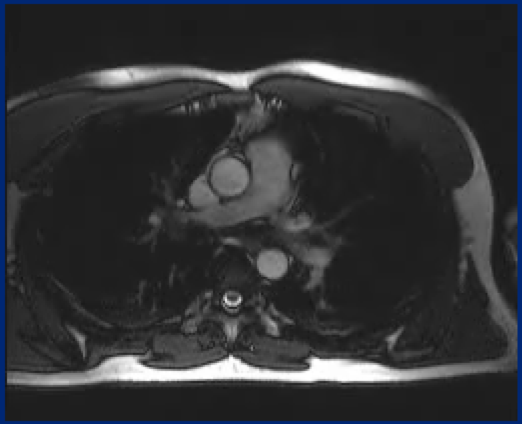
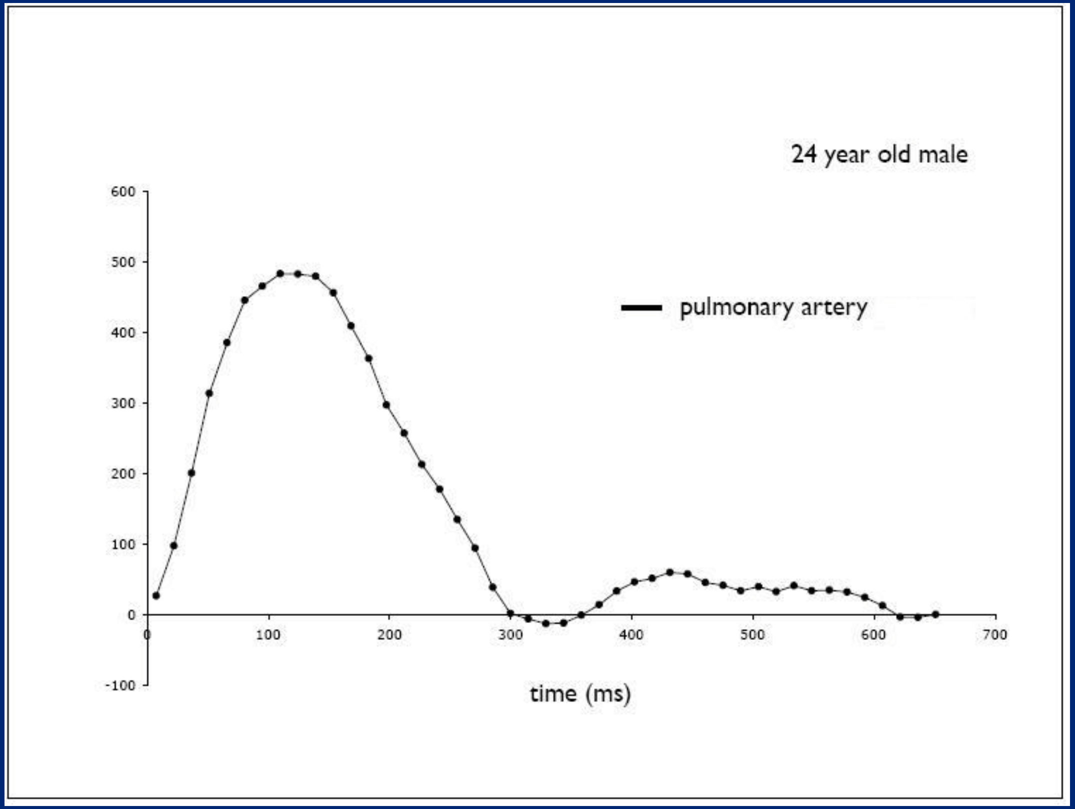
Inflow data - pulmonary artery





Have good quality flow measurements in the large vessels

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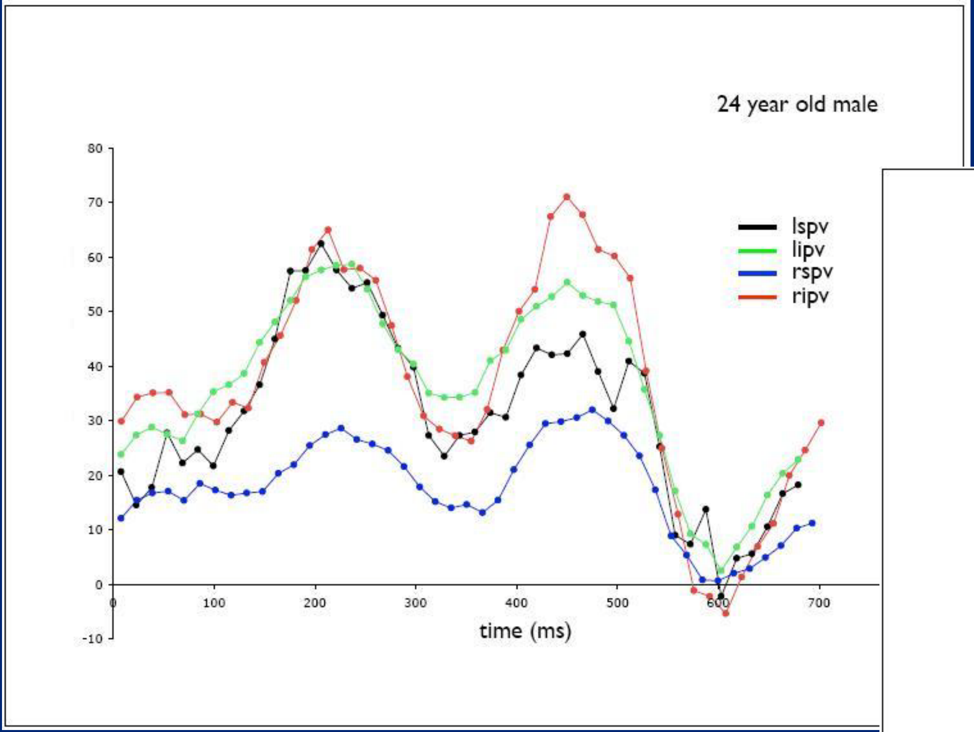
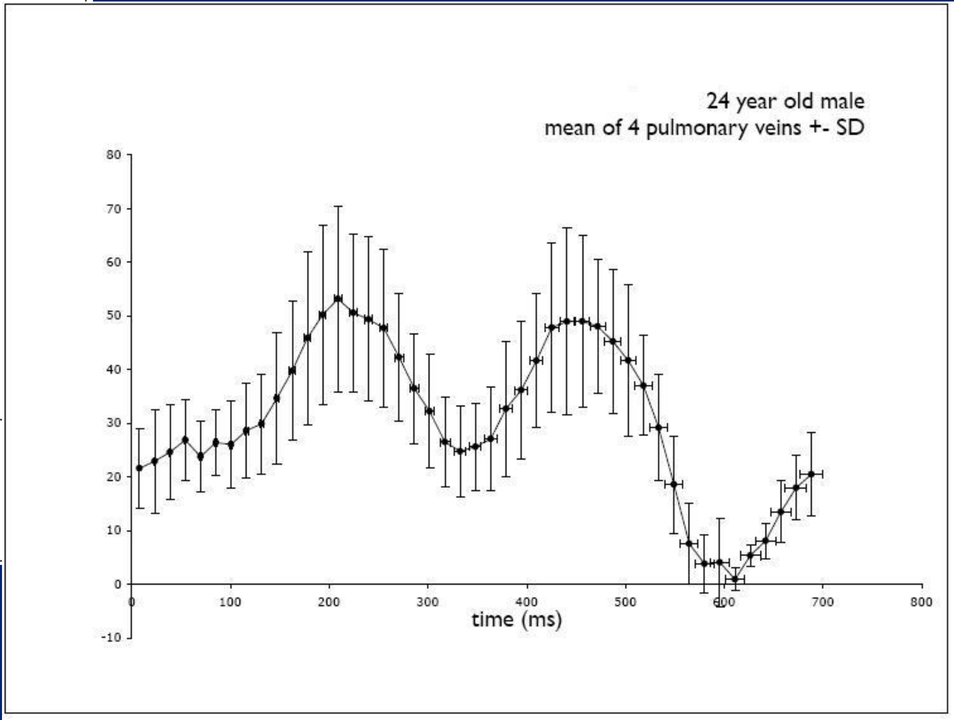
Pulmonary Vein Return Flow





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Small pulmonary arterioles and venules

- Assume arterial and venous trees are topologically similar so that trees of vascular beds can be linked together.
- Material and geometrical properties are different.
- Obtain a matching condition to link the large arteries with the large veins by calculating an overall admittance for the whole bed of small vessels.

Governing equations

$$\frac{\partial u}{\partial t} + \frac{1}{\rho}\frac{\partial p}{\partial x} = \frac{\nu}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u}{\partial r}\right)$$

$$p(x,t) = P(x)e^{i\omega t}$$

$$q(x,t) = Q(x)e^{i\omega t}$$

$$\begin{aligned} Q &= 2\pi\int_0^{r_0} U r dr \\ \Leftrightarrow i\omega Q &= \frac{-A_0}{\rho}\frac{\partial P}{\partial x}(1-F_J) \end{aligned}$$

$$F_J = \frac{2J_1(w_0)}{w_0 J_0(w_0)}$$

$w_0^2 = i^3 w^2$ ($w^2 = r_0^2\omega/\mu$ is the Womersley number)

$$i\omega C P + \frac{\partial Q}{\partial x} = 0$$

$$\frac{\omega^2}{c^2}Q + \frac{\partial^2 Q}{\partial x^2} = 0$$

$$c = \sqrt{\frac{A_0(1-F_J)}{\rho C}}.$$

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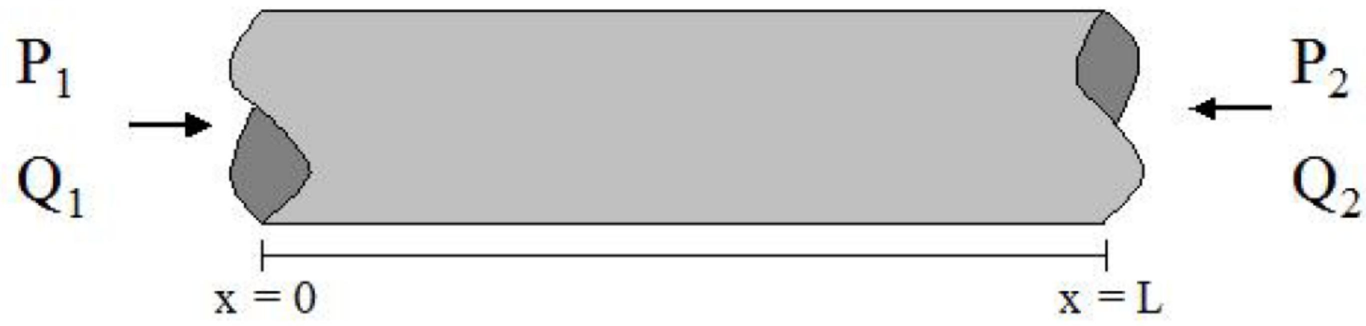


$$Q(x,\omega) = a\cos(\omega x/c) + b\sin(\omega x/c)$$

$$P(x,\omega) = (i/g_\omega)(-a\sin(\omega x/c) + b\cos(\omega x/c))$$

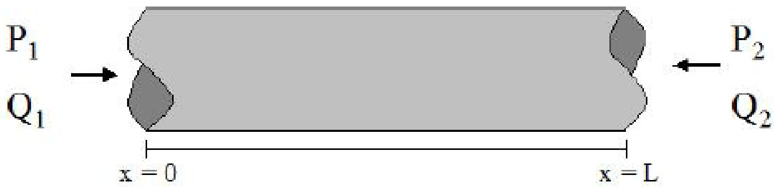
$$\begin{pmatrix} Q_1 \\ Q_2 \end{pmatrix} = \frac{i g_\omega}{S_L} \begin{pmatrix} -C_L & 1 \\ 1 & -C_L \end{pmatrix} \begin{pmatrix} P_1 \\ P_2 \end{pmatrix}$$

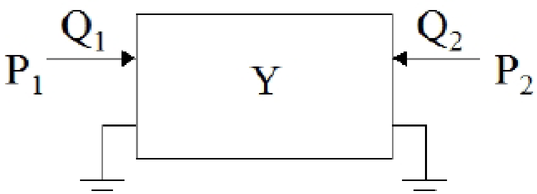
where $C_L \equiv \cos(\omega L/c)$ and $S_L \equiv \sin(\omega L/c)$, meaning that

$$\mathbf{Y}(\omega) = \frac{i g_\omega}{S_L} \begin{pmatrix} -C_L & 1 \\ 1 & -C_L \end{pmatrix}$$

is the admittance matrix for any one artery or vein when $\omega \neq 0$.

Admittance Matrix





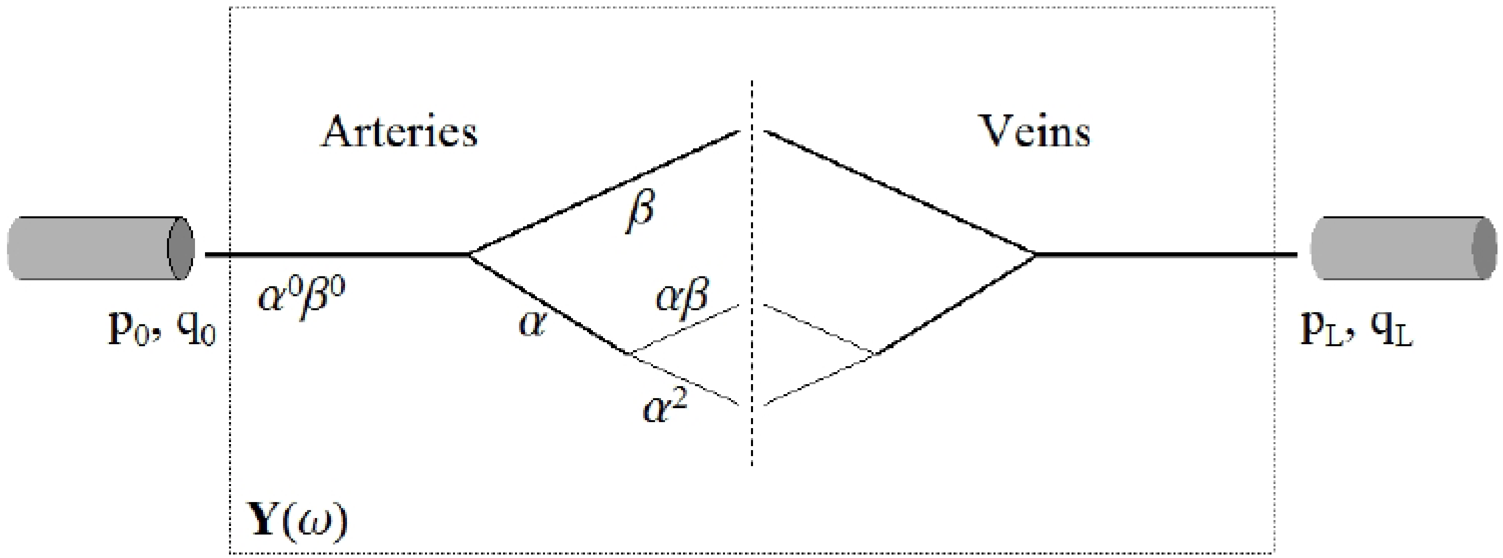
- When $\omega \neq 0$

$$\mathbf{Y}(\omega) = \frac{ig_\omega}{S_L}\frac{\rho g l}{q_c}\begin{pmatrix} -C_L & 1 \\ 1 & -C_L \end{pmatrix} \quad (12)$$

- When $\omega = 0$

$$\mathbf{Y}(0) = \frac{\rho g l}{q_c}\frac{\pi r_0^4}{8\mu L}\begin{pmatrix} 1 & -1 \\ -1 & 1 \end{pmatrix} \quad (13)$$

Linking an Arterial and Venous tree



- Two Vessels in Parallel

$$\mathbf{Y} = \mathbf{Y}^A + \mathbf{Y}^B \tag{14}$$

- Two Vessels in Series

$$\mathbf{Y} = \frac{1}{Y_{22}^A + Y_{11}^B} \begin{pmatrix} det(\mathbf{Y}^A) + Y_{11}^A Y_{11}^B & -Y_{12}^A Y_{12}^B \\ -Y_{21}^A Y_{21}^B & det(\mathbf{Y}^B) + Y_{22}^A Y_{22}^B \end{pmatrix} \tag{15}$$

Matching conditions for the large arteries and veins

$$\begin{pmatrix} Q_A(L,\omega) \\ Q_V(0,\omega) \end{pmatrix} = \begin{pmatrix} Y_{11}(\omega) & Y_{12}(\omega) \\ Y_{21}(\omega) & Y_{22}(\omega) \end{pmatrix} \begin{pmatrix} P_A(L,\omega) \\ P_V(0,\omega) \end{pmatrix}$$

which leads to convolution integrals in real space

$$q_A(L,t) = \int_0^T \left(p_A(L,t-\tau)y_{11}(\tau) + p_V(0,t-\tau)y_{12}(\tau)\right) d\tau$$

$$q_V(0,t) = \int_0^T \left(p_A(L,t-\tau)y_{21}(\tau) + p_V(0,t-\tau)y_{22}(\tau)\right) d\tau$$

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Pulmonary disease

- **Group I - Pulmonary Arterial Hypertension** - in this group of conditions, the pathophysiology is located in pulmonary arteries and arterioles of less than 500μm diameter, with increased stiffness and resistance in the smaller vessels [7] [12].

- **Group III - Pulmonary Hypertension in association with hypoxic lung disease** - this group includes conditions that involve pulmonary vascular remodelling (typically affecting vessels of less than 500μm diameter) and loss of the pulmonary vascular bed (vascular rarefaction) due to underlying respiratory disease [15].

- **Group IV - Chronic Thromboembolic Pulmonary Hypertension** - here, the problem is initially located in larger vessels with increased stiffness and decreased cross-sectional area. Eventually there may be involvement of the small vessels in the same way as Pulmonary Arterial Hypertension [2] [3].

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Pulmonary Hypertension, Lankhaar et al. 2006

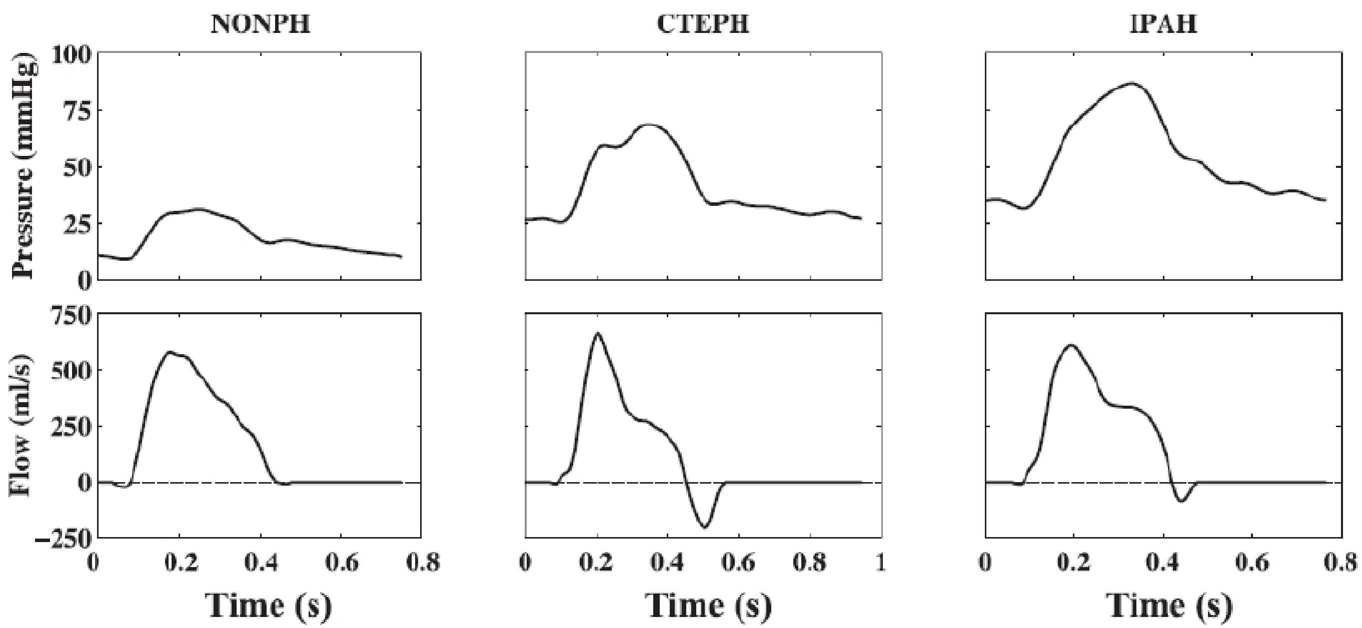

Fig. 2. Example of a preprocessed and synchronized pressure-flow pair for each patient group. Note that diastolic flow is set equal to zero. NONPH, no pulmonary hypertension (control); CTEPH, chronic thromboembolic pulmonary hypertension; IPAH, idiopathic pulmonary arterial hypertension.

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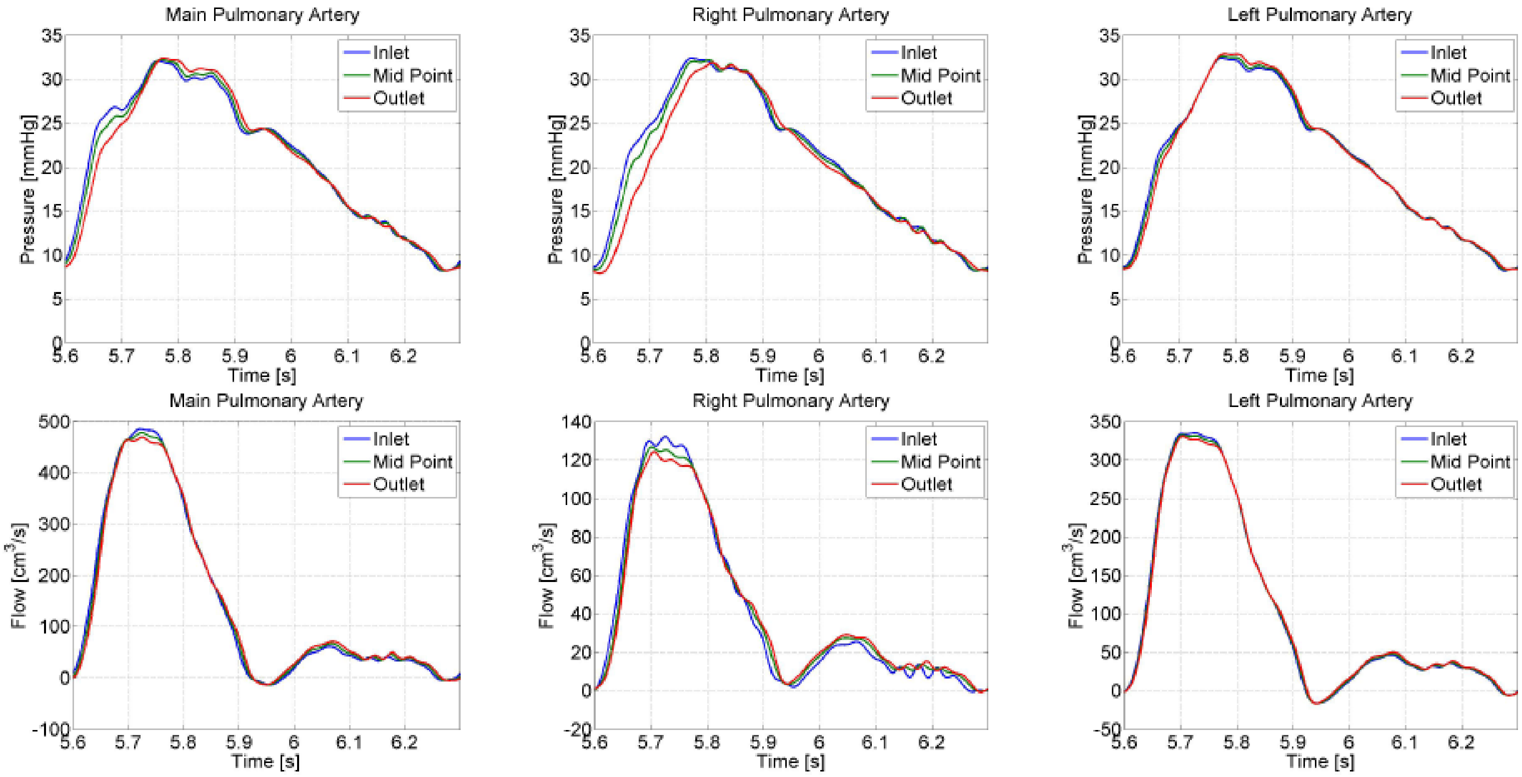
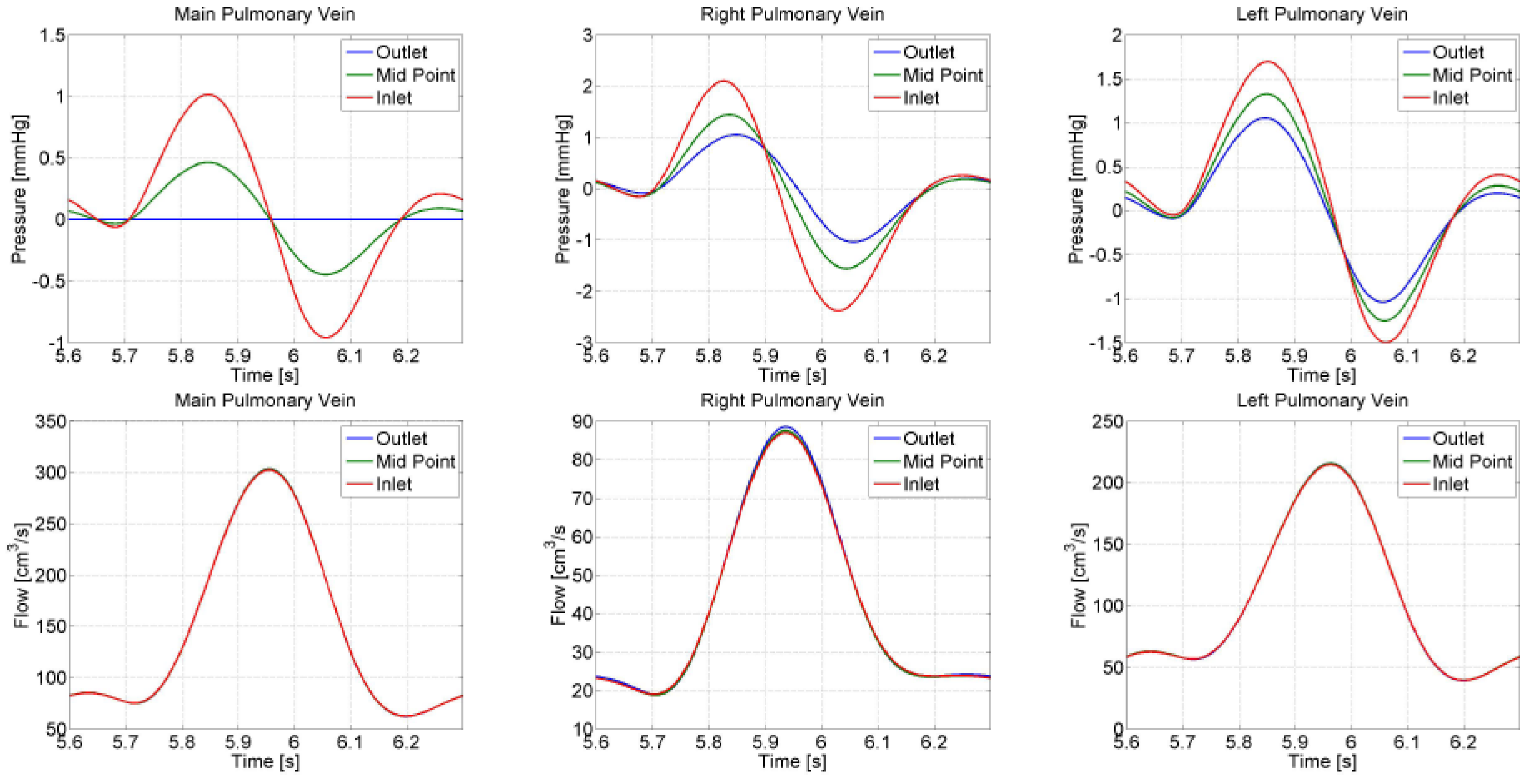
Pulmonary Arteries



Pulmonary Veins



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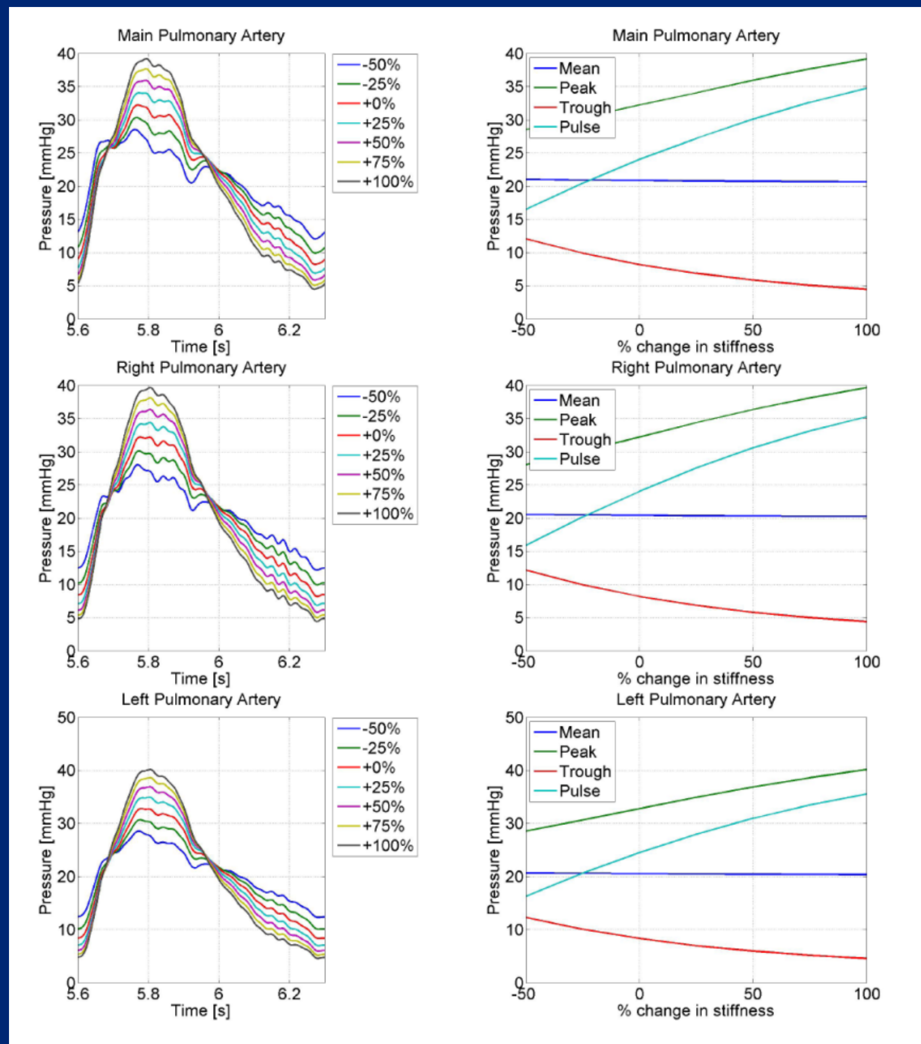

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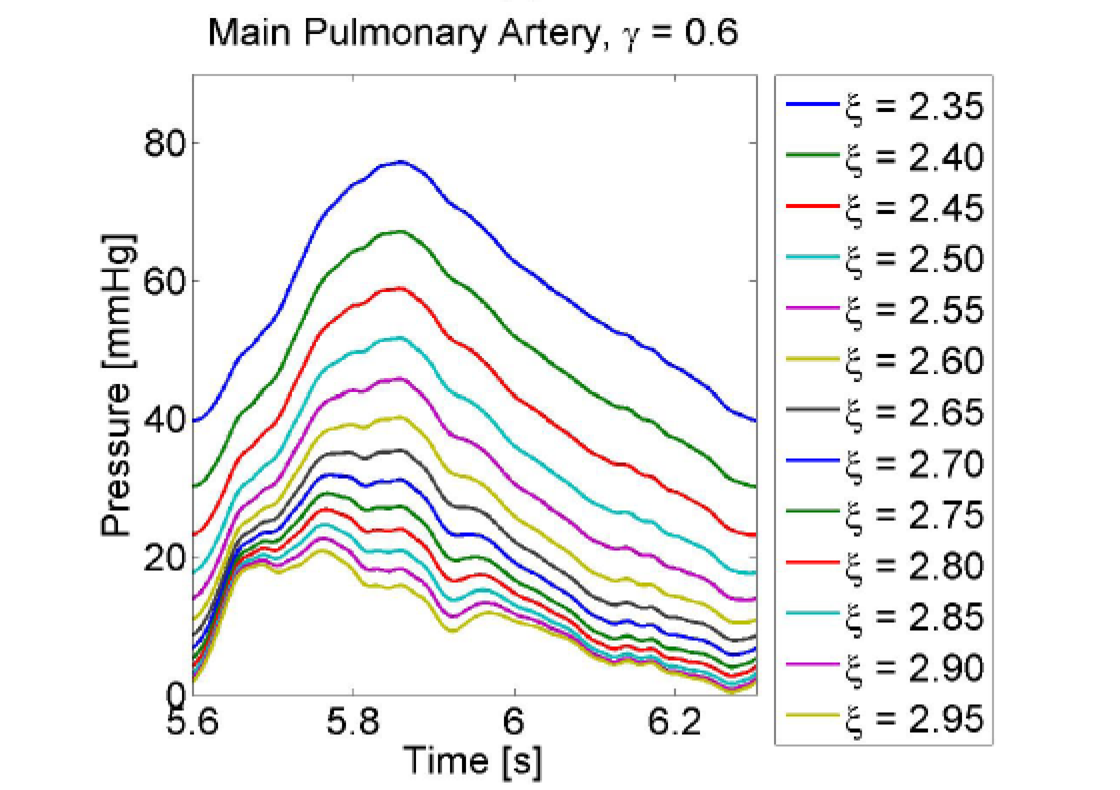

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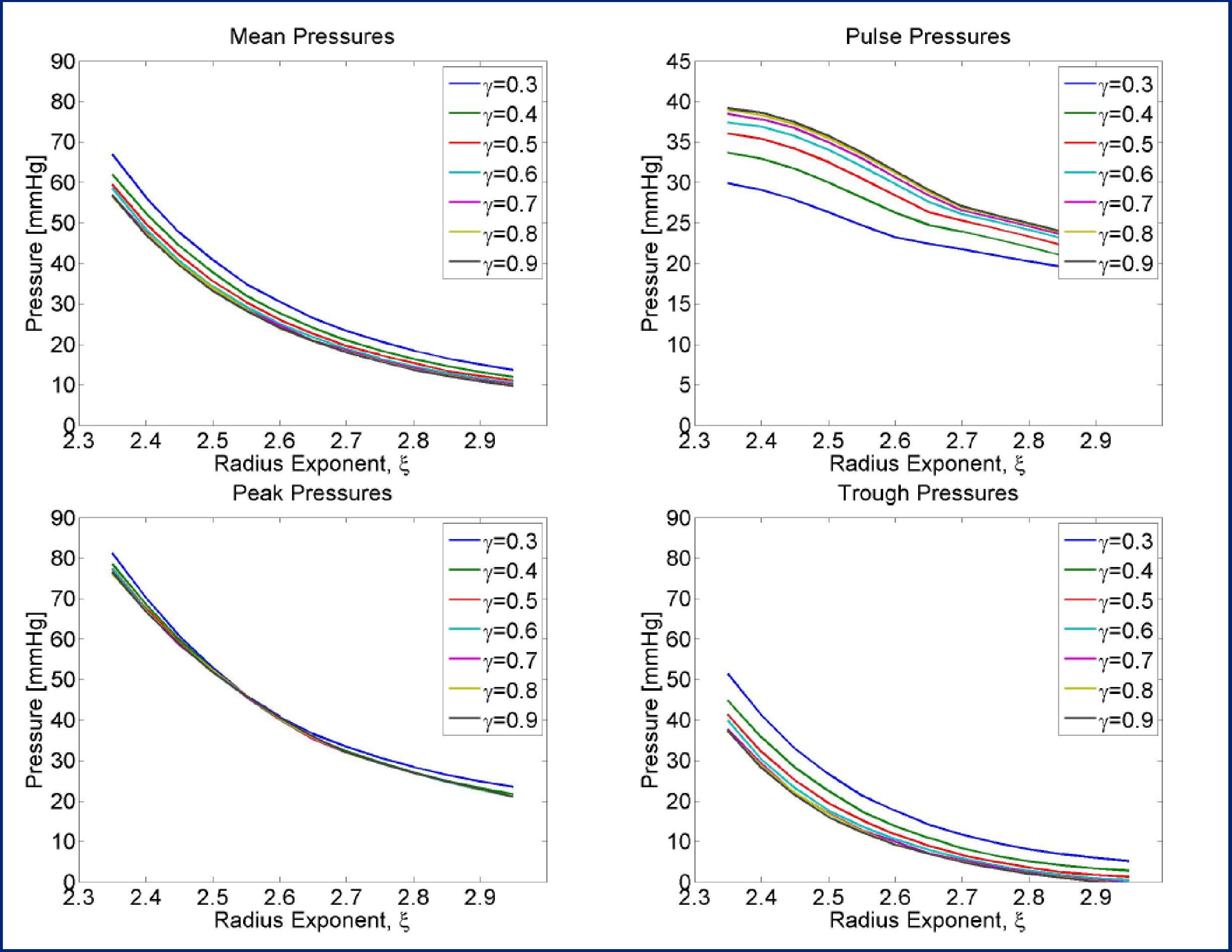
Effects of rarefaction



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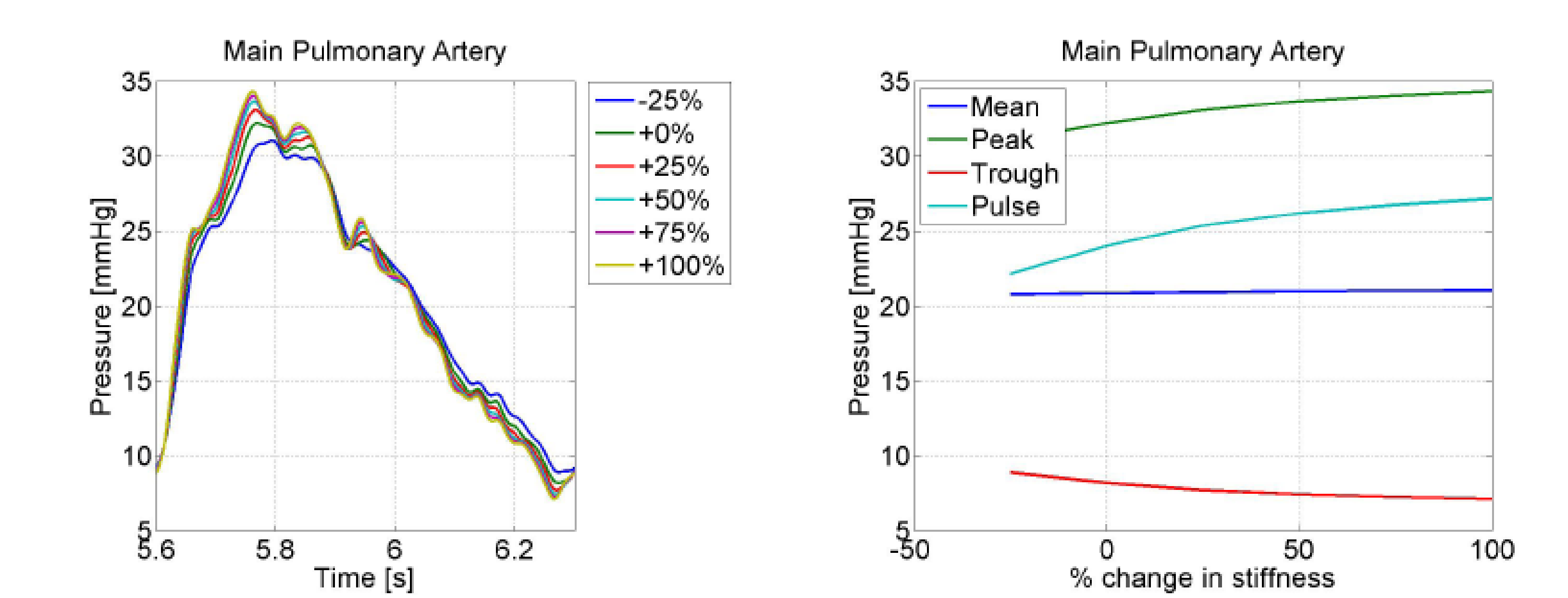
- **Group IV - Chronic Thromboembolic Pulmonary Hypertension** - here, the problem is initially located in larger vessels with increased stiffness and decreased cross-sectional area. Eventually there may be involvement of the small vessels in the same way as Pulmonary Arterial Hypertension [2] [3].



Note earlier arrival of pressure peak

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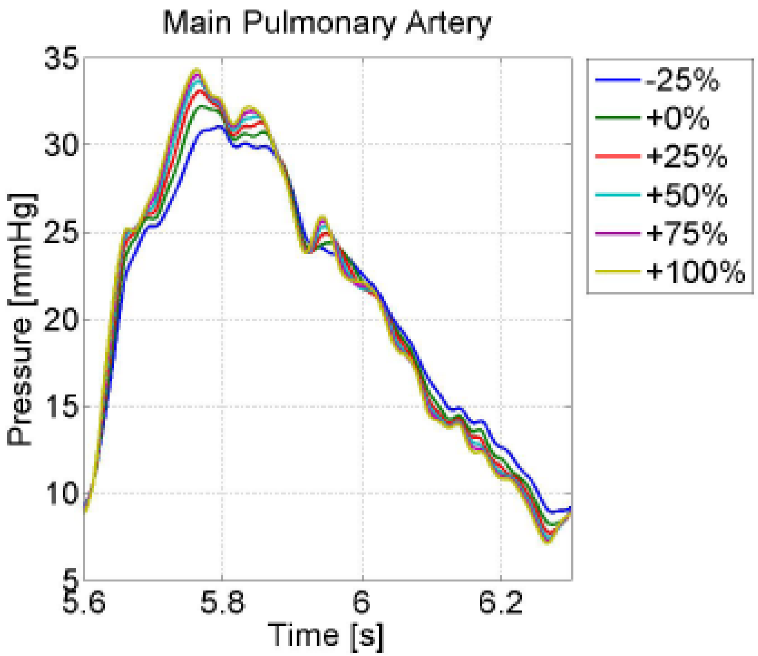

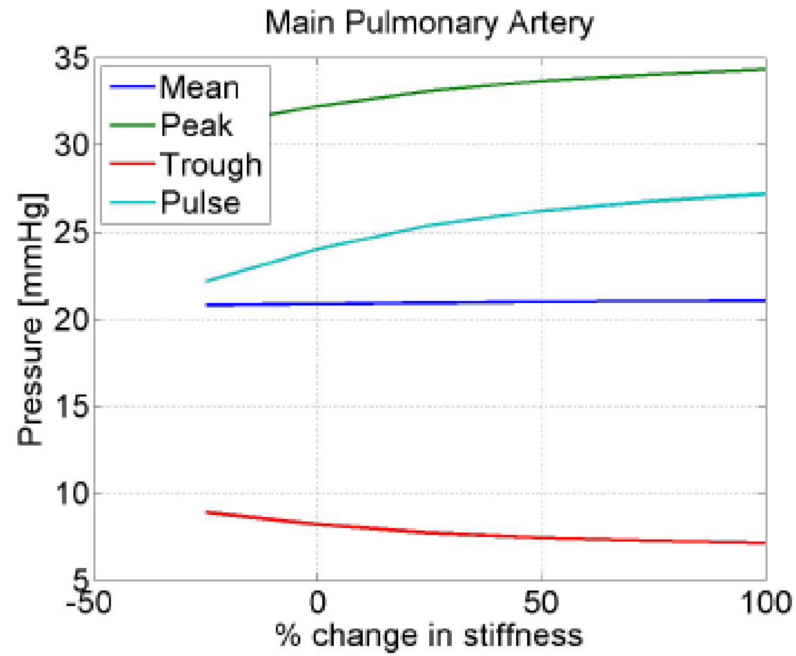

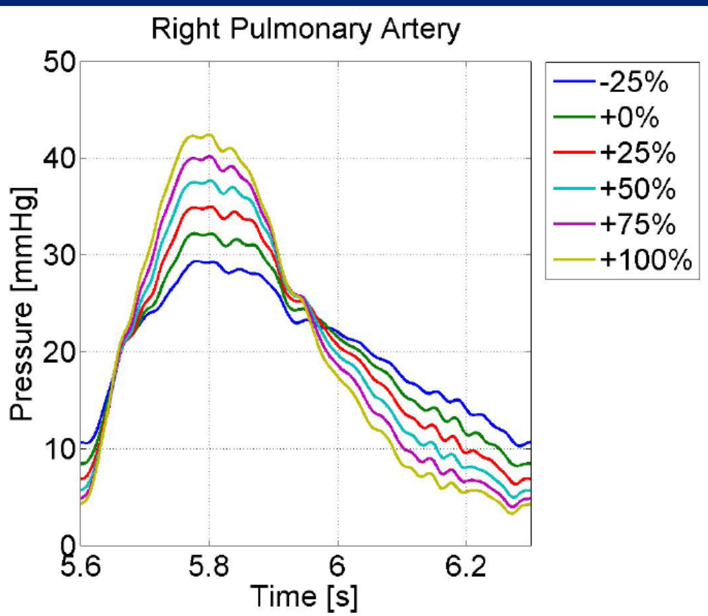

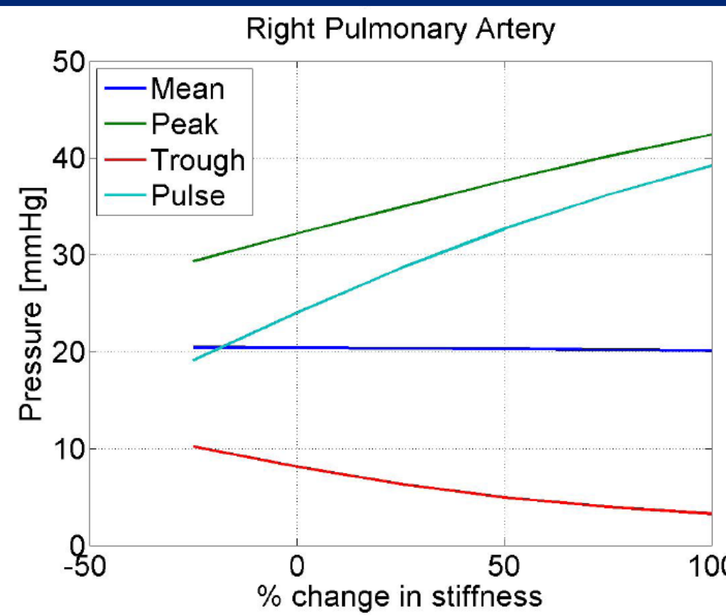

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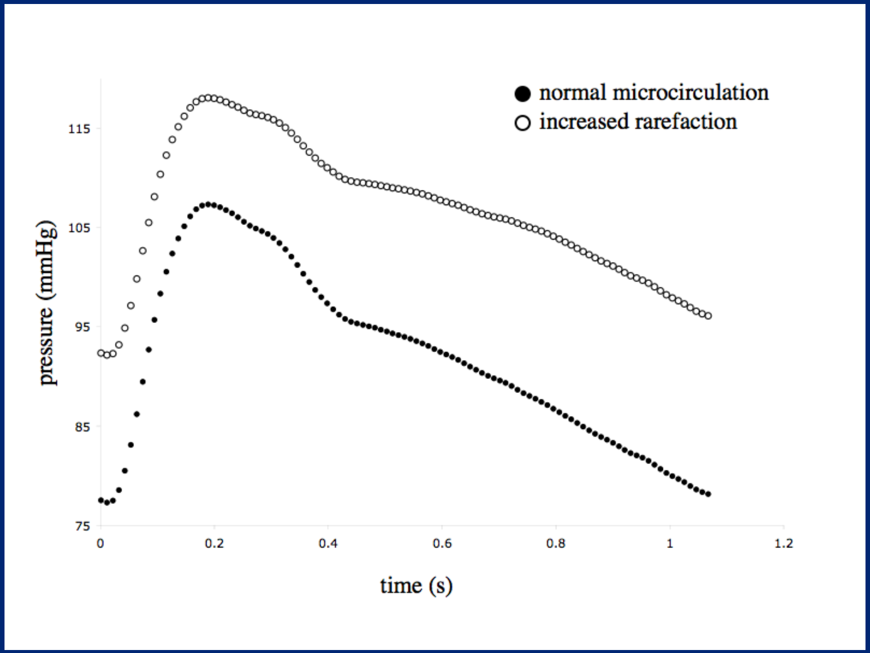
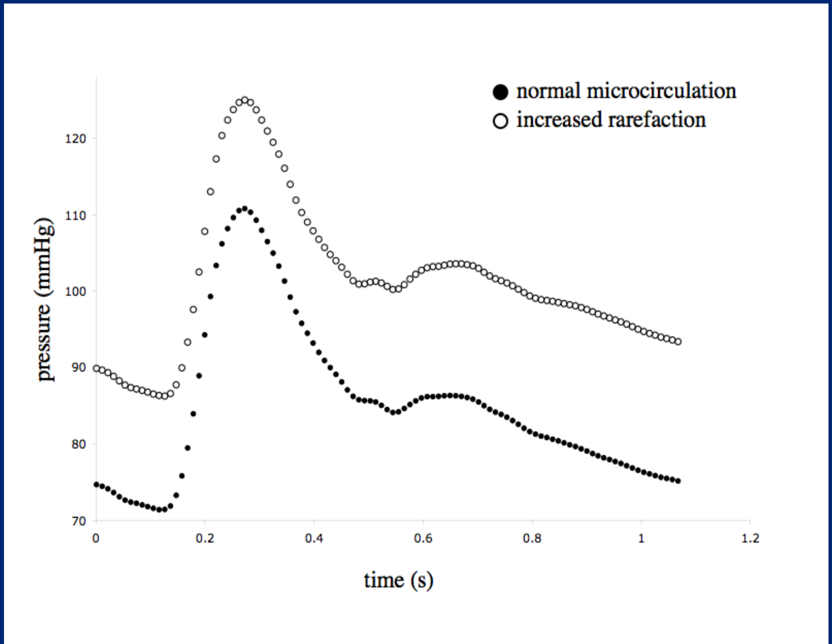
3. Normal v. Increased Rarefaction in the Microcirculation - Pressure



Ascending aorta



Right radial artery

Pressure waveforms: averages of 7 waveforms from 7 healthy individuals. Normal microcirculation – solid circle. Increased rarefaction – open circle.

$$\eta = (r_{d1}^2 + r_{d2}^2) / r_{pa}^2 = 1.16 \,\&\, 1.08$$

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Parameters determining parent/daughter radius ratios

$$\eta = (r_{\mathrm{d1}}^2 + r_{\mathrm{d2}}^2) / r_{\mathrm{pa}}^2 = 1.16 \,\&\, 1.08$$

$$r_{\mathrm{pa}}^{\xi} = r_{\mathrm{d1}}^{\xi} + r_{\mathrm{d2}}^{\xi}, \xi = 2.7$$

$$\alpha = r_{\mathrm{d1}} / r_{\mathrm{pa}} \text{ and } \beta = r_{\mathrm{d2}} / r_{\mathrm{pa}}$$

$$\gamma = \alpha / \beta = r_{\mathrm{d1}} / r_{\mathrm{d2}}$$

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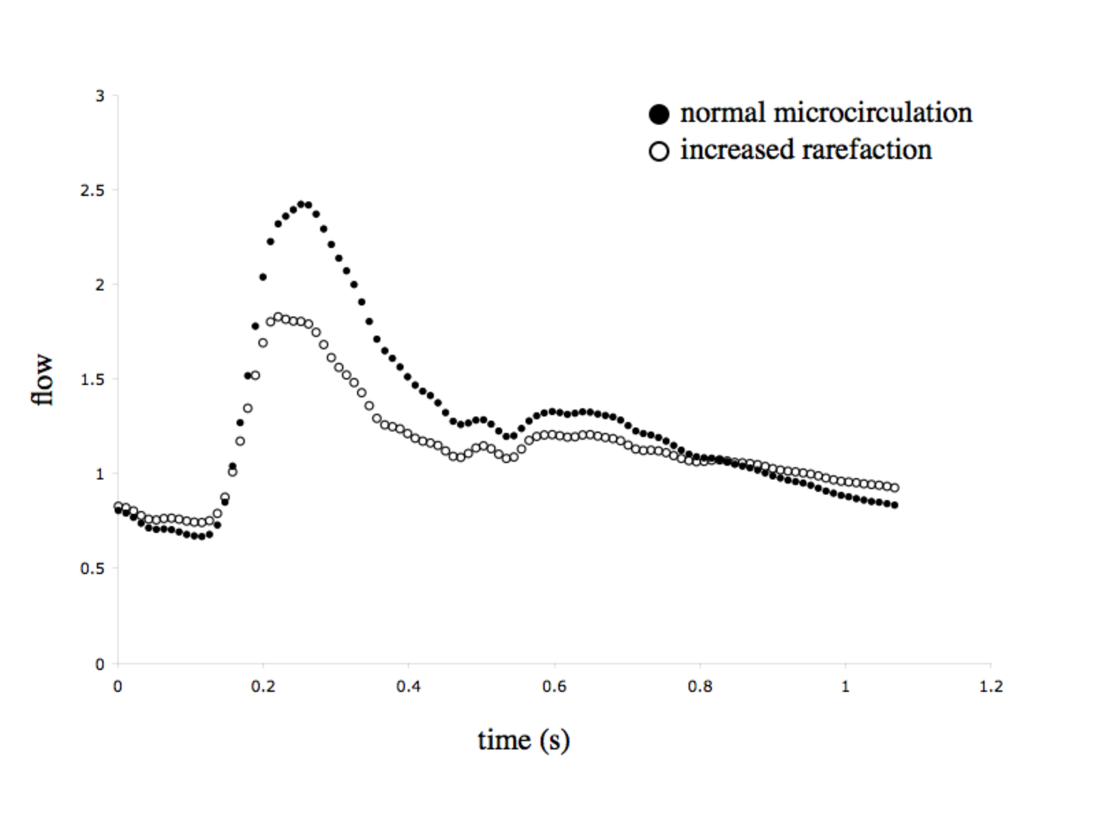
Normal vs Increased Rarefaction in the Microcirculation - Flow



Flow waveform at right radial artery: averages of 7 healthy individuals. Normal microcirculation – solid circle. Increased rarefaction – open circle.

$$\eta = (r_{d1}^2 + r_{d2}^2) / r_{pa}^2 = 1.16 \,\&\, 1.08$$

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Conclusions

- First numerical simulations of periodic pulsatile flow in the full pulmonary circulation.

- First calculations of pressure drop in small arteries.

- Comparisions between clinical data and model results.

- Evidence of changes in large vessel waveforms associated with changes in physiology of vascular beds, similar to those seen clinically.

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The Real System

Many challenges: flexible, complex, individual, able to sustain a great range of flow rates and regimes.

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