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POLITECNICO DI MILANO

MOX

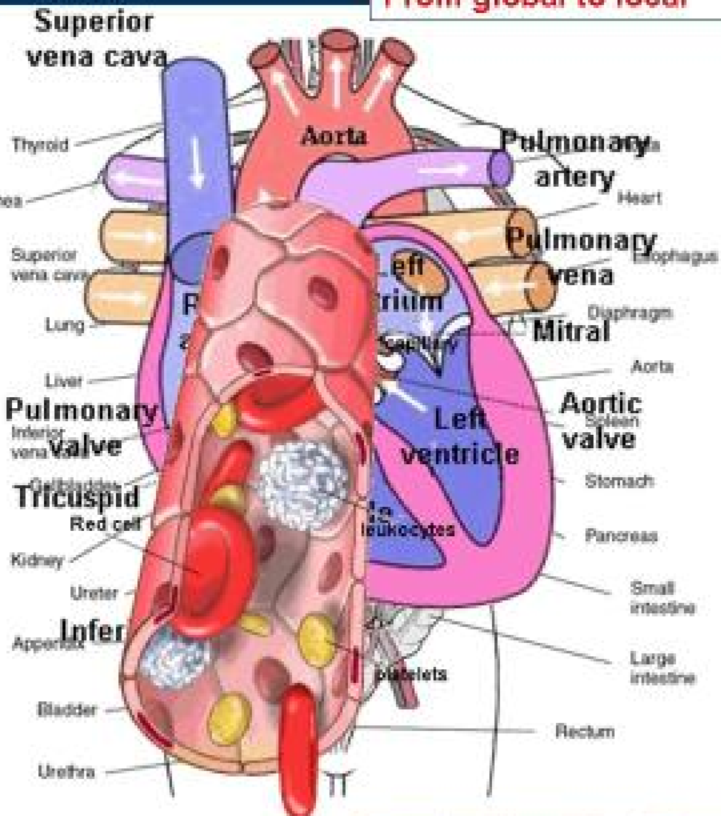
EPFL

INTRODUCTION to CARDIOVASCULAR MATHEMATICS - 06

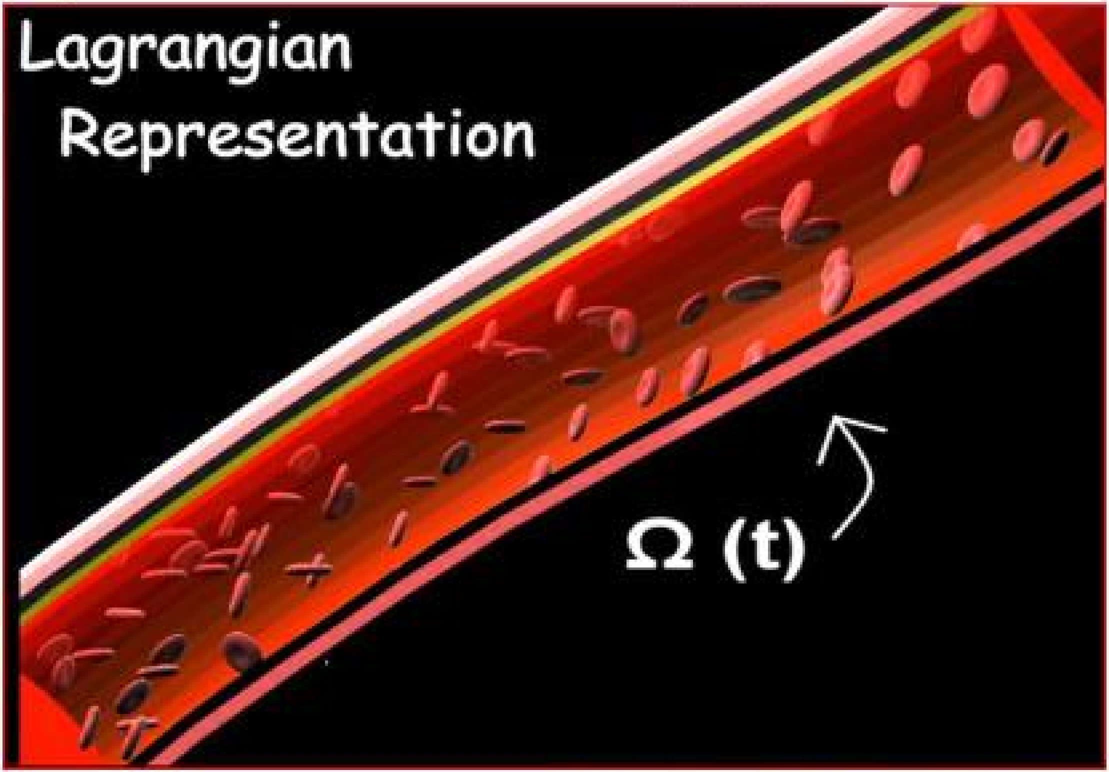
MATHEMATICAL MODEL

From global to local

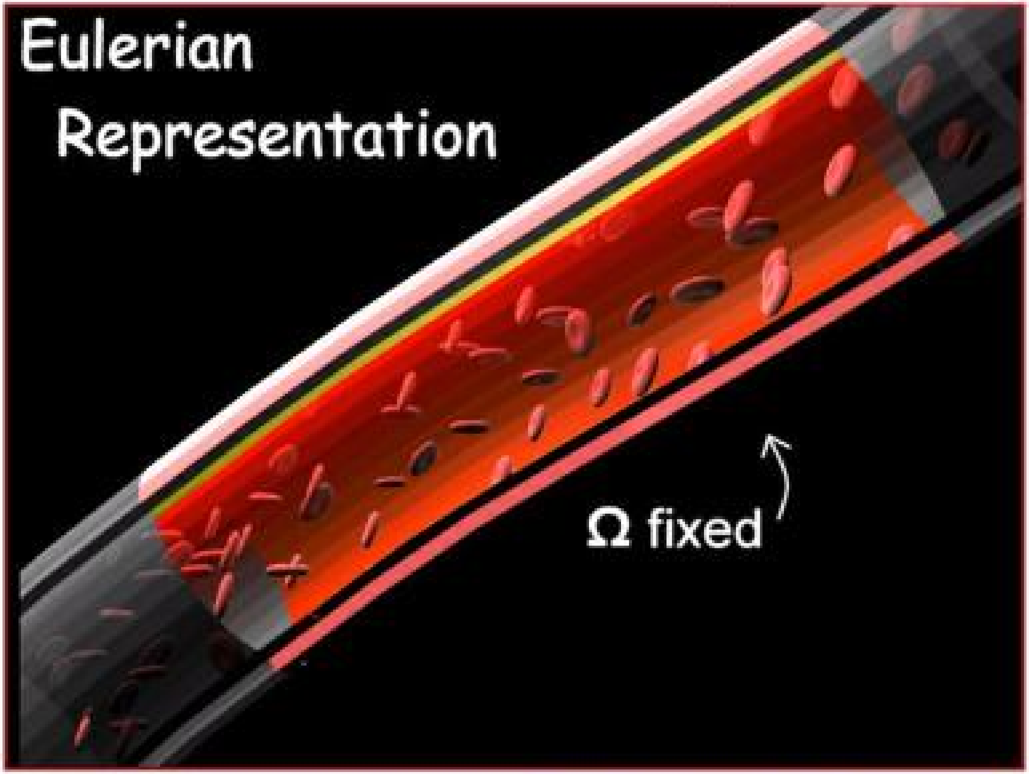
Blood is a suspension of **red cells, leukocytes** and **platelets** on a liquid suspension called **plasma**



Representation Framework: Neither Lagrangian…

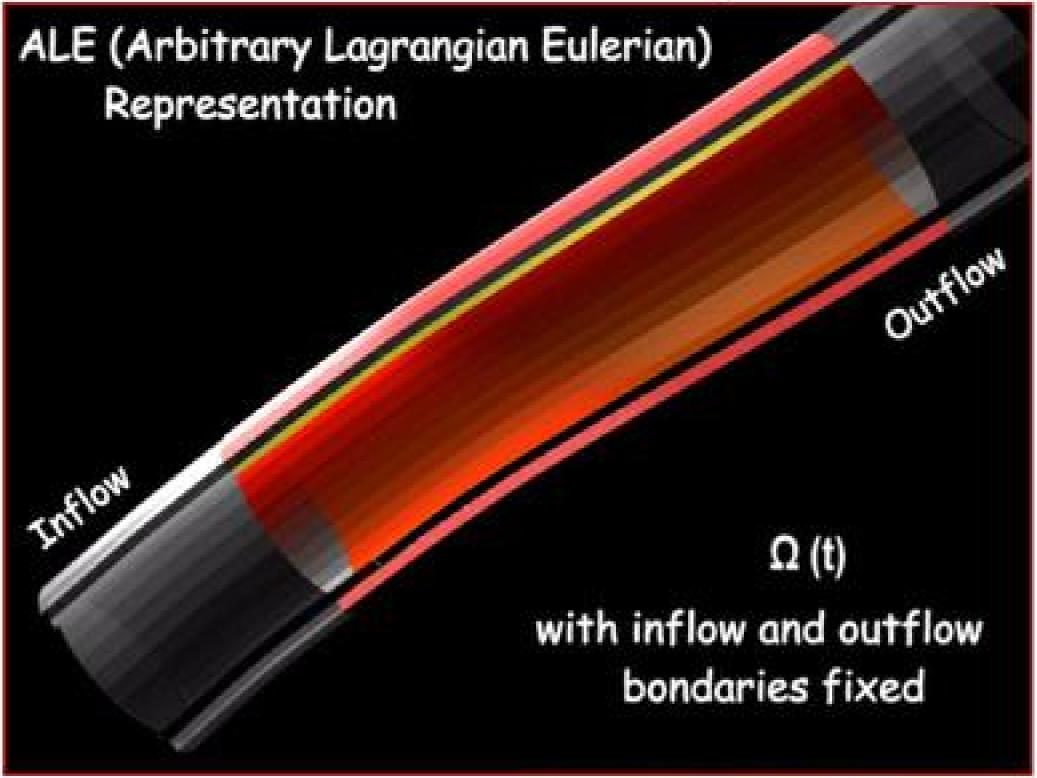


… nor Eulerian…

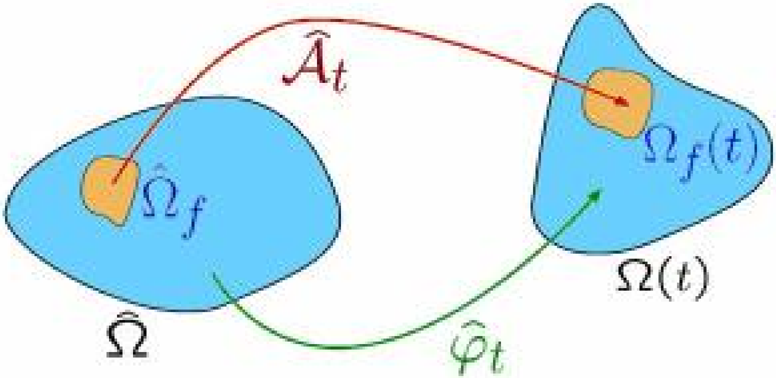


MATHEMATICAL MODEL

... ALE!



ALE framework: an abstract setting



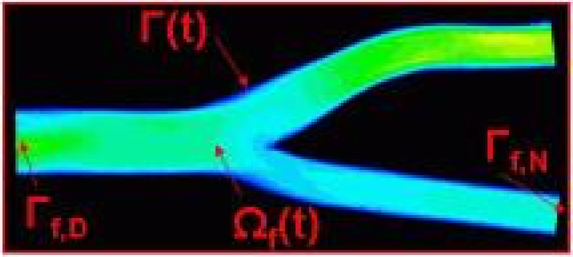
The moving control domain

$$\hat{\mathbf{w}} = \frac{\partial \hat{\mathcal{A}}_t}{\partial t}$$

Fluid equations

Assumptions on the fluid (in large arteries):

- Homogeneous
- Newtonian $(\mu = constant)$



$$\sigma_f(\mathbf{u}_f, P) = -P\mathbf{I} + 2\mu\epsilon(\mathbf{u}_f)$$

Cauchy stress tensor

Strain rate tensors

$$\epsilon(\mathbf{u}_f) = \frac{1}{2}(\nabla\mathbf{u}_f + (\nabla\mathbf{u}_f)^T)$$

Incompressible Navier-Stokes equations in ALE conservation form:

$$\frac{\rho_f}{J_{\bar{\mathcal{A}}}}\frac{\partial J_{\bar{\mathcal{A}}}\mathbf{u}_f}{\partial t}\Big|_{\bar{x}} + \mathrm{div}(\rho_f\mathbf{u}_f \otimes (\mathbf{u}_f - \mathbf{w}) - \sigma_f(\mathbf{u}_f, P)) = 0, \quad \text{in } \Omega_f(t)$$

$$\mathrm{div}\mathbf{u}_f = 0, \quad \text{in } \Omega_f(t)$$

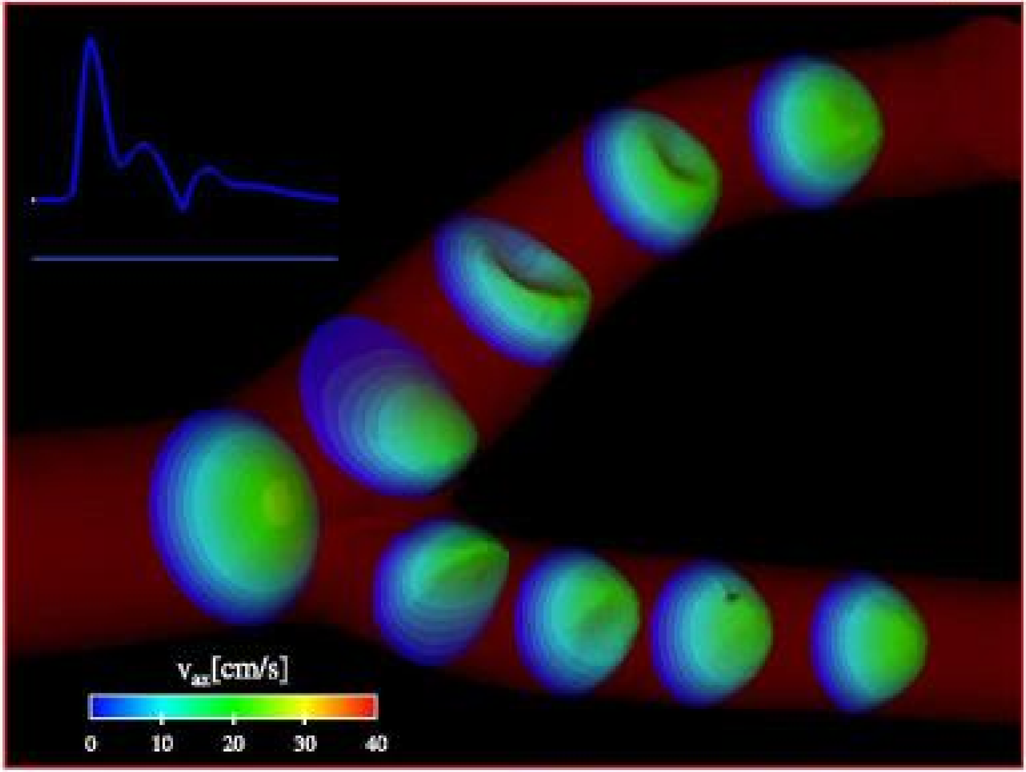
$$\mathbf{u}_f = \mathbf{u}_{f,D}, \quad \text{on } \Gamma_{f,D}$$

$$\sigma_f(\mathbf{u}_f, P)\mathbf{n}_f = \mathbf{g}_{f,N}, \quad \text{on } \Gamma_{f,N}$$

$$\mathbf{u}_f = \mathbf{u}_\Gamma, \quad \text{on } \Gamma(t)$$

MATHEMATICAL MODEL

Velocity profiles in carotid bifurcation (rigid boundaries, Newtonian)



(M.Prosi)

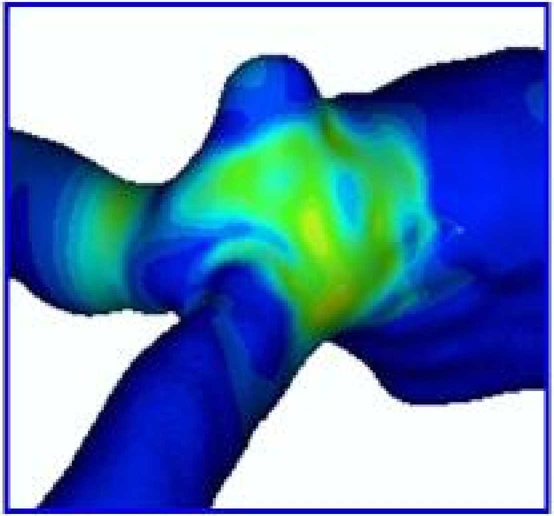
MATHEMATICAL MODEL

WSS (Wall Shear Stress) - an indicator of atherosclerosis

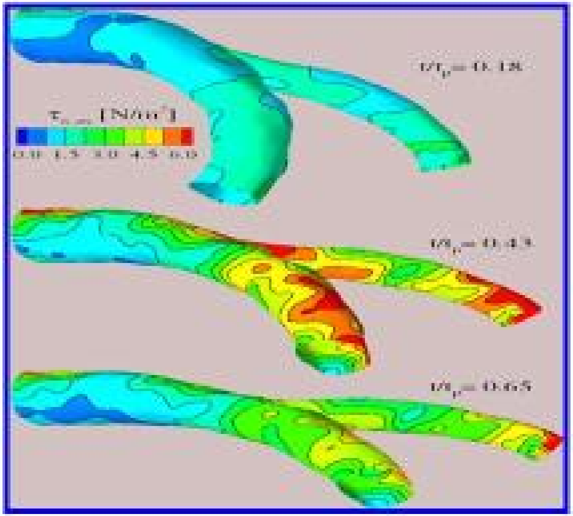
$$WSS = \mu\left(\frac{\partial \mathbf{u}}{\partial \mathbf{n}} \cdot \boldsymbol{\tau}\right)\Big|_{wall}$$

$\mathbf{u}$ velocity field

$\mathbf{n}$, $\boldsymbol{\tau}$ normal and tangential unit vectors to the vessel wall



WSS pulmonary artery (congenital heart disease)



WSS on coronaries (M.Prosi, K.Perktold TU-Graz)

MATHEMATICAL MODEL

Viscosity depends on shear rate and vessel radius

Rouleax aggregation

Red blood cells aggregate as in stack of coins

Fahraeus-Lindquist effect

In small vessels (below 1mm radii) red blood cells move toward the central part of the vessel, whence blood viscosity shifts toward plasma viscosity (much lower)

Non-Newtonian Models

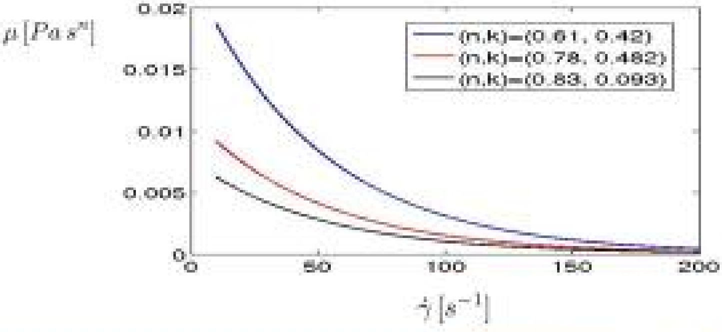
$\sigma_f(\mathbf{u}_f, P) = -P\mathbf{I} + 2\mu\epsilon(\mathbf{u}_f)$ Cauchy stress tensor

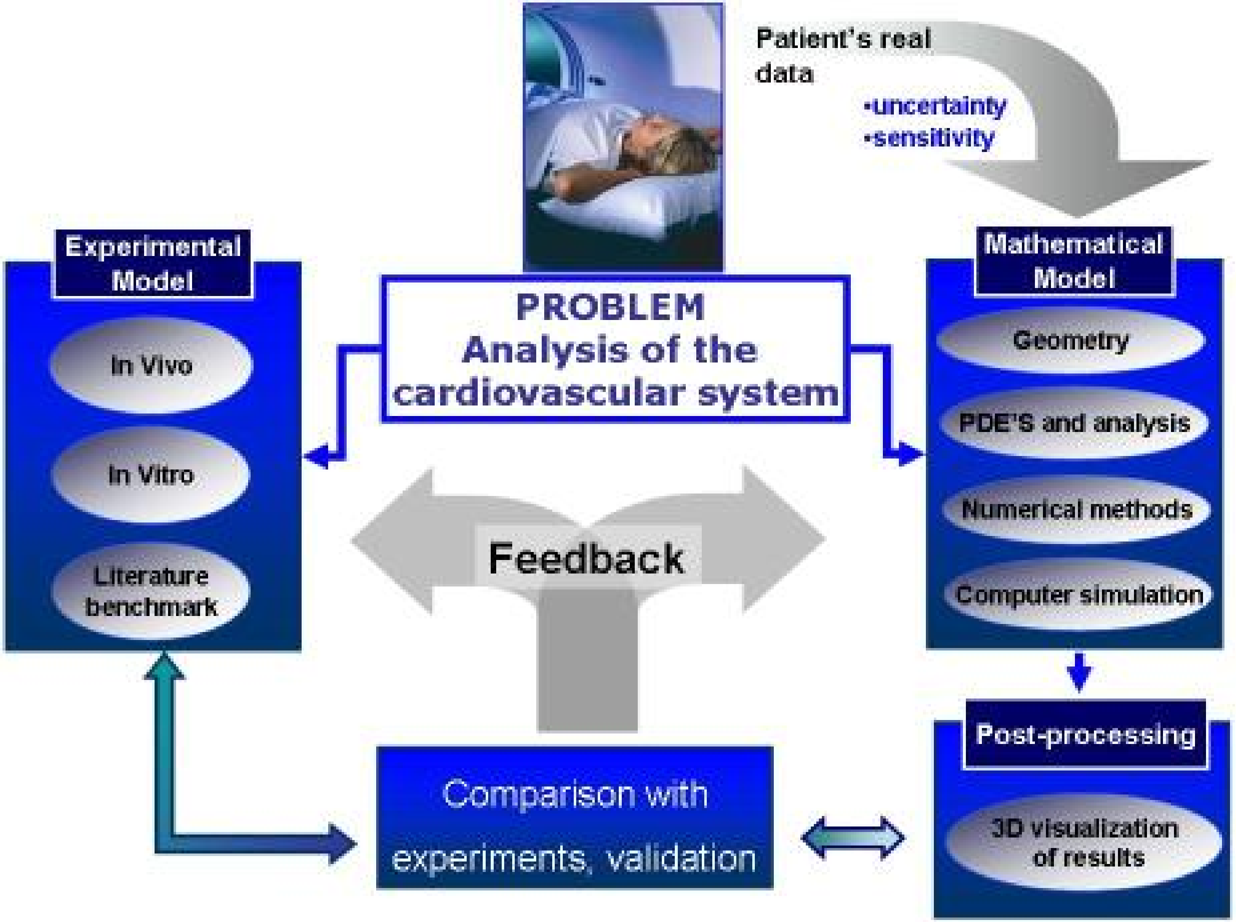
Generalized Newtonian model:

$\mu = \mu(\dot\gamma) \quad \dot\gamma = \sqrt{2\mathrm{tr}(\epsilon^2)}$ ($\dot\gamma$ Rate of deformation, or shear rate)

POWER LAW model: $\mu(\dot\gamma) = k\dot\gamma^{n-1}$

Shear thinning if n<1, μ is a decreasing function of $\dot\gamma$




Patient's real data
•uncertainty
•sensitivity
Experimental Model
In Vivo
In Vitro
Literature benchmark
PROBLEM
Analysis of the cardiovascular system
Mathematical Model
Geometry
PDE'S and analysis
Numerical methods
Computer simulation
Feedback
Post-processing
3D visualization of results
Comparison with experiments, validation

Some Generalized Non-Newtonians Models

$$\mu_0 = \lim_{\dot\gamma \to 0} \mu(\dot\gamma) = 0.056\, Pa\, s$$

$$\mu_\infty = \lim_{\dot\gamma \to \infty} \mu(\dot\gamma) = 0.00345\, Pa\, s$$

MODEL	$\frac{\mu(\dot\gamma) - \mu_\infty}{\mu_0 - \mu_\infty}$	MATERIAL CONSTANTS FOR BLOOD
POWELL-EYRING	$\frac{sinh^{-1}(\lambda\dot\gamma)}{\lambda\dot\gamma}$	$\lambda = 5.383\, s$
CROSS	$(1 + (\lambda\dot\gamma)^m)^{-1}$	$\lambda = 1.007\, s,\ m = 1.028$
MODIFIED CROSS	$(1 + (\lambda\dot\gamma)^m)^{-a}$	$\lambda = 3.736\, s,\ m = 2.406,\ a = 0.254$
CARREAU	$(1 + (\lambda\dot\gamma)^2)^{(n-1)/2}$	$\lambda = 3.313\, s,\ n = 0.3568$
CARREAU-YASUDA	$(1 + (\lambda\dot\gamma)^a)^{(n-1)/a}$	$\lambda = 1.902\, s,\ n = 0.22,\ a = 1.25$

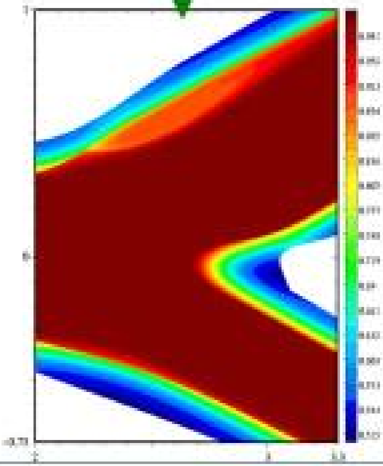
(Y.I.Cho and K.R.Kensey, Biorheology, 1991)

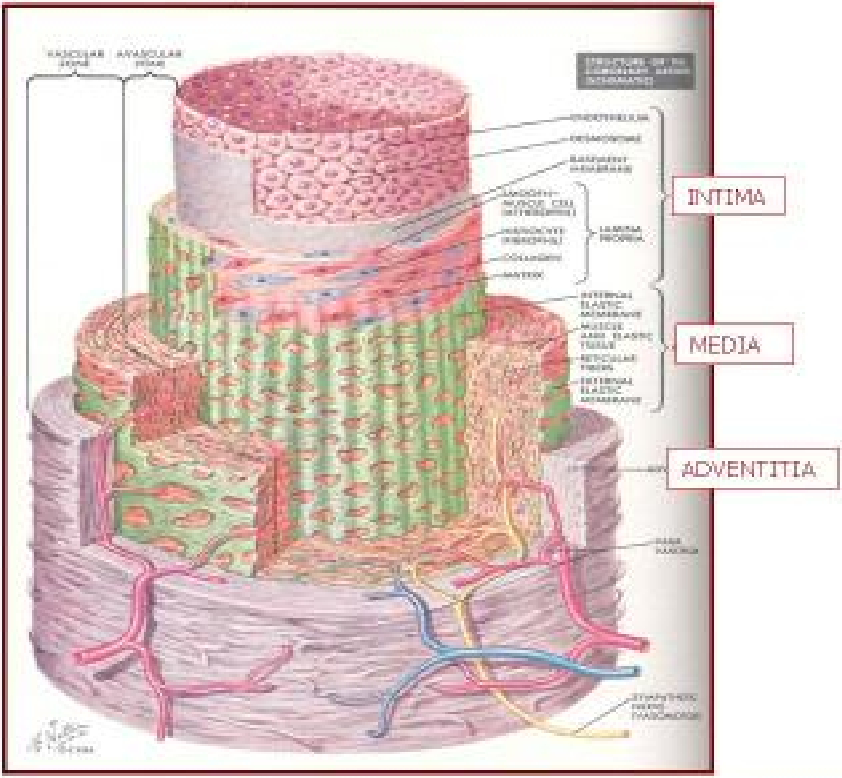
MATHEMATICAL MODEL

Model of the arterial vessel

Mechanical interaction
(Fluid-wall coupling)

Biochemical interactions
(Mass-transfer processes: macromolecules, drug delivery, Oxygen,...)





Mechanical interaction: equations for the solid wall

The momentum conservation (elastodynamic) equation

(Lagrangian approach)

$$\hat{\rho}_{s,0}\frac{\partial^2\hat{\eta}_s}{\partial t^2} - \mathrm{div}_{\hat{\mathbf{x}}}(\hat{\mathbf{F}}_s\hat{\Sigma}) = 0 \quad \text{in} \quad \hat{\Omega}_s$$

where:

$\hat{\mathbf{F}}_s$	deformation gradient
$\hat{J}_s = \det\hat{F}_s$	Jacobian
$\hat{\Sigma} = \hat{\mathbf{F}}_s^{-1}\hat{\Pi}_{\sigma_s} = \hat{J}_s\hat{\mathbf{F}}_s^{-1}\hat{\sigma}_s\hat{\mathbf{F}}_s^{-T}$	second Piola-Kirchoff tensor
$\hat{\rho}_{s,0} = \hat{\rho}_s\hat{J}_s$	density in reference configuration

Solid wall equations

We assume the solid to be a hyper-elastic material:

$$\hat{\Sigma} = \frac{\partial \hat{W}}{\partial \hat{\mathbf{E}}}(\hat{\mathbf{E}})$$

$\hat{W}$ is a given density of elastic energy

$\hat{\mathbf{E}} = \frac{1}{2}\left[\hat{\mathbf{F}}_s^T \hat{\mathbf{F}}_s - \mathbf{I}\right]$ is the Green-Lagrange strain tensor

Equilibrium of a hyper-elastic solid:

$$\hat{\rho}_{s,0}\frac{\partial^2 \hat{\eta}_s}{\partial t^2} - \mathrm{div}_{\hat{\mathbf{x}}}(\hat{\mathbf{F}}_s \hat{\Sigma}) = 0, \quad \text{in} \quad \hat{\Omega}_s$$

$$\hat{\eta}_s = 0 \quad \text{on} \quad \hat{\Gamma}_{s,D}$$

$$\hat{\mathbf{F}}_s \hat{\Sigma} \hat{\mathbf{n}}_s = \hat{J}_s |\hat{\mathbf{F}}_s^{-T} \hat{\mathbf{n}}_s| \hat{\mathbf{g}}_{s,N}, \quad \text{on} \quad \hat{\Gamma}_{s,N}$$

$$\hat{\mathbf{F}}_s \hat{\Sigma} \hat{\mathbf{n}}_s = \hat{J}_s |\hat{\mathbf{F}}_s^{-T} \hat{\mathbf{n}}_s| \hat{\mathbf{g}}_{\Gamma}, \quad \text{on} \quad \hat{\Gamma}$$

The coupled fluid-structure problem

Equations for the geometry:

$$\hat{\eta}_f = \mathrm{Ext}(\hat{\eta}_{s|\hat{\Gamma}}),\ \hat{\mathbf{w}} = \frac{\partial \hat{\eta}_f}{\partial t},\ \Omega_f(t) = (I + \hat{\eta}_f)(\hat{\Omega}_f)$$

Equations for the fluid:

$$\frac{\rho_f}{J_{\tilde{\mathcal{A}}}} \frac{\partial J_{\tilde{\mathcal{A}}} \mathbf{u}_f}{\partial t}\Big|_{\hat{x}} + \mathrm{div}(\rho_f \mathbf{u}_f \otimes (\mathbf{u}_f - \mathbf{w}) - \sigma_f(\mathbf{u}_f, P)) = 0, \text{ in } \Omega_f(t)$$

$$\mathrm{div}\,\mathbf{u}_f = 0, \quad \text{in} \quad \Omega_f(t)$$

$$\mathbf{u}_f = \mathbf{u}_D, \quad \text{on} \quad \Gamma_{f,D}$$

$$\sigma_f(\mathbf{u}_f, P)\mathbf{n}_f = \mathbf{g}_{f,N}, \quad \text{on} \quad \Gamma_{f,N}$$

$$\mathbf{u}_f = \mathbf{w}, \quad \text{on} \quad \Gamma(t)$$

Equations for the structure:

$$\hat{\rho}_{s,0} \frac{\partial^2 \hat{\eta}_s}{\partial t^2} - \mathrm{div}_{\hat{\mathbf{x}}}(\hat{\mathbf{F}}_s \hat{\Sigma}) = 0, \quad \text{in} \quad \hat{\Omega}_s$$

$$\hat{\eta}_s = 0 \quad \text{on} \quad \hat{\Gamma}_{s,D}$$

$$\hat{\mathbf{F}}_s \hat{\Sigma} \hat{\mathbf{n}}_s = \hat{J}_s |\hat{\mathbf{F}}_s^{-T} \hat{\mathbf{n}}_s| \hat{\mathbf{g}}_{s,N}, \quad \text{on} \quad \hat{\Gamma}_{s,N}$$

$$\hat{\mathbf{F}}_s \hat{\Sigma} \hat{\mathbf{n}}_s = \hat{J}_s \hat{\sigma}_f(\mathbf{u}_f, P) \hat{\mathbf{F}}_s^{-T} \hat{\mathbf{n}}_s, \quad \text{on} \quad \hat{\Gamma}$$

Energy balance

For homogeneous boundary data (isolated system):

$$\mathbf{u}_f = 0 \quad on \quad \partial\Omega_f(t)\backslash\Gamma(t)$$

$$\hat{\mathbf{F}}_s\hat{\Sigma}\hat{\mathbf{n}}_s = 0 \quad on \quad \partial\hat{\Omega}_s\backslash\hat{\Gamma}$$

$$\frac{d}{dt}[EK(\mathbf{u}_f,\mathbf{u}_s)+EP(\hat{E})]+\mathrm{Diss}(\mathbf{u}_f)= 0$$

with $\mathbf{u}_s = \dfrac{\partial\hat{\eta}_s}{\partial t}$

$$EK(\mathbf{u}_f,\mathbf{u}_s) = \int_{\Omega_f(t)}\frac{\rho_f}{2}|\mathbf{u}_f|^2 d\mathbf{x} + \int_{\hat{\Omega}_s}\frac{\hat{\rho}_{s,0}}{2}|\mathbf{u}_s|^2 d\hat{\mathbf{x}}$$ Kinetic energy

$$EP(\hat{E}) = \int_{\hat{\Omega}_s}\hat{W}(\hat{E})d\hat{\mathbf{x}}$$ Elastic potential energy

$$\mathrm{Diss}(\mathbf{u}_f) = \int_{\Omega_f(t)} 2\mu|\varepsilon(\mathbf{u}_f)|^2 d\mathbf{x}$$ Viscous dissipation

MATHEMATICAL MODEL

Some references

(Existence of strong or weak solutions, control, stability of time-discretizations in time-dependent domains)

Le Tallec and Mouro (95),

Beirao da Veiga (04),

Desjardin and Esteban (99),

Osses and Puel (99),

Grandmont and Maday (00-02),

J.L.Lions and Zuazua (95),

Zhang and Zuazua (04-06),

Murea and Vazquez (05),

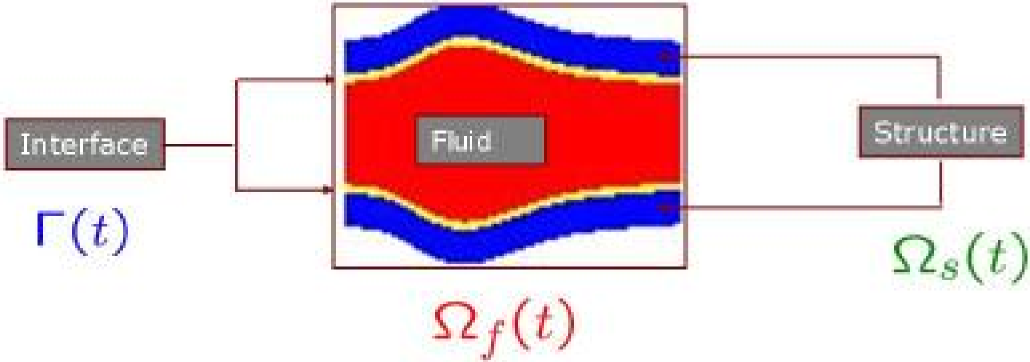
Cheng, Coutand and Shkoller (06)

L.Formaggia and F.Nobile (99-04)

D.Boffi and L.Gastaldi (04)

Dimensional reduction: working at interface

Role of Interface



Interface Problem: Domain Decomposition Formulation, I

Steklov-Poincare' equation

$$\mathrm{SP_f}(\overrightarrow{\lambda}) + \mathrm{SP_S}(\overrightarrow{\lambda}) = 0$$

Construction of the Steklov-Poincare' (**Dirichlet-to-Neumann**) maps SP_f and SP_s:

$$\overrightarrow{\lambda} \to (\overrightarrow{u}, p) = Res_f(\overrightarrow{\lambda}) \to SP_f(\overrightarrow{\lambda}) = \sigma_f(\overrightarrow{u}, p) \cdot \overrightarrow{n}_f$$

$$\overrightarrow{\lambda} \to (\overrightarrow{u}, p) = Res_s(\overrightarrow{\lambda}) \to SP_s(\overrightarrow{\lambda}) = \sigma_s(\overrightarrow{u}, p) \cdot \overrightarrow{n}_s$$

DD Formulation, II: Preconditioned Iterations

$$\mathrm{SP_f}(\vec{\lambda}) + \mathrm{SP_S}(\vec{\lambda}) = 0$$

1. Compute the residual stress from a given displacement

$$\vec{\sigma}^k = -(\mathrm{SP_f}(\vec{\lambda}^k) + \mathrm{SP_S}(\vec{\lambda}^k))$$

2. Apply the inverse of the preconditioner to the stress

⇨ recover displacement

$$\vec{\mu}^k = P^{-1}\vec{\sigma}^k$$

3. Update displacement

$$\vec{\lambda}^{k+1} = \vec{\lambda}^k + \omega^k \vec{\mu}^k$$

$$P^{-1} = \alpha_f^k(\mathrm{SP}_f'(\vec{\lambda}^k))^{-1} + \alpha_S^k(\mathrm{SP}_S'(\vec{\lambda}^k))^{-1}$$

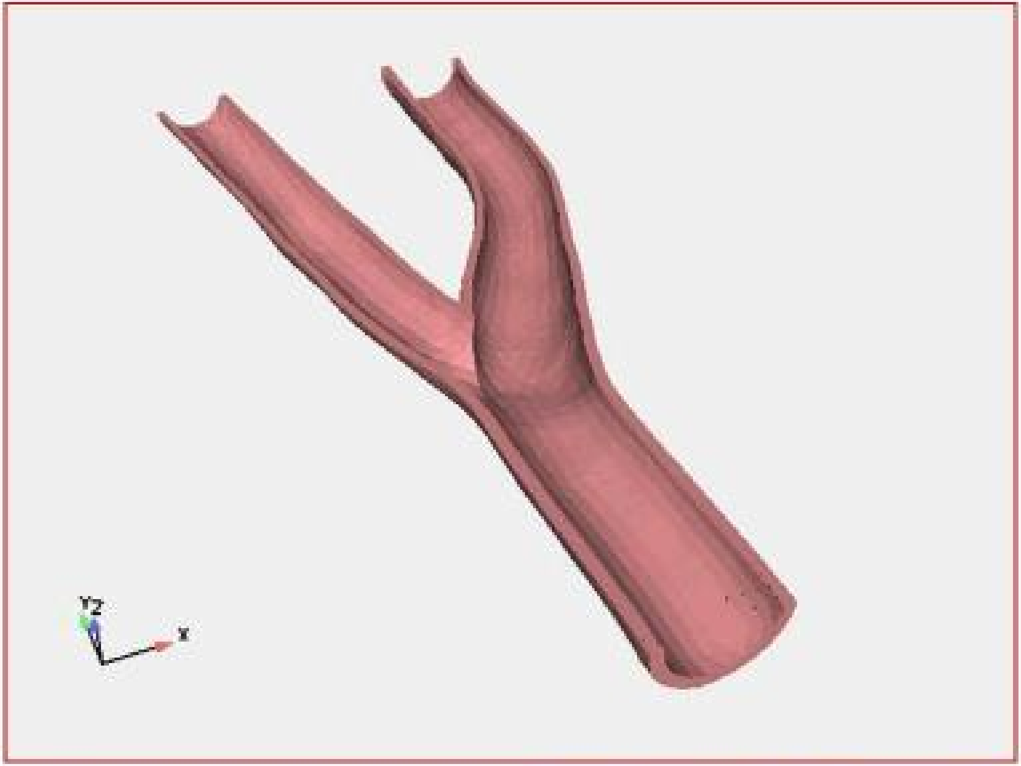
(S. Deparis, M. Discacciati, G.Fourestey and A.Q. 2004)

GEOMETRIC PRE-PROCESSING

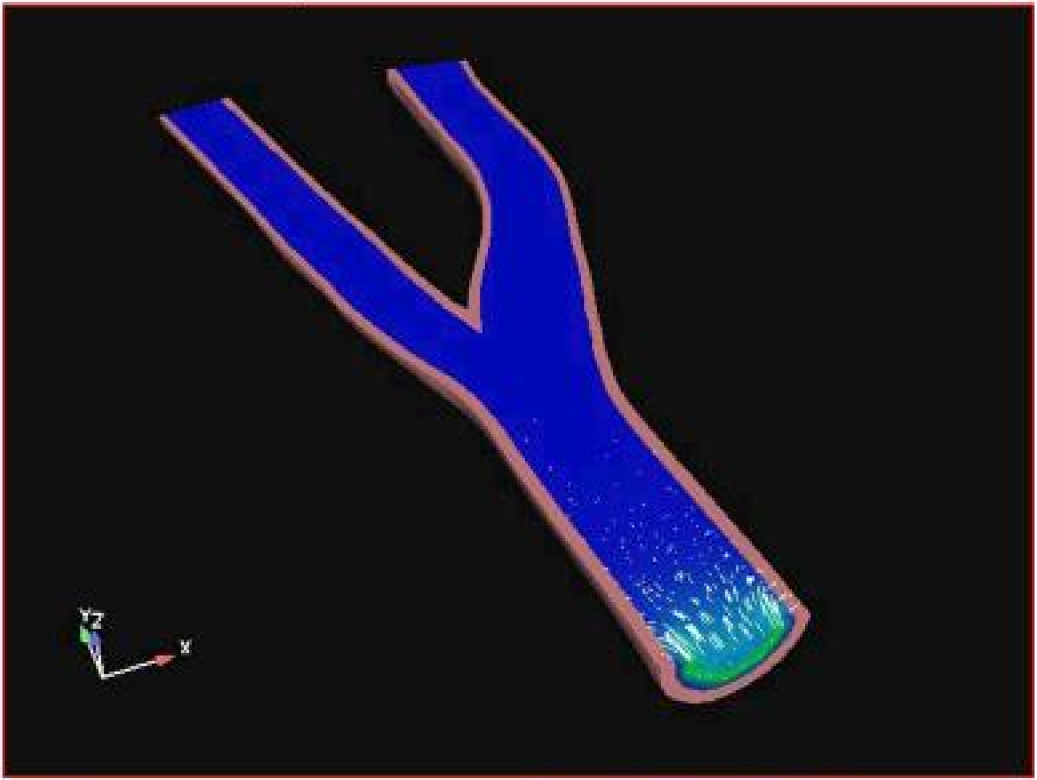
Geometric Pre-Processing

- Extraction of 3D geometric model from medical images (anatomy)
- Statistical analysis and classification (according to clinical protocols)
- Generation of boundary and initial conditions (physiology)
- Generation of computational mesh for surfaces and volumes (2D and 3D)

FSI for carotid bifurcation : wall deformation



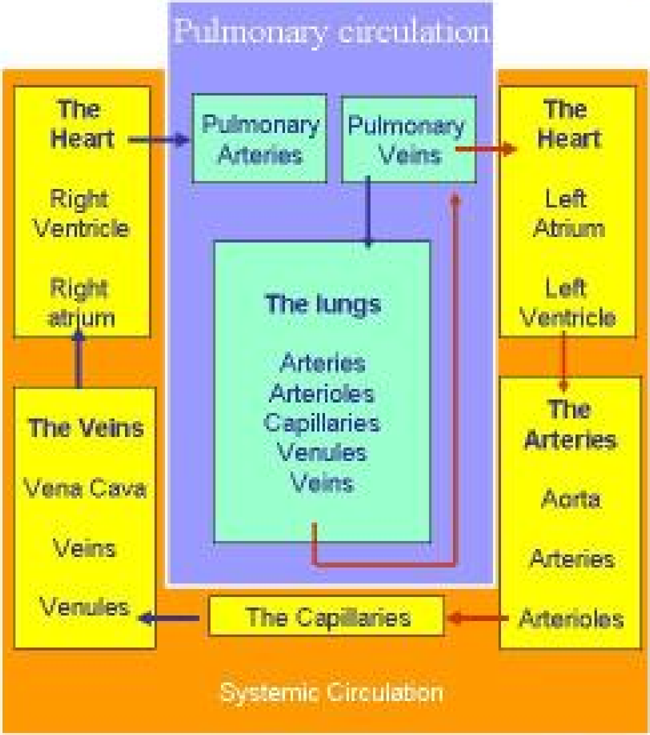
Flowfield

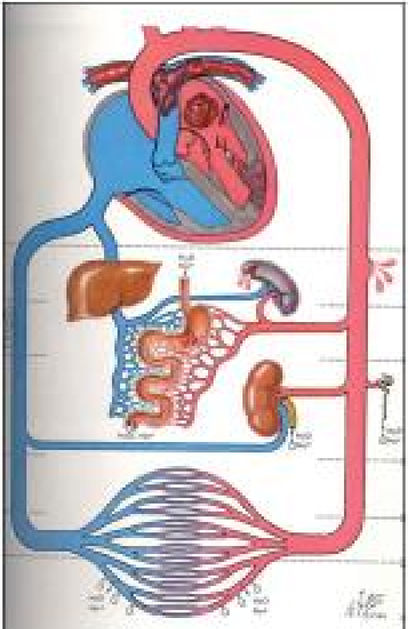


Spurious reflections with free-stress outflow conditions

Geometric Multiscale

Cardiovascular System: Functionality





Representative fluid dynamics values

- Geometrical and mechanical parameters of blood vessels vary highly from the arterial scale to the capillary one
- Customarily, the flow has a laminar regime

Vessel	Number	Diameter [cm]	Wall thickness [cm]	Velocity [cm/s]	Average Reynolds number
Aorta	1	2.5	0.2	48	3400
Arteries	159	0.5	0.1	45	500
Arterioles	1.4e6	0.004	0.002	5	0.7
Capillaries	3.2e9	0.0008	0.0001	0.1	0.002
Venules	20e6	0.007	0.0002	0.2	0.01
Veins	40	0.5	0.05	10	140
Vena cava	2	3	0.3	38	3300

Full scale turbulence (high Re) can develop in a few cases only:

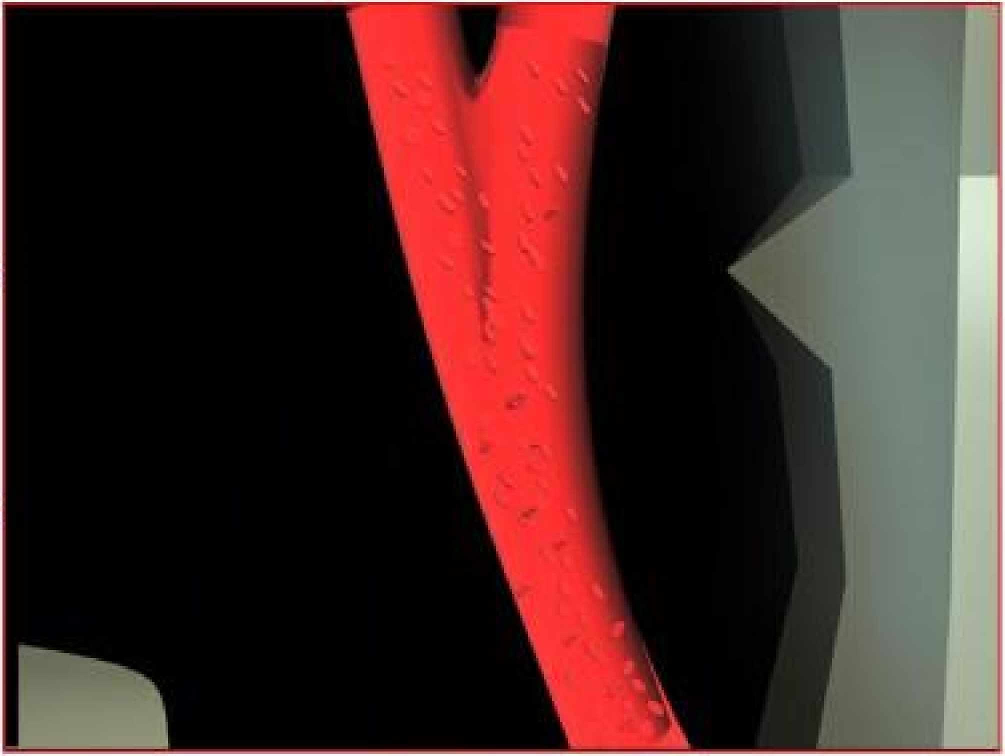
1. High cardiac output (exercise)
2. Stenoses
3. Low blood density (for example: anemia)

A local-to-global approach

Local (level1):
3D flow model

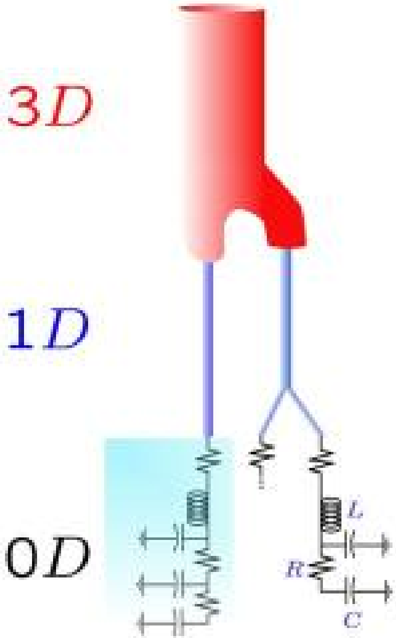
Global (level 2):
1D network of major arteries and veins

Global (level 3):
0D capillary network



MATHEMATICAL MODEL

Dimensional reduction by geometric multiscale



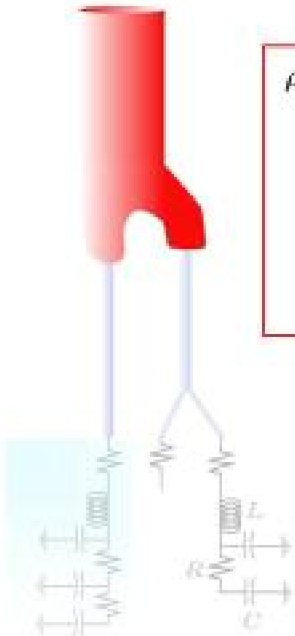
3D Navier-Stokes (F) +
3D ElastoDynamics (V-W)

1D Euler (F) +
Algebraic pressure law

0D lumped parameters
(system of linear ODEs)

MATHEMATICAL MODEL

Geometric multiscale models



3D Navier-Stokes (F) + 3D ElastoDynamics (V-W)

$$
\begin{aligned}
\rho_f[\partial_t \mathbf{u} + (\mathbf{u} - w)\cdot\nabla\mathbf{u}] - \mu\Delta\mathbf{u} + \nabla p &= 0 && \text{in } \Omega_f \\
\text{div } \mathbf{u} &= 0 && \text{in } \Omega_f \\
\partial_{tt}\eta - \text{div } \sigma(\eta) &= f(\eta) && \text{in } \Omega_w \\
\sigma(\eta)\cdot n &= T(\mathbf{u}, p)\cdot n && \text{on } \Gamma \\
\mathbf{u} &= \partial_t \eta && \text{on } \Gamma
\end{aligned}
$$

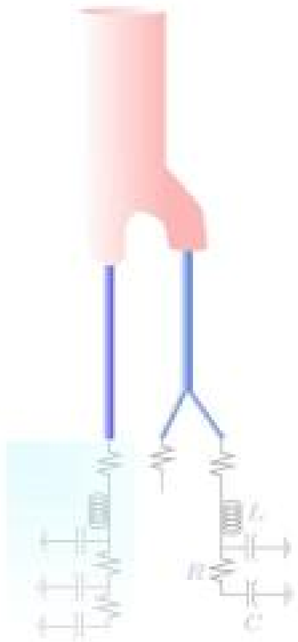
Assume that:

- $u_z >> u_x, u_y$
- u_z has a prescribed steady profile
- average over axial sections
- static equilibrium for the vessel

Then we obtain a 1D problem.

MATHEMATICAL MODEL

Geometric multiscale model



1D Euler(F) + Algebraic pressure law

$$
\begin{aligned}
\partial_t A + \partial_x Q &= 0, \\
\partial_t Q + \partial_x \left(\frac{\alpha Q}{A} \right) + \frac{A}{\rho} \partial_x P &= -K_r \frac{Q}{A}, \\
P(A) &= \beta \frac{\sqrt(A) - \sqrt(A_0)}{A_0}
\end{aligned}
$$

Assume to

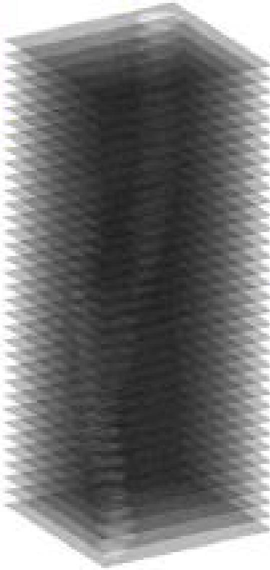
- linearize 1D equations
- consider average internal variables
- relate interface values to averaged ones

Then we obtain a 0D problem (ODE).

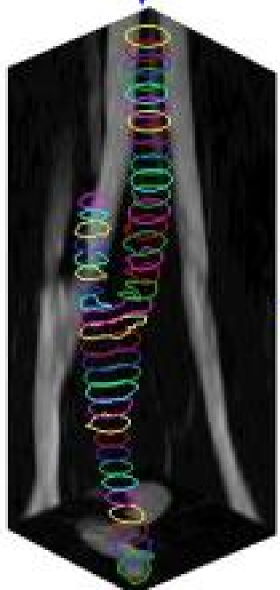
GEOMETRIC PRE-PROCESSING

Extracting geometry from medical images

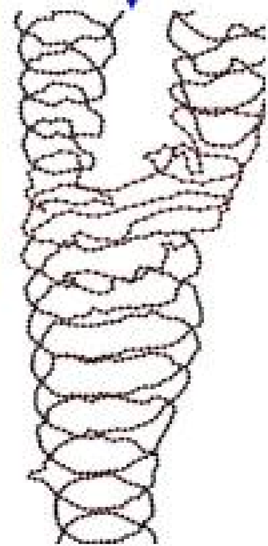
MR (Magnetic Resonance)



Stack of images from MRI (1mm)



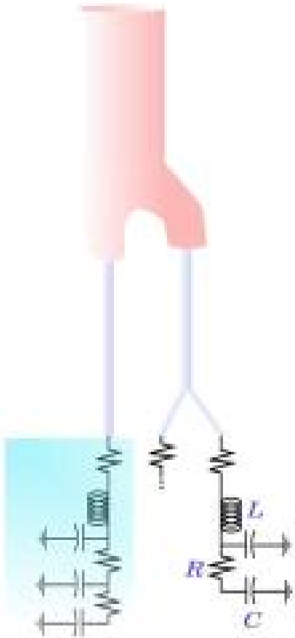
Contour extraction by segmentation (using B-Splines)



Sample points on extracted geometry

MATHEMATICAL MODEL

Geometric multiscale model



0D Lumped parameters (system of linear ODE's)

$$C\frac{dP_i}{dt} = -(Q_{i+1} - Q_i),$$

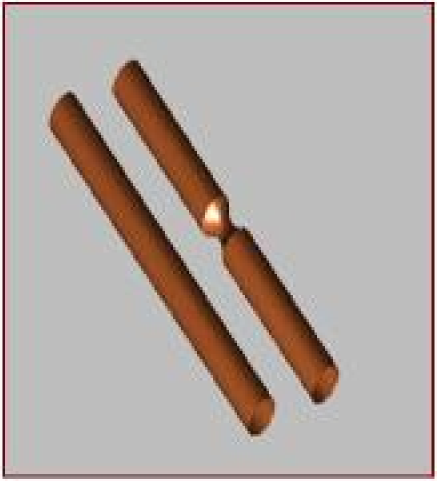
$$L\frac{dQ_i}{dt} = -(P_i - P_{i-1}) - RQ_i$$

The analogy

Fluid dynamics	Electrical circuits
Pressure	Voltage
Flow rate	Current
Blood viscosity	Resistance R
Blood inertia	Inductance L
Wall compliance	Capacitance C

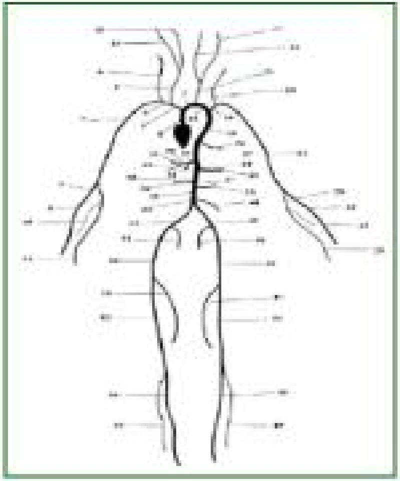
- RLC circuits model "large" arteries
- RC circuits account for capillary bed
- Can describe compartments (such as peripheral circulation)

One-dimensional models



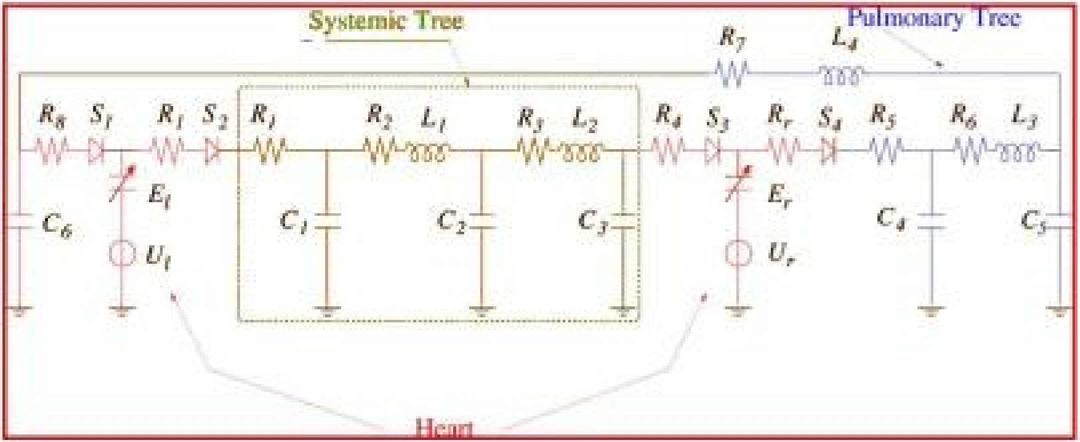
Stenosed artery

Junction of three arteries
(stented abdominal aorta)



Network of 55 arteries

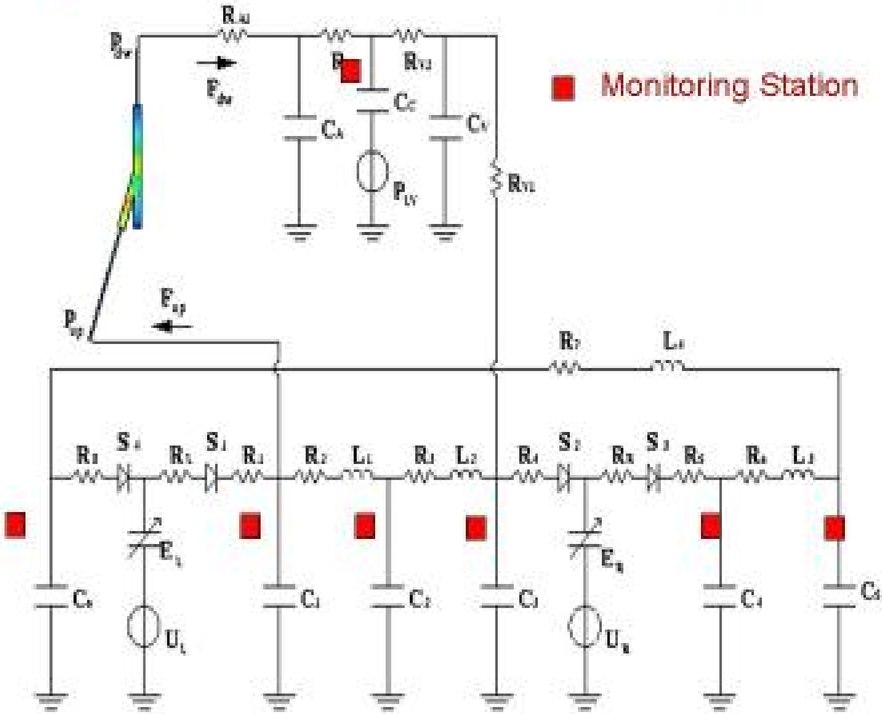
A 0D model of the whole circulation



Continuity of fluxes and pressure yields the DAE system:

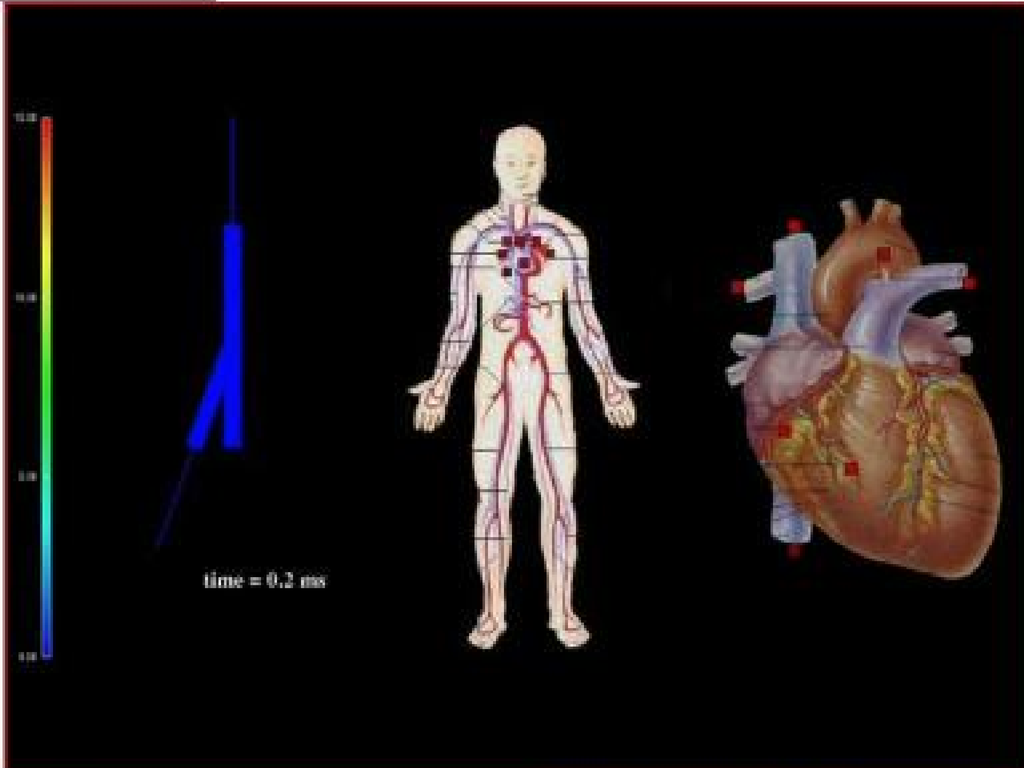
$$\begin{cases} \dfrac{d\mathbf{y}}{dt} = B(\mathbf{y}, \mathbf{z}, t) \quad t \in (0, T] \\ G(\mathbf{y}, \mathbf{z}) = 0 \end{cases}$$

A full geometric multiscale model: 0D-1D-2D (or 3D) coupling

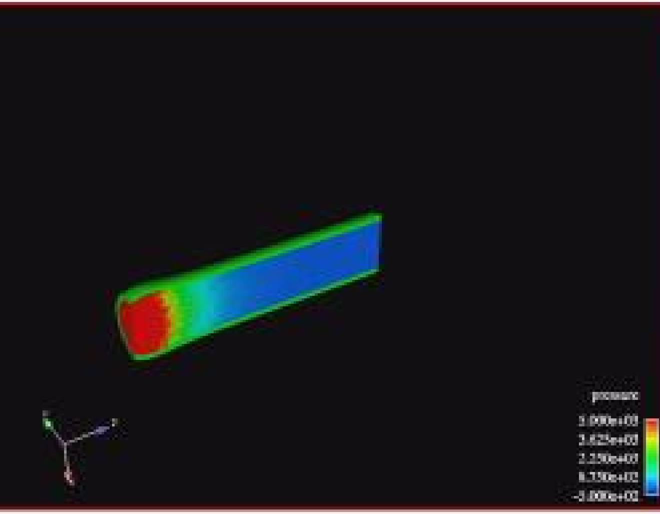


MATHEMATICAL MODEL

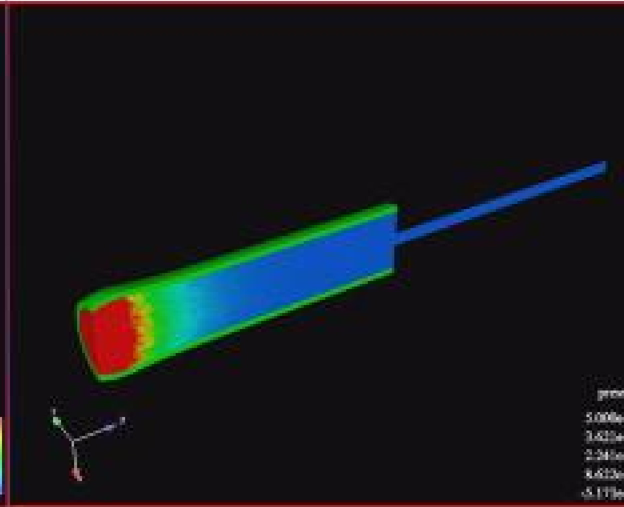
3D - 1D - 0D



3D and 1D for a cilindrical artery: pressure pulse



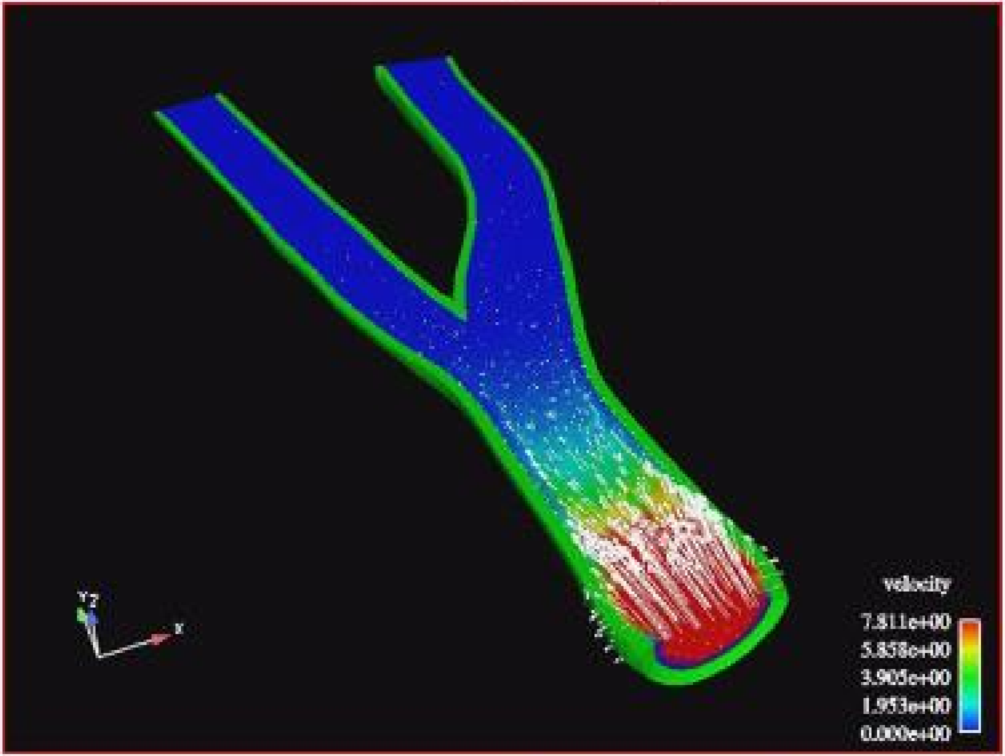
3D model (spurious reflections)



3D-1D coupled model

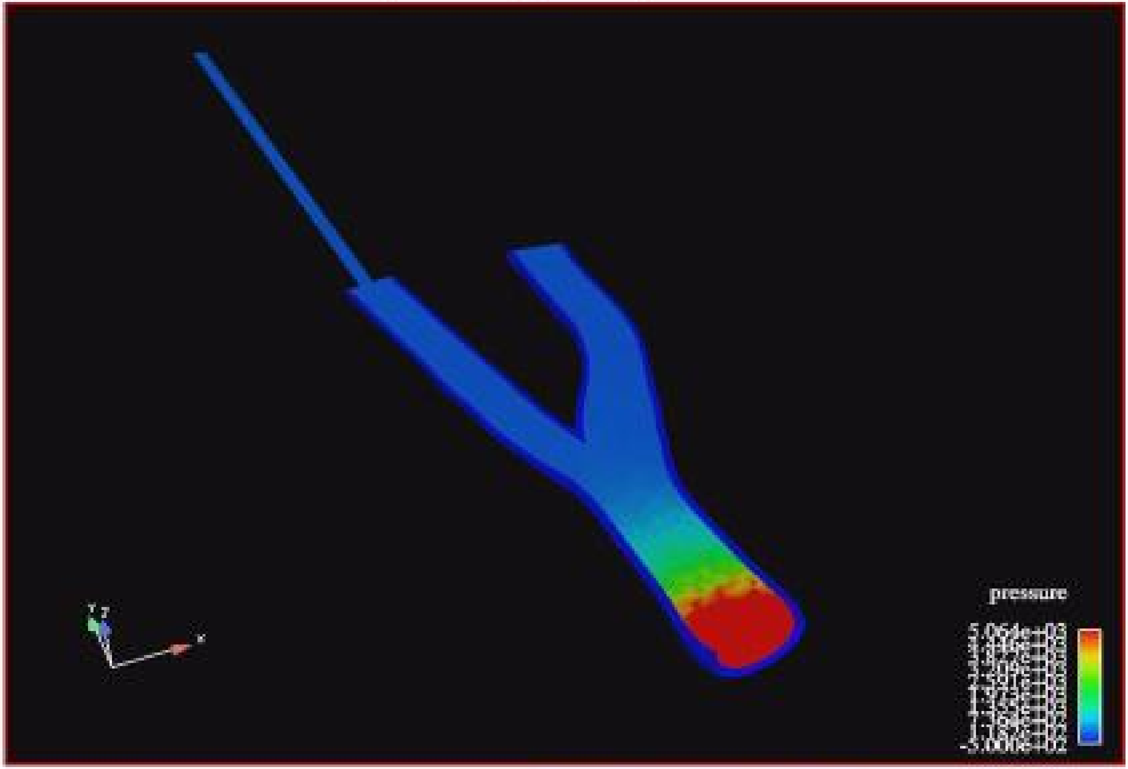
(A. Moura)

3D-1D for the carotid: velocity field



(A. Moura)

3D-1D for the carotid: pressure pulse



(A. Moura)

MATHEMATICAL MODEL

Some references on the 1D system

L.Euler, Principia pro motu sanguinis per arteria determinando, 1775

Continuous dependence of 1D: L.Formaggia. J.F. Gerbeau, F. Nobile, A. Q., 2001

Existence of local-in-time regular solution for in the half-space for 1D: S. Canic, E.H. Kim, 2003, S.Canic and A.Mikelic, 2004

Asymptotic analysis for 1D-0D coupling: M.Fernandez, V.Milisic and A.Q., 2004

Existence of regular global solution on bounded domains without source term and special b.c:

D.Amadori, S. Ferrari and L.Formaggia, 2006

Treatment of interfaces between models of different dimension

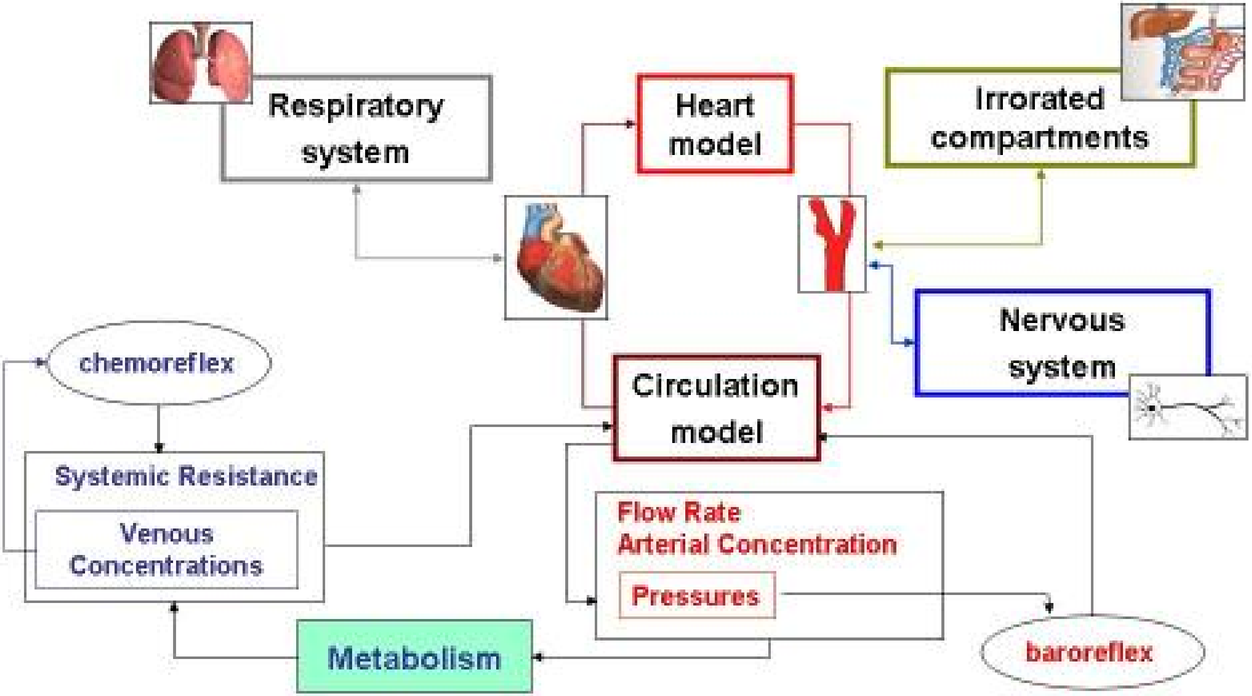
(A.Q. and A. Veneziani, MMS SIAM, 2004 (3D-0D, Shauder fixed point)

L.Formaggia, J.F.Gerbeau, F.Nobile and A.Q., 2002

A.Veneziani, C.Vergara, 2006, L.Formaggia, A.Veneziani, C.Vergara, 2006

(by either Lagrange multipliers or optimal control)

A Global Scenario: An Outlook



Building the surface S from sample points

$$S = \{\mathbf{x} \in \mathbb{R}^3 : \ \phi(\mathbf{x}) = 0\}$$ Implicit definition

$$\phi(\mathbf{x}) = \sum_i w_i \varphi(||\mathbf{x} - \mathbf{x}_i||)$$ Radial basis expansion

Two possible choices: $\varphi(r) = r$ or $\varphi(r) = r^3$

Extracting infomation from the surface :

$$H_h(\mathbf{x}) = \frac{H(\mathbf{x})}{|\nabla \phi(\mathbf{x})|}, \quad \mathbf{x} \in S$$ **Normalized Hessian**

Allows computation of curvature:

$$\sigma(H_h) = \{0, k_{min}, k_{max}\}$$

POST-PROCESSING and MODEL VALIDATION

Post-processing and model validation

Error analysis (comparison with exact solutions on benchmark problems and results in literature)

Comparison with experimental results (in vivo / in vitro)

Assessment by M.D. and clinicians

APPLICATIONS

1 - Cavo-pulmonary shunt

2 - Cerebral aneurysms

3 – Stents

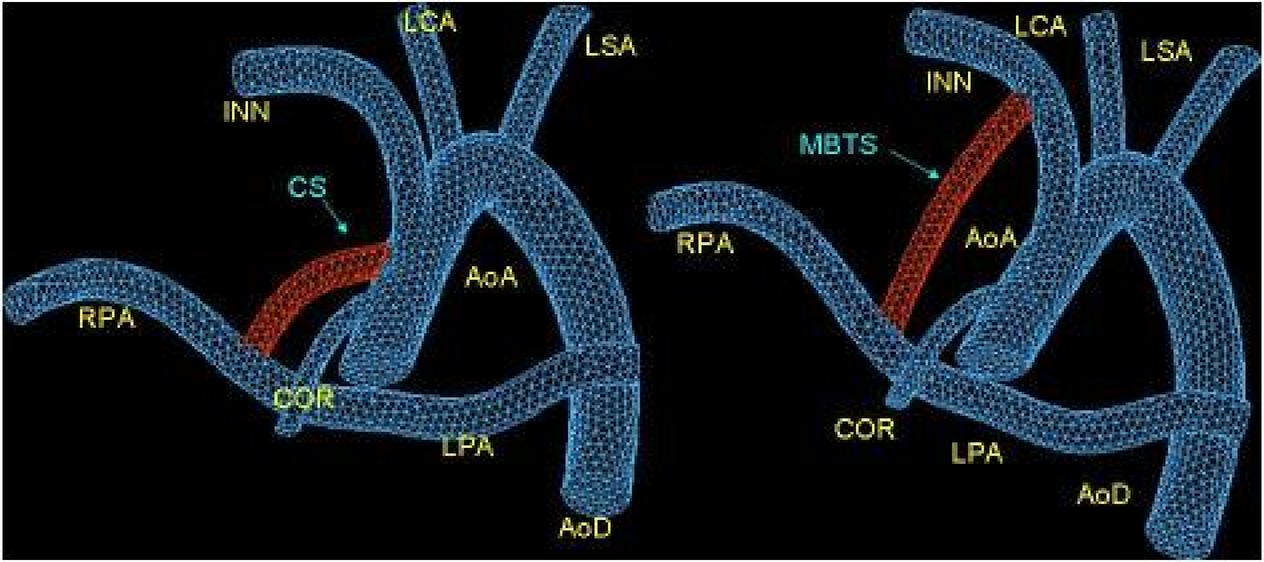
1 - Cavopulmonary Shunt

LABS, Politecnico of Milan
Cariplo Foundation
Great Ormond Street Hospital, London

APPLICATION 1: CAVOPULMONARY SHUNT

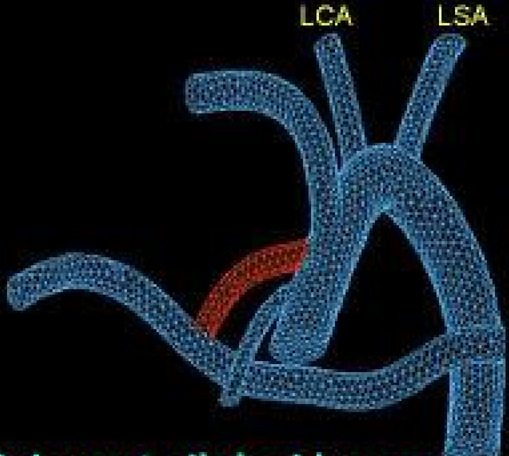
Shunt for restoring heart-pulmonary circulation

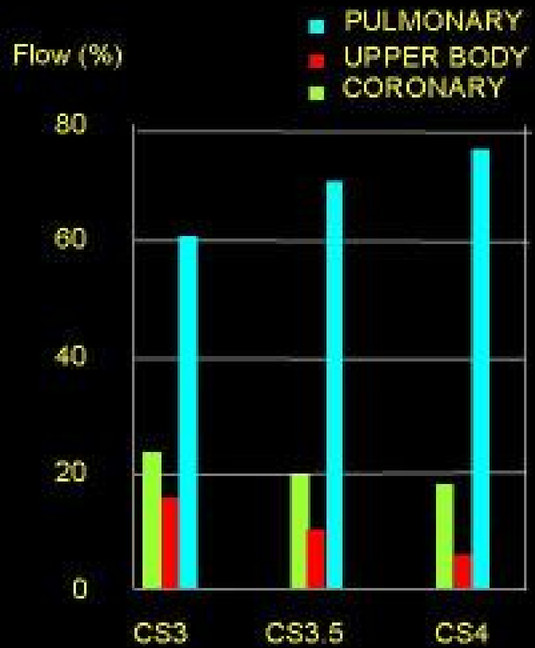
Central Shunt (CS) | Modified Blalock-Taussig Shunt (MBTS)



APPLICATION 1: CAVOPULMONARY SHUNT

Central Shunt
(CS)



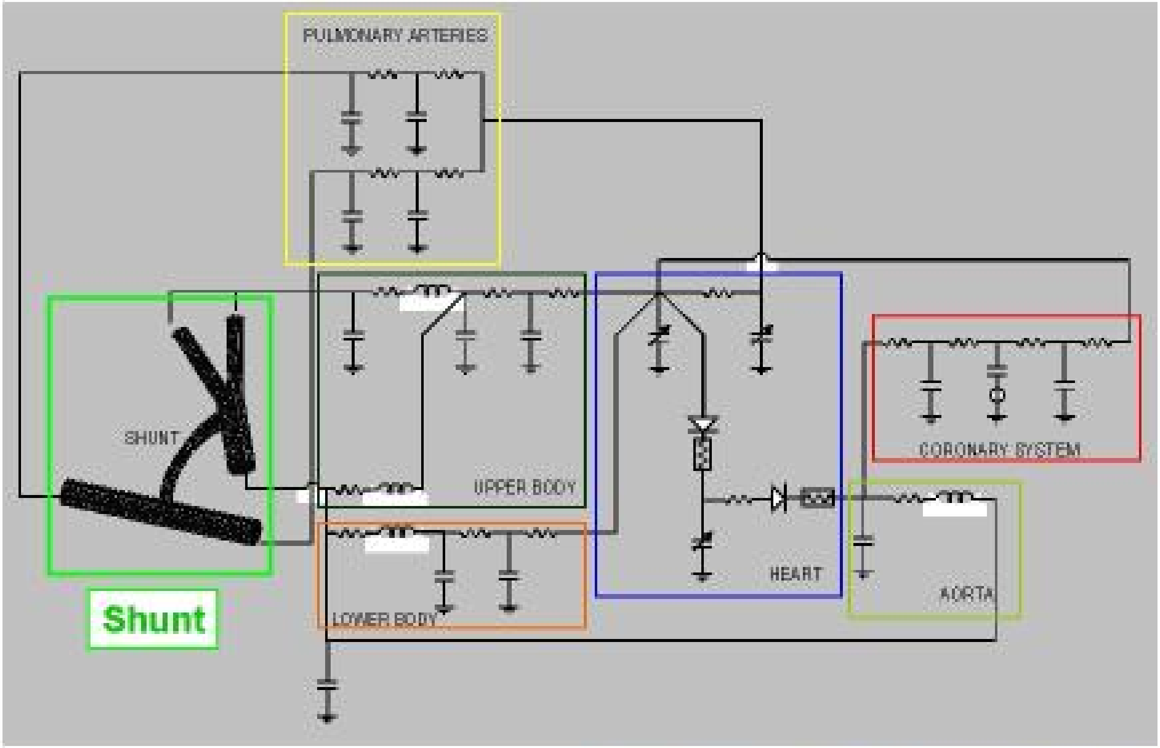


Relevant clinical issues:

- shunt radius choice
- systemic/pulmonary flux balancing
- coronary flux

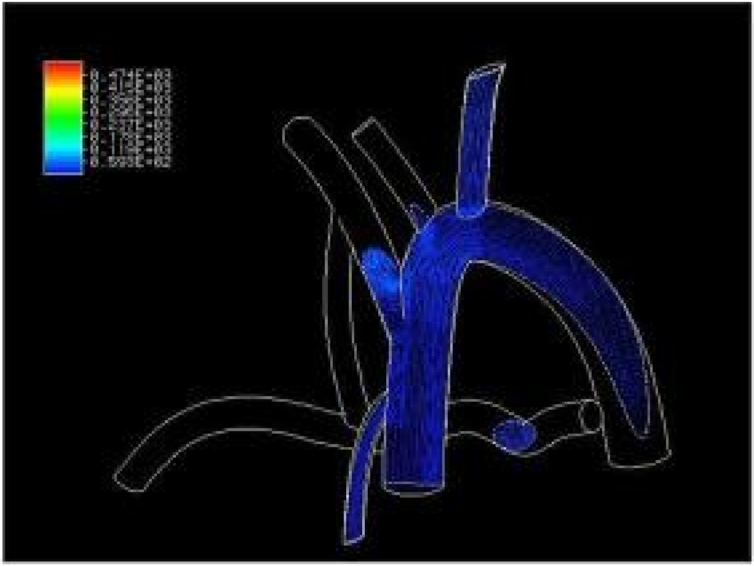
APPLICATION 1: CAVOPULMONARY SHUNT

A multiscale 3D-0D model



APPLICATION 1: CAVOPULMONARY SHUNT

Flow reversal in the pulmonary artery



2 - Cerebral Aneurysms

The ANEURISK Project

Siemens Italia

Niguarda Hospital, Milan

Lab of Biological Structures – Politecnico of Milan

APPLICATION 2: THE ANEURISK PROJECT

Project description

CEREBRAL ANEURYSMS are lesions arising on cerebral vessels characterized by a bulge of the vessel wall. Quite often they are subject to rupture, yielding dangerous cerebral haemorrhage.

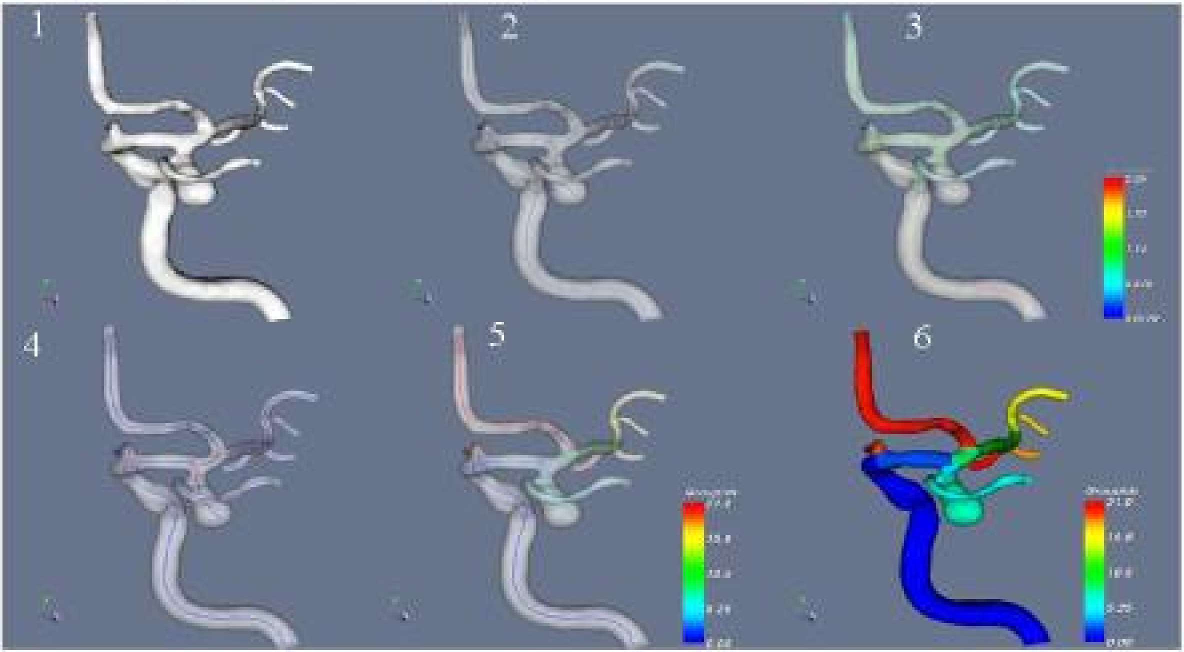
"It is estimated that 5% of the population has some type of aneurysm in the brain. The incidence of ruptured aneurysm is approximately 10 out of 100,000 people per year. …About 10% of patients who have one aneurysm will have at least one more." *National Library of Medicine, NIH US,* http://www.nlm.nih.gov

PROJECT GOAL:
To highlight the possible relationships between **vascular morphology** and risk of development and rupture of aneurysms

METHODS:
Integration of extensive data analysis and numerical simulations

APPLICATION 2: THE ANEURISK PROJECT

Morphological Analysis

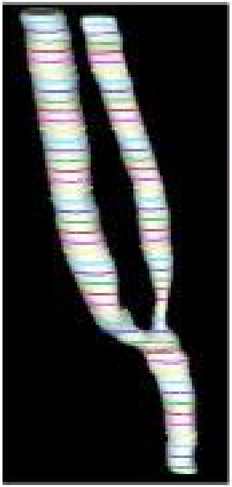


1. Model
2. Centerlines
3. Maximal Inscribed Sphere Radius
4. Bifurcations Identification
5. Centerlines of each branch
6. Branch Identifications

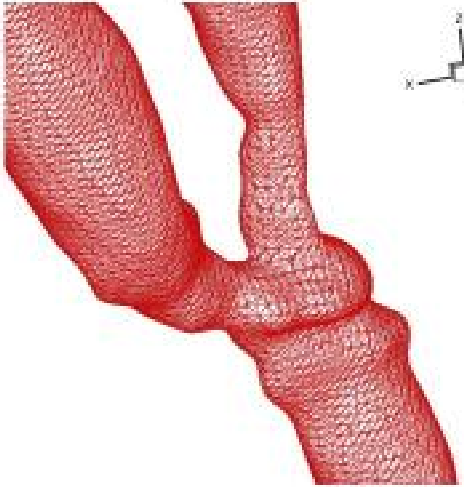
GEOMETRIC PRE-PROCESSING

Generating a computational mesh

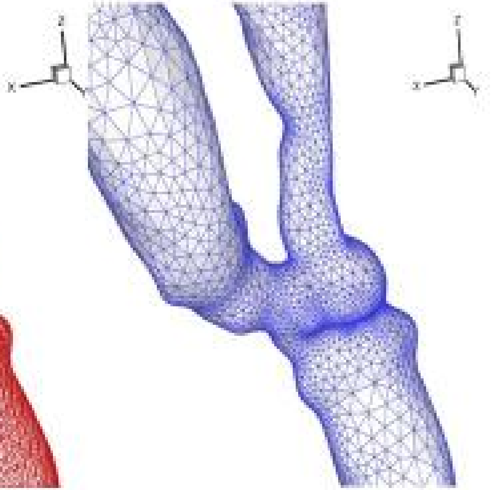
Constrained optimization procedures are needed to maximize a suitable measure of the grid quality (to avoid triangle distorsion) while keeping the desired accuracy of surface representation



Splines on sections



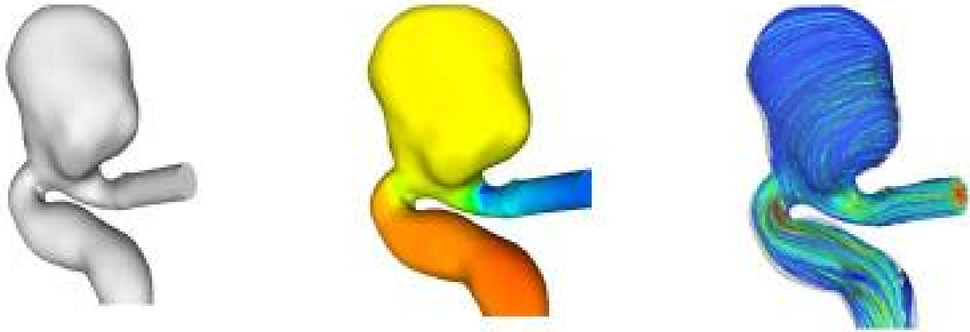
Original grid (marching cube algorithm, J.Bloomenthal,1994)



Optimized grid (J. Peiro et al, 2006)

APPLICATION 2: THE ANEURISK PROJECT

From geometric reconstruction to numerical simulations



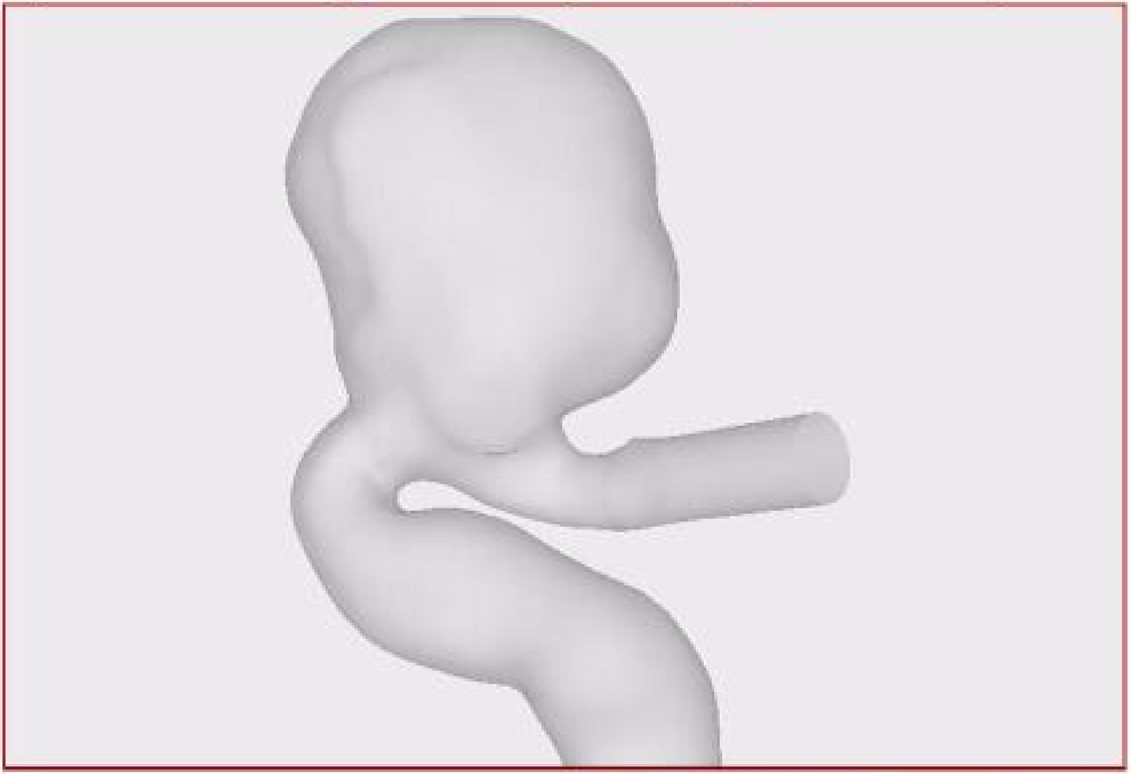
Reconstruction
of the aneurism's geometry

Pressure field

Velocity streamlines

APPLICATION 2: THE ANEURISK PROJECT

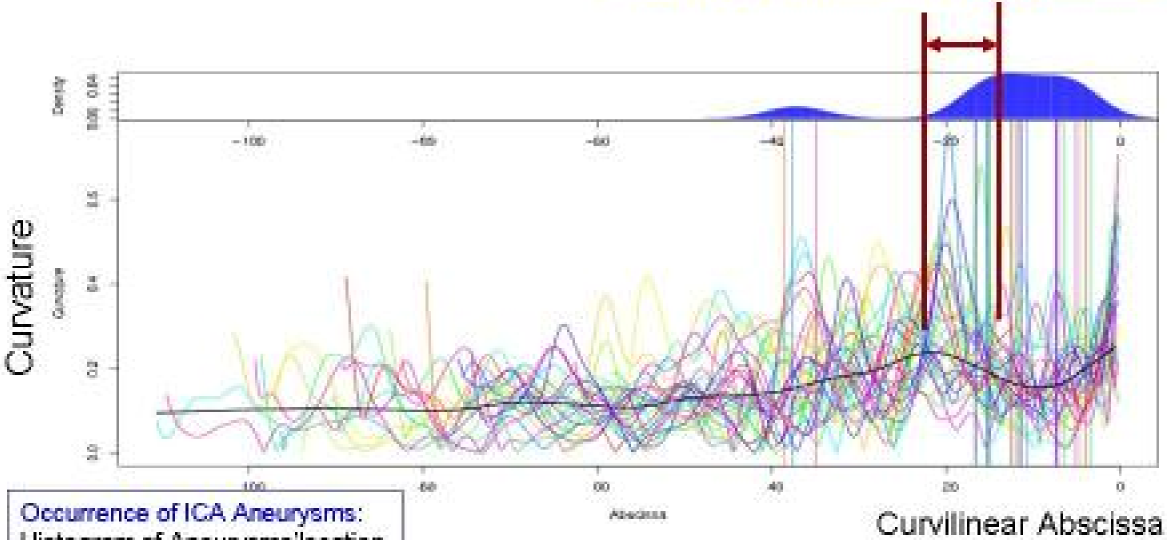
Particle tracing in an aneurysm during a full cardiac pulse



APPLICATION 2: THE ANEURISK PROJECT

Statistical analysis and CFD on 65 patients

Peak in ICA aneurysms density is slightly downstream the peak of vessel curvature, suggesting a correlation with fluid dynamics



Occurrence of ICA Aneurysms:
Histogram of Aneurysms'location shows that ICA aneurysms occur essentially in two sites

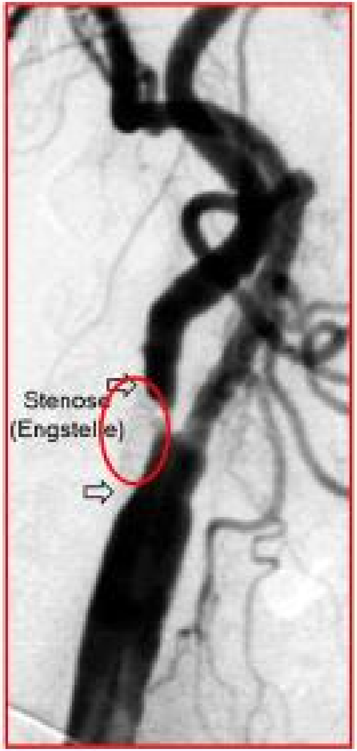
Classes introduced in Hassan et al., J. Neurosurgery, 2005

3- Drug Eluting Stents

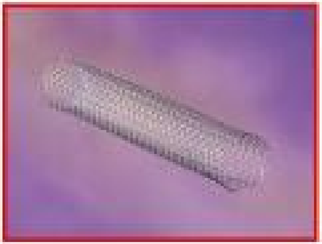
Haemodel EU Project, 6th Framework
MIUR, Italian Ministry of Research and University
FNS, Swiss National Funds
Fondazione Cariplo

APPLICATION 3: DRUG ELUTING STENTS

Stenosys in the carotid bifurcation

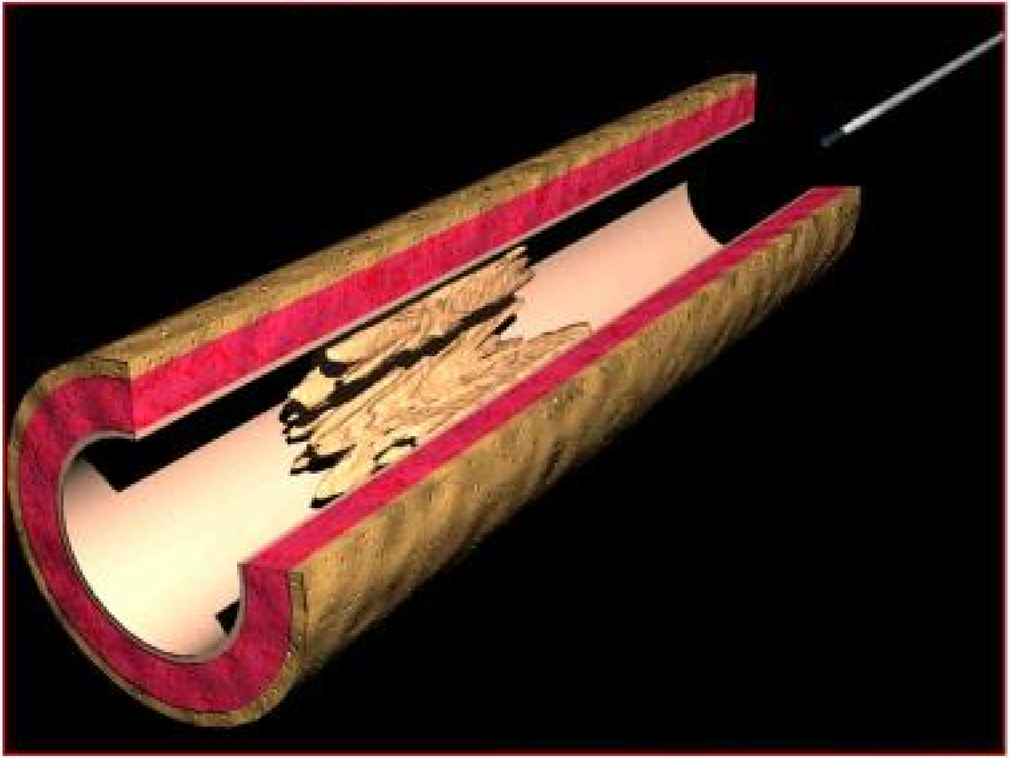


Angiography after stent placement



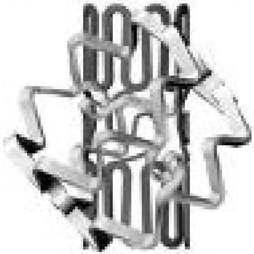
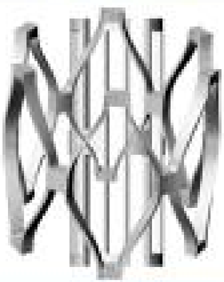
APPLICATION 3: DRUG ELUTING STENTS

Stent deployment



APPLICATION 3: DRUG ELUTING STENTS

Four commercial coronary stents

CORDIS	JOSTENT
	
SORIN	**PALMAZ**
	

Different stent design may affect the local drug distribution across the arterial wall

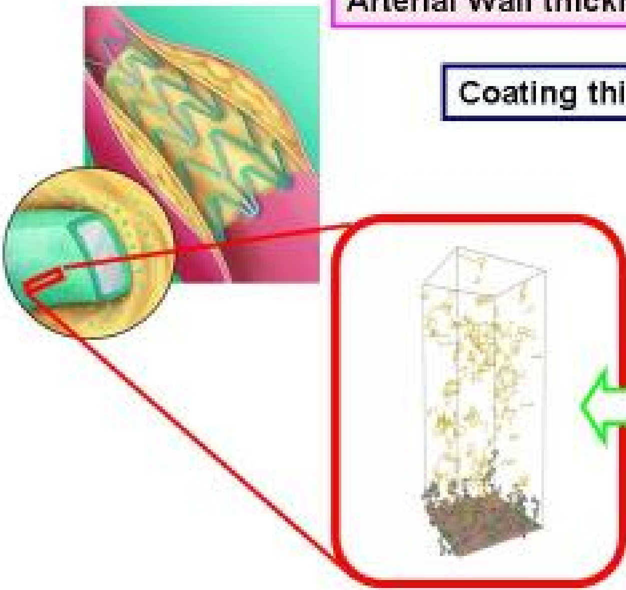
The final configuration reached after the stent deployment has to be taken into account: an incorrect expansion may cause sites of toxic dose

APPLICATION 3: DRUG ELUTING STENTS

Mathematical Model

Arterial Wall thickness: 0.4 – 1.0 mm

Coating thickness: 5 μ m



Modelled with three phases:

- **Effective solid phase** (drug bound to the polymer)
- **Virtual solid phase** (polymer swelled – free interface)
- **Liquid phase** (drug dissolved in plasma)

APPLICATION 3: DRUG ELUTING STENTS

A Multi-Domain/Multi-Phase Problem

$$\frac{\partial c}{\partial t} = D\Delta c + \mathbf{u}\nabla c$$

Macroscale, mm (in the arterial wall)

Macroscale, µm (in the coating matrix)

$$\frac{\partial C_L}{\partial t} = \underbrace{\frac{1}{r^2}\frac{\partial}{\partial r}\left(D \cdot r^2 \cdot \frac{\partial C_L}{\partial r}\right)}_{\text{Diffusion}} + \underbrace{C_{Se} \cdot K_{Lero}}_{\text{Erosion}} + \underbrace{\frac{\partial C_{Se}}{\partial t}(1 - K_{Lero} \cdot t)}_{\text{Dissolution}}$$

LIQUID PHASE

$$\frac{\partial C_S}{\partial t} = -\frac{\partial C_{Se}}{\partial t}(1 - K_{Lero} \cdot t) - C_{Se} \cdot K_{Lero}$$

VIRTUAL SOLID PHASE (free interface)

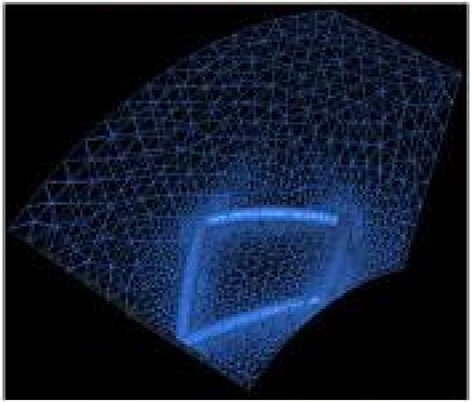
$$\frac{\partial C_{Se}}{\partial t} = -K_{dis}(\epsilon C_{sat} - C_L)$$

EFFECTIVE SOLID PHASE (dynamics of polymer concentration)

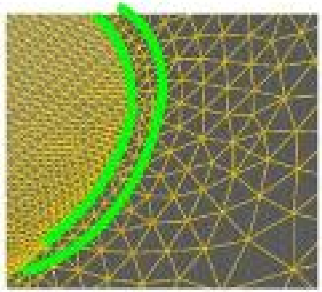
K_{dis}, K_{Lero}, D **Depend on polymer characteristics (porosity, tortuosity,...)**
Determined by stochastic models

APPLICATION 3: DRUG ELUTING STENTS

Numerical strategy

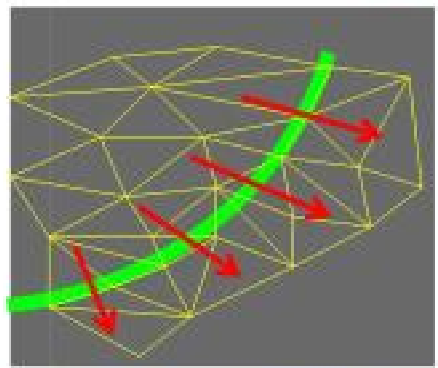


Grid around the stent



Coating as a 3D domain

Don't consider the coating as a 3D domain, rather approximate the transient flux at the interface to the arterial wall

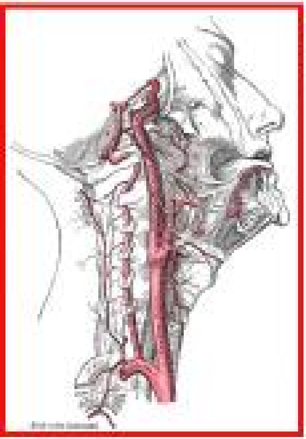


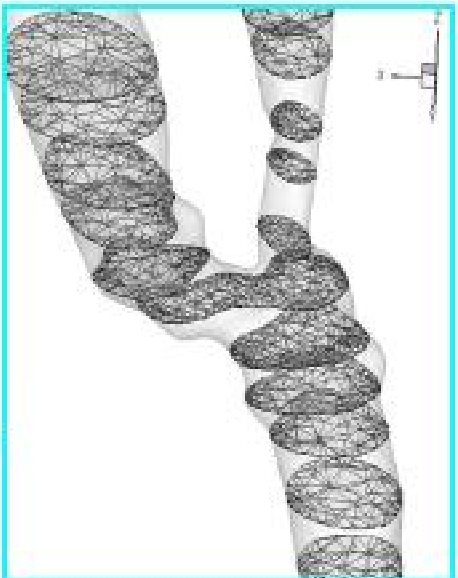
	in stent coating	in the wall
#Elements	965.081	1.018.475

(many more for realistic geometries)

Volume-grid generation

A good surface mesh is a key factor for the generation of a 3D volume grid for the numerical simulation of blood flow



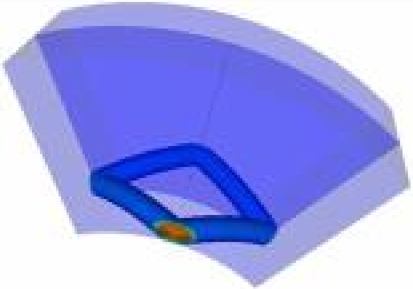


QuickTime™ and a Cinepak decompressor are needed to see this picture.

(A.Veneziani)

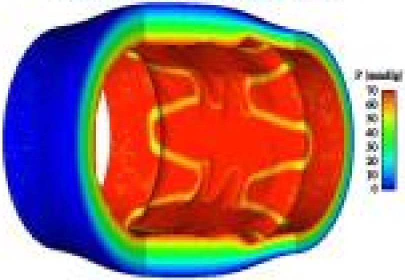
APPLICATION 3: DRUG ELUTING STENTS

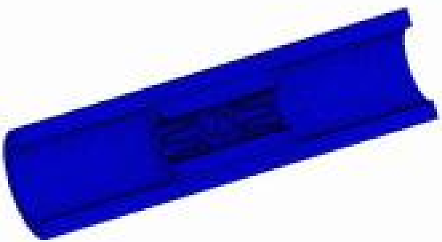
Heparin release from stent coating



Concentration around a simplified geometry
Effective time: 1 day (uniform coating)

Blood plasma pressure distribution for a realistic model (deployed stent)





Simulation of stent expansion and drug release

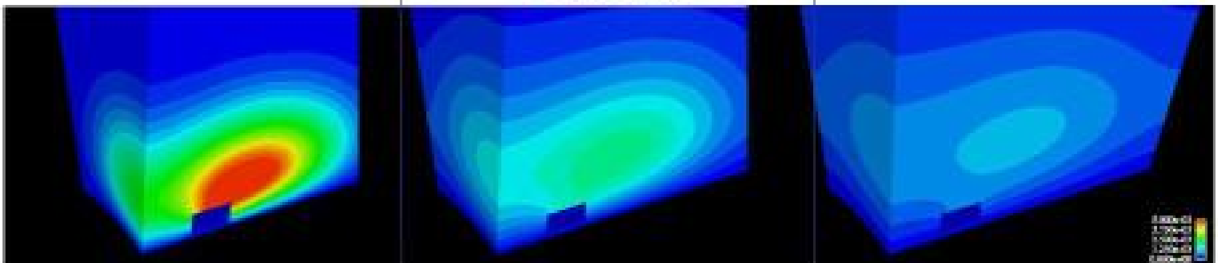
(M.Prosi)

APPLICATION 3: DRUG ELUTING STENTS

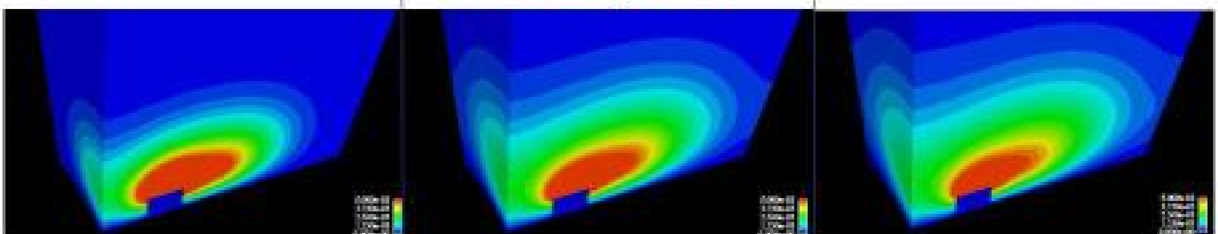
Uniform vs multilayered coating: release dynamics

1 day | 2 days | 3 days

Uniform



Multi-layered



(M.Prosi)

CONCLUSIONS/OUTCOME

Better understanding of physiological processes (basic research)

Assessment of risk indicators for pathological uprises (clinical diagnosys)

Tool for therapeutic/surgical planning (optimization)

NEW MATHEMATICAL DEVELOPMENTS

ACKNOWLEDGMENTS

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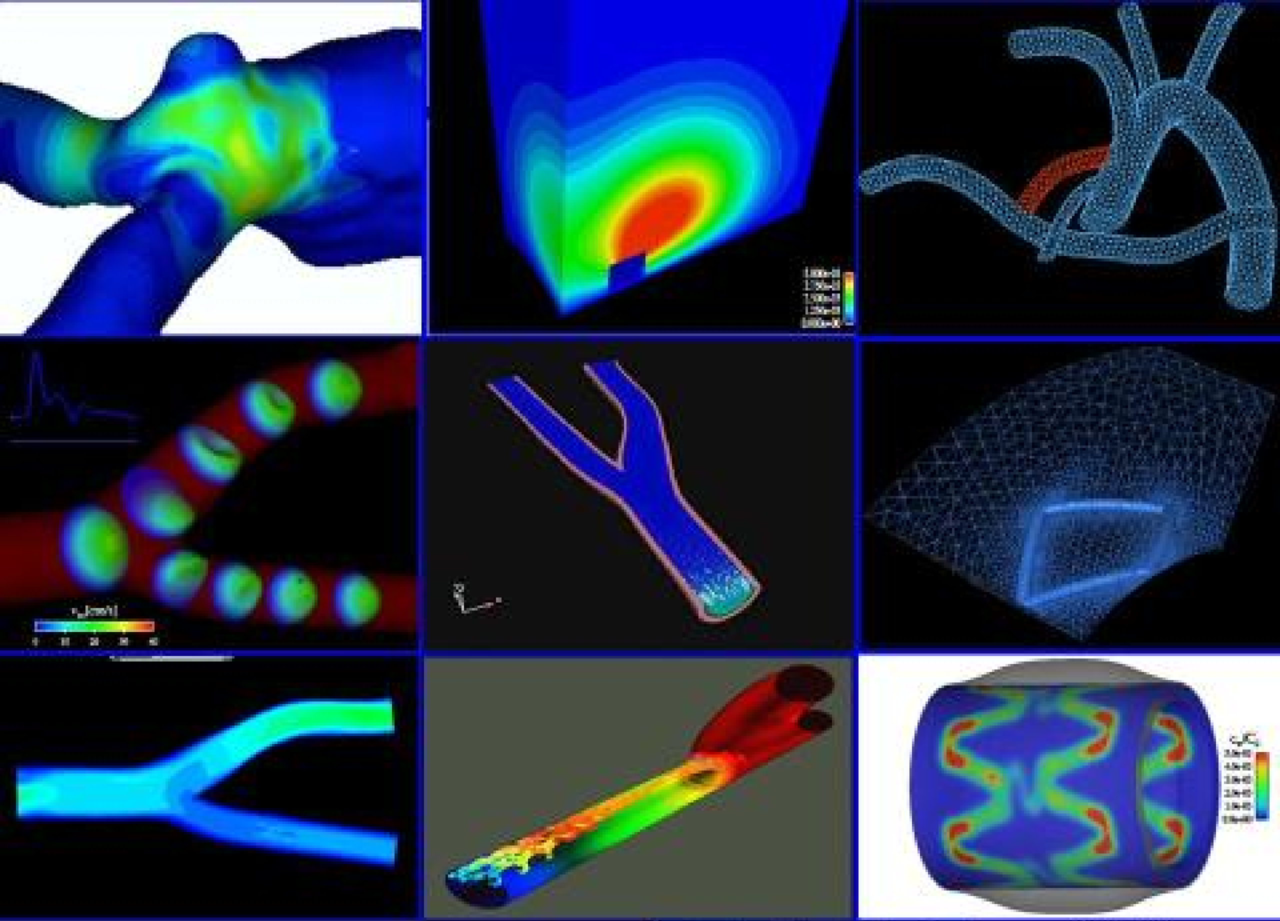
MOX

C.D'Angelo,G. Fourestey, C.Vergara

EPFL

CHUV University Hospital (Lausanne), Great Hormond Street Hospital (London), Niguarda Hospital (Milan), Haemodel EU Project, Siemens (Milan), Laboratory of Biological Structures (Politecnico of Milan)

External Collaborations



MATHEMATICAL MODEL

Mathematical Model

- Identification of patient's parameters
  (blood viscosity, density, properties of arterial walls)
- Set-up of PDEs model
  (well-posedness analysis)
- Set-up of numerical methods
  (stable, efficient and accurate)
- Computer simulation
- Control and optimization

MATHEMATICAL MODEL

1. Local analysis

2. Fluid-structure interaction

3. Geometric multiscale

4. A global scenario