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Modeling and Complexity Reduction in PDES for Multiphysics Modeling the Circulatory System

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### The Context

# I. From clinical imaging to computational grid

# 2. Mathematical Modeling

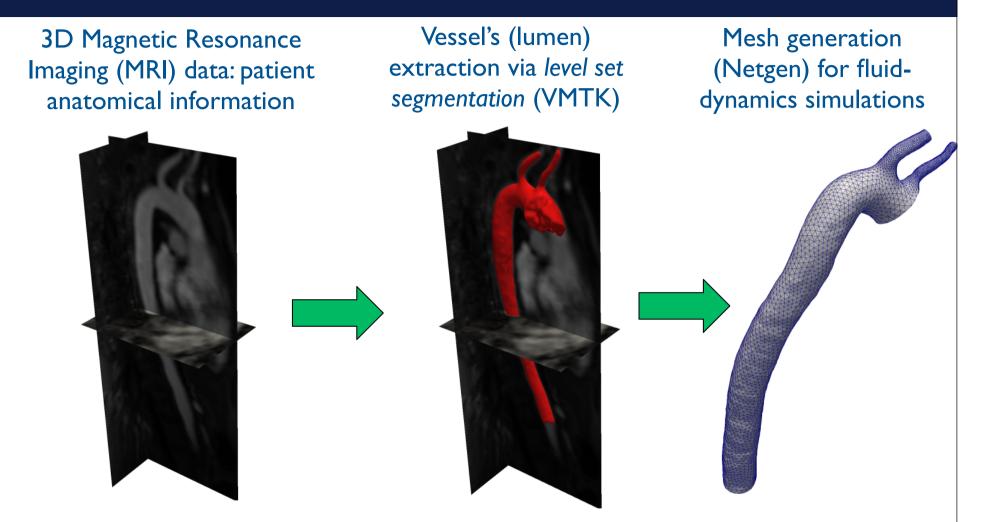
### 3. Computing

# 4. Verification Validation

### 5. Clinical Applications

# From Images to Grid

### Image Processing and Volume Reconstruction



This "snapshot" has been obtained as an average over the cardiac cycle that could be considered as the diastolic configuration

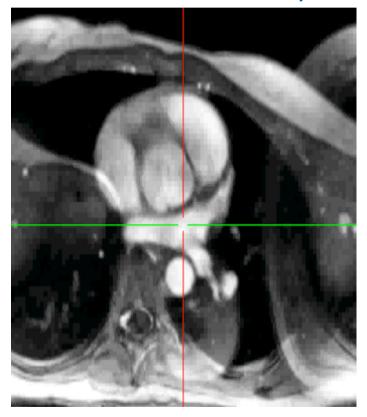
Aortic arch (courtesy of MD Luciani and MD Puppini, Ospedale Borgo Trento, Verona, Italy) (E.Faggiano, G.B.Luciani, G.Puppini, C.Vergara, 2010)

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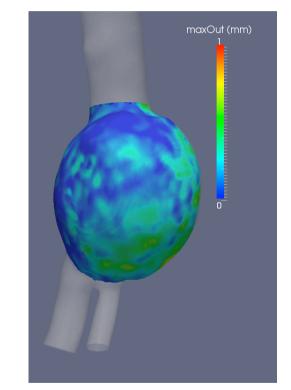
### Image Processing (cont'd) 4D Displacement Data

### **AAA - Aneurysm in the Abdominal Aorta**

4D MRI data: anatomical information of the patient at 10-20 instants over the cardiac cycle



Vessel segmentation and surface registration → displacement analysis (VMTK)



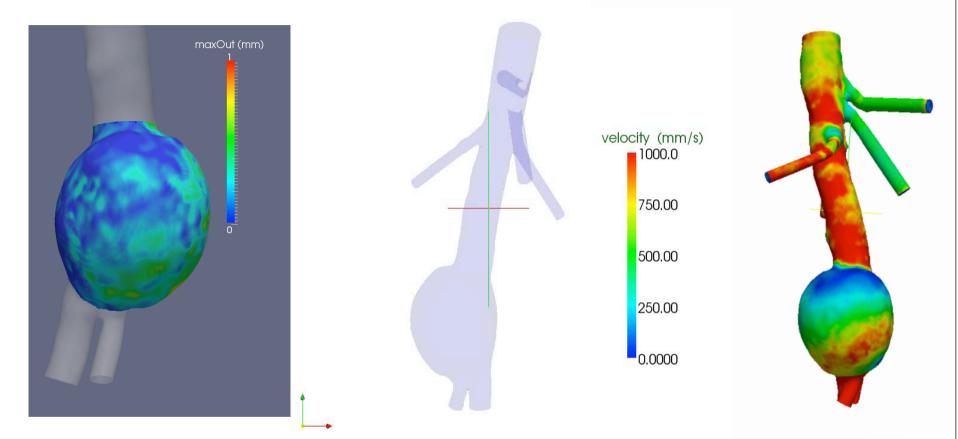
Normalized maximum (in time) displacement with respect to the diastolic configuration

Aortic arch, courtesy of MD M. Domanin, Policlinico di Milano, Italy

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### Image Processing (cont'd) 4D Displacement Data

### **AAA - Aneurysm in the Abdominal Aorta**



Normalized maximum (in time) displacement with respect to the diastolic configuration

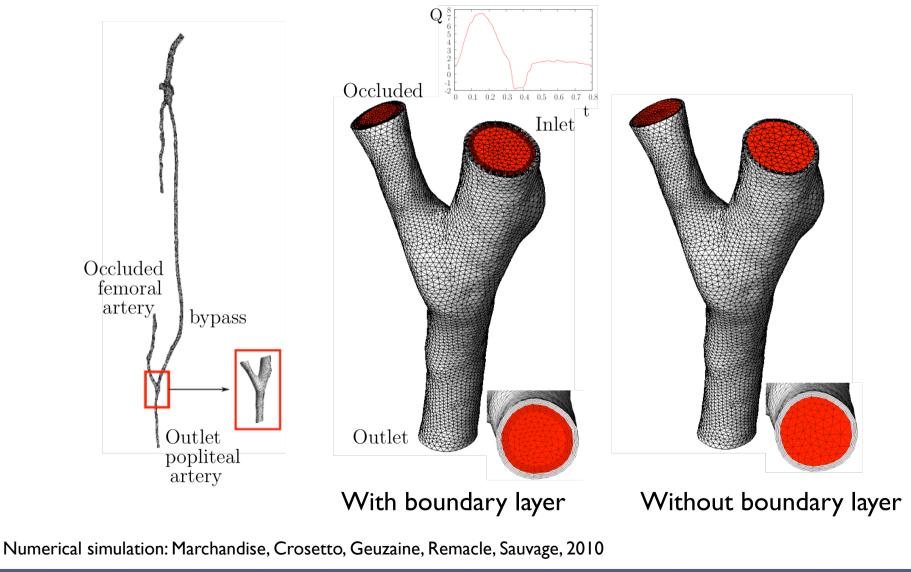
Numerical simulation (LIFEV): blood velocity pattern and WESS (Courtesy: M.Piccinelli and C.Vergara)

The zone of highest jet's incidence is the one of maximum displacement on the figure on the left

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### Importance of grid quality: FSI simulation in a femoral bypass

### Patient-specific geometry and boundary conditions



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### FSI in a femoral bypass

### Influence of boundary layer grid on wall shear stress (WSS)

Three different grids, meshes with and without BL

Boundary layer grids

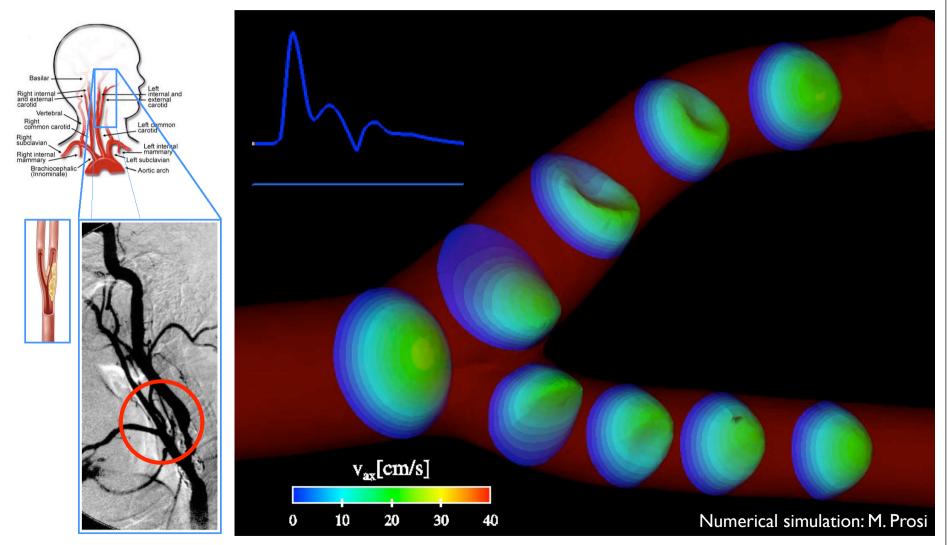
Grids without boundary layer WSS (dyn/cm^2) 10

All three meshes without boundary layer (lower) fail to capture the correct WSS. Fluid meshes ranging from 9,000 to 213,000 nodes

# Modeling

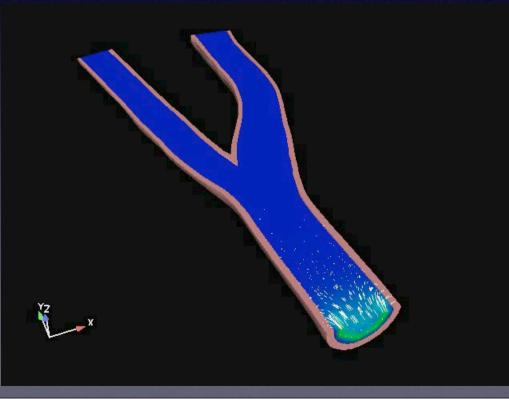
### Local flow analysis - Incompressible Newtonian Flow

- Navier-Stokes equations in carotid artery with rigid walls
- Pulsatile inflow defective b.c at outflow



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### Modeling: Vessel Compliance



### Abstract setting - FSI: the ALE frame of reference

$$\Omega_{f,0}$$
  $\mathcal{A}_t$   $\Omega_f(t)$ 

### • ALE mapping

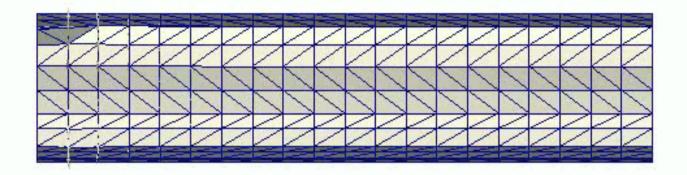
The computational domain  $\Omega$  in the Eulerian formulation. It is a fixed portion of space filled by the medium during its motion

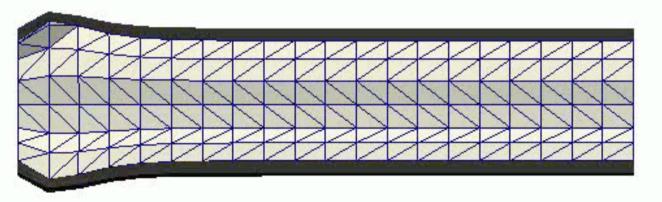
### ALE derivative

$$\left. \frac{\partial q}{\partial t} \right|_{\widetilde{\mathcal{A}}} = \mathbf{w} \cdot \nabla q + \frac{\partial q}{\partial t}$$

### The moving grid and the ALE velocity

### A coupled fluid-structure problem







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Let  $\widetilde{\omega}_0 \subset \widetilde{\omega}$  be a subdomain in the ALE reference configuration and  $\omega_0(t) = \widetilde{\mathcal{A}}(\widetilde{\omega}_0, t) \subset \omega(t)$  it image by the ALE map. Then for any continuously differentiable field:

$$\frac{\mathrm{d}}{\mathrm{d}\,t} \int_{\omega_0(t)} f \,\mathrm{d}\mathbf{x} = \int_{\omega_0(t)} \left( \frac{\partial f}{\partial t} \bigg|_{\widetilde{\mathcal{A}}} + f \,\mathrm{div}\,\boldsymbol{w} \right) \mathrm{d}\mathbf{x}$$
$$= \int_{\omega_0(t)} \left( \frac{\partial f}{\partial t} + \mathrm{div}\,(f\boldsymbol{w}) \right) \mathrm{d}\mathbf{x}$$

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### Blood flow FSI - The equations

### A coupled fluid-structure problem

Equations for the geometry:

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

Equations for the fluid:

$$\frac{\rho_{f}}{J_{\hat{\mathcal{A}}}} \frac{\partial J_{\hat{\mathcal{A}}} \mathbf{u}_{f}}{\partial t}_{|_{\hat{\mathbf{x}}}} + \operatorname{div}(\rho_{f} \mathbf{u}_{f} \otimes (\mathbf{u}_{f} - \mathbf{w}) - \sigma_{f}(\mathbf{u}_{f}, P)) = 0, \text{ in } \Omega_{f}(t)$$

$$\operatorname{div} \mathbf{u}_{f} = 0, \text{ in } \Omega_{f}(t)$$

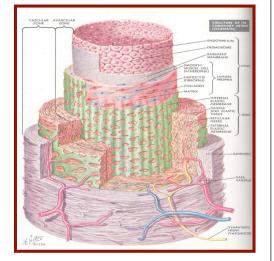
$$\mathbf{u}_{f} = \mathbf{u}_{D}, \text{ on } \Gamma_{f,D}$$

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

$$\mathbf{u}_{f} = \mathbf{w}, \text{ on } \Gamma(t)$$

Equations for the structure:

$$\begin{split} \widehat{\rho}_{s,0} \frac{\partial^2 \widehat{\eta}_s}{\partial t^2} - \operatorname{div}_{\widehat{\mathbf{x}}}(\widehat{\mathbf{F}}_s \widehat{\boldsymbol{\Sigma}}) &= 0, & \text{in } \widehat{\Omega}_s \\ \widehat{\eta}_s &= 0 & \text{on } \widehat{\Gamma}_{s,D} \\ \widehat{\mathbf{F}}_s \widehat{\boldsymbol{\Sigma}} \widehat{\mathbf{n}}_s &= \widehat{J}_s |\widehat{\mathbf{F}}_s^{-T} \widehat{\mathbf{n}}_s| \widehat{\mathbf{g}}_{s,N}, & \text{on } \widehat{\Gamma}_{s,N} \\ \widehat{\mathbf{F}}_s \widehat{\boldsymbol{\Sigma}} \widehat{\mathbf{n}}_s &= \widehat{J}_s \widehat{\sigma}_f(\mathbf{u}_f, P) \widehat{\mathbf{F}}_s^{-T} \widehat{\mathbf{n}}_s, & \text{on } \widehat{\Gamma} \end{split}$$



### Surface registration

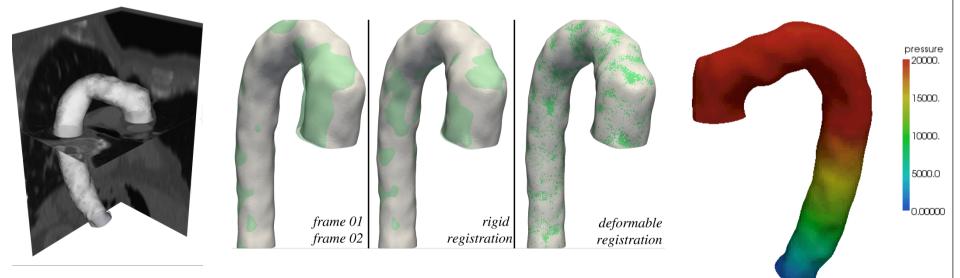
### Surface registration:

find the alignment of the surfaces of two consecutive time frames

• construction of a **displacement field**  $\eta_{meas}$  which maps the surface points

Surface registration could be used to solve a FSI problem without solving the structure:

Solve the ALE fluid problem in a moving domain with known boundary



Acknowledgement: A. Veneziani, M. Piccinelli, L. Mirabella, T. Passerini

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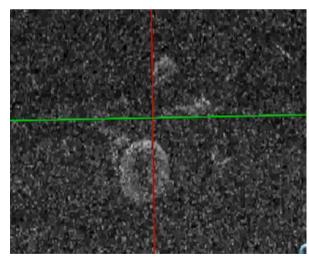
### (Variational) data assimilation

# I) Based on surface registration Example: determine the rigidity of a vessel Find the minimum of c

$$\mathcal{J} = \int\limits_{\Sigma} \left( oldsymbol{\eta}_{meas}(oldsymbol{x}, au_k) - oldsymbol{\eta}(oldsymbol{x}, au_k) 
ight)^2 d\sigma.$$

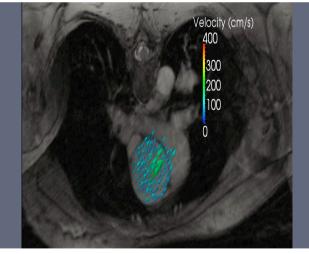
under the constraint given by the **FSI** problem

### II) Based on volumetric data



4D Phase-contrast MRI data: blood velocity at specific slices at 10-20 instants over the cardiac cycle

> Velocity vectors extraction



(M.Perego, A.Veneziani, C.Vergara, A variational approach for estimating the compliance of the cardiovascular tissue, SIAM J Sci Comp, 2011)

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### Computing -Complexity

## Geometric Multiscaling

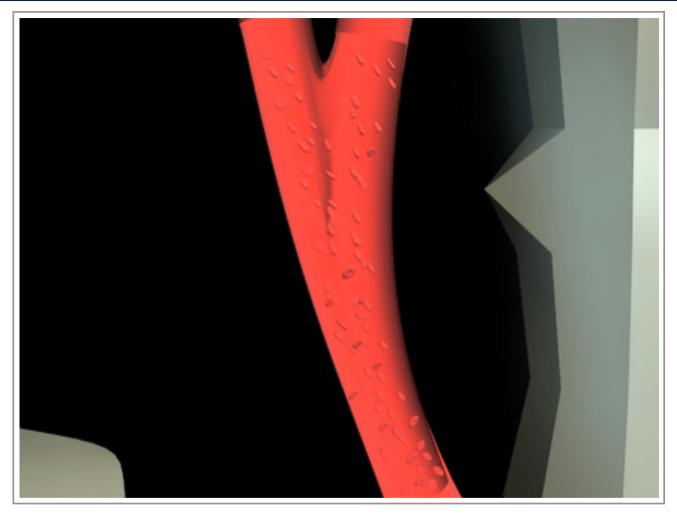
### Global Flow Analysis: System's Complexity

Morphological complexity: the diameter of blood vessels ranges from 10<sup>-2</sup> m down to 10<sup>-6</sup> m. Consequently, the flow regime varies considerably.

Vessel	Radius(cm)	Number	Reynolds number
Aorta	1.25	1	3400
<u>Arteries</u>	0.2	159	55
Arterioles	1.5 x 10 <sup>-3</sup>	5.7 x 10 <sup>7</sup>	0.7
<u>Capillaries</u>	3 x 10 <sup>-4</sup>	<b>1.6 x 10</b> <sup>10</sup>	0.002
Venules	1 x 10 <sup>-3</sup>	1.3 x 10 <sup>9</sup>	0.01
<u>Veins</u>	0.25	200	140
Vena cava	1.5	1	3300

• **Functional complexity**: the cardiovascular system is able to react to changes in the external environment and presents several 'non-linear' components (e.g. valves). We need to account for the local/systemic interactions.

### Geometric multiscaling in the circulatory system

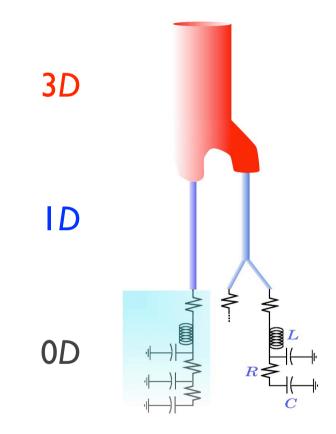


Local: 3D FSI flow model

Global: ID network of arteries and veins (Euler hyperbolic system) Global: 0D capillary network (DAE system)

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### Geometric multiscaling in the circulatory system



3D Navier-Stokes (F) + 3D ElastoDynamics (V-W) ID Euler (F) + Algebraic pressure law 0D lumped parameters

(system of linear ODEs)

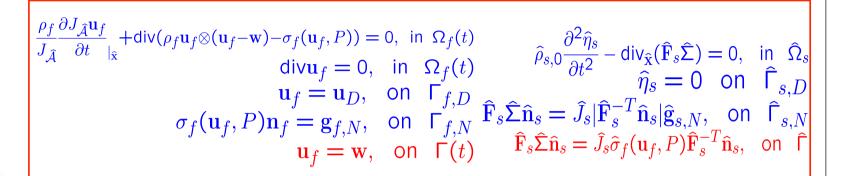
(L. Formaggia, A.Q, A. Veneziani: Cardiovascular Mathematics, Springer, 2009)

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### Mathematical Model

3D

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



Assume to:

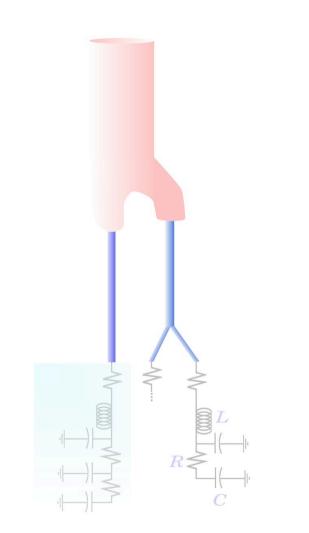
- $u_z >> u_x, u_y$
- $u_z$  has a prescribed steady profile
- average over axial sections
- static equilibrium for the vessel

Then we obtain a ID problem

### Mathematical Model

ID

### ID Euler(F) + Algebraic pressure law



$$\partial_t A + \partial_x Q = 0,$$
  

$$\partial_t Q + \partial_x \left(\frac{\alpha Q}{A}\right) + \frac{A}{\rho} \partial_x P = -K_r \frac{Q}{A},$$
  

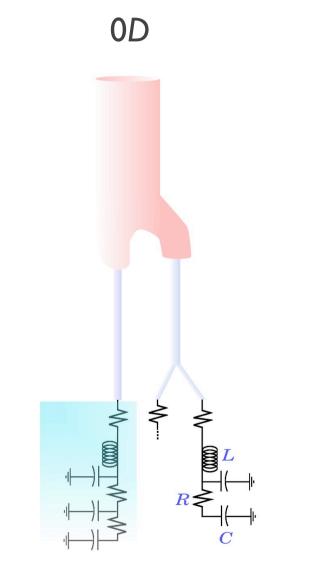
$$P(A) = \beta \frac{\sqrt{(A) - \sqrt{(A_0)}}}{A_0}$$

### Assume to:

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

Then we obtain a 0D problem (ODE)

### Mathematical Model



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

$$C\frac{dP_i}{dt} = -(Q_{i+1} - Q_i),$$
$$L\frac{dQ_i}{dt} = -(P_i - P_{i-1}) - RQ_i$$

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)

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### The ID Network

At a bifurcation we prescribe

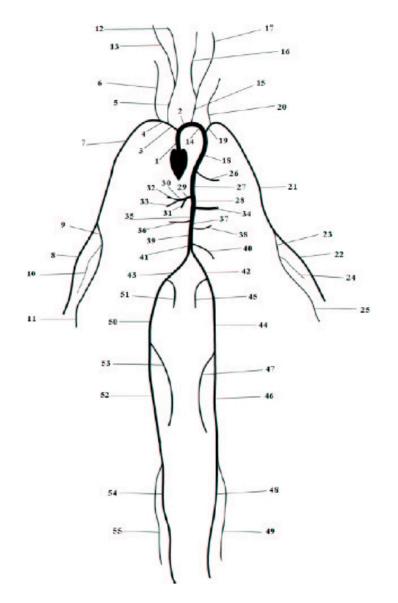
- ✓ Continuity of total pressure:  $p_{t,l} = p_{t,2} = p_{t,3}$
- ✓ Conservation of mass:  $\Sigma_i Q_i = 0$

### Mathematical Analysis

The coupled problem satisfies a stability estimate similar to that of the single artery model. No shock waves developing, explicit form of characteristic variables available

In principle, it is possible to account for curvature, tapering, and for the bifurcation angle through an energy loss term.

In practice, this has a minor impact on numerical results

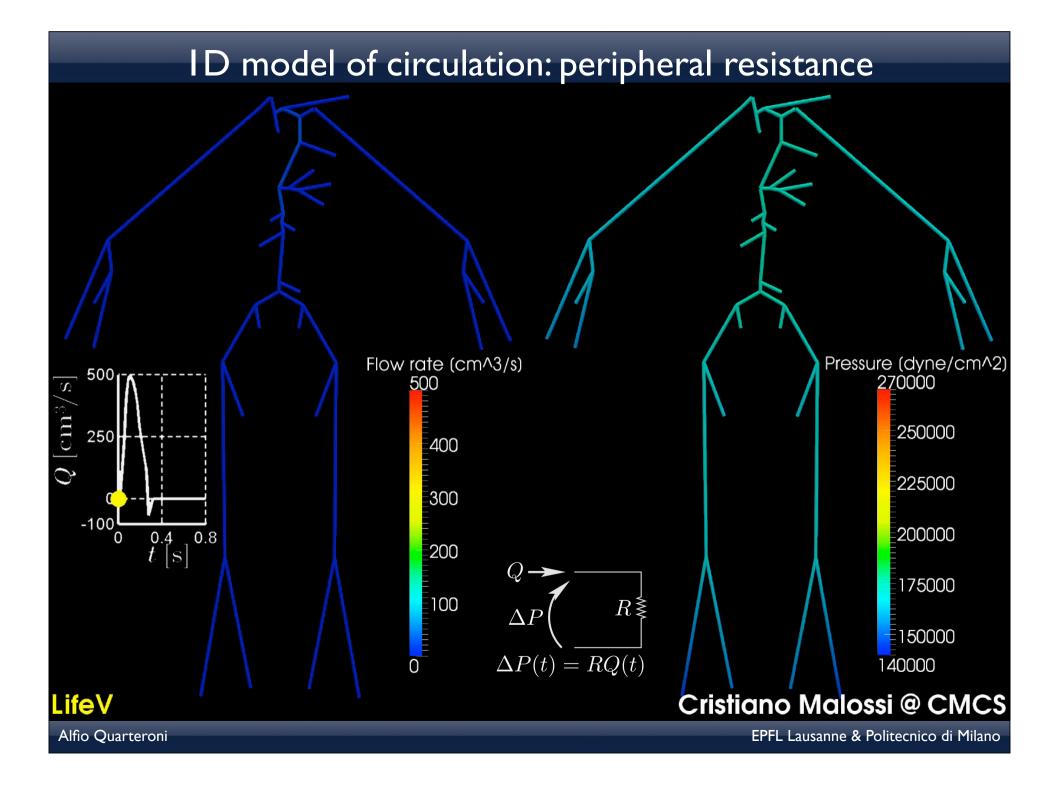


Peripheral branches: Absorbing b.c Colormap: A/A<sub>0</sub>-I

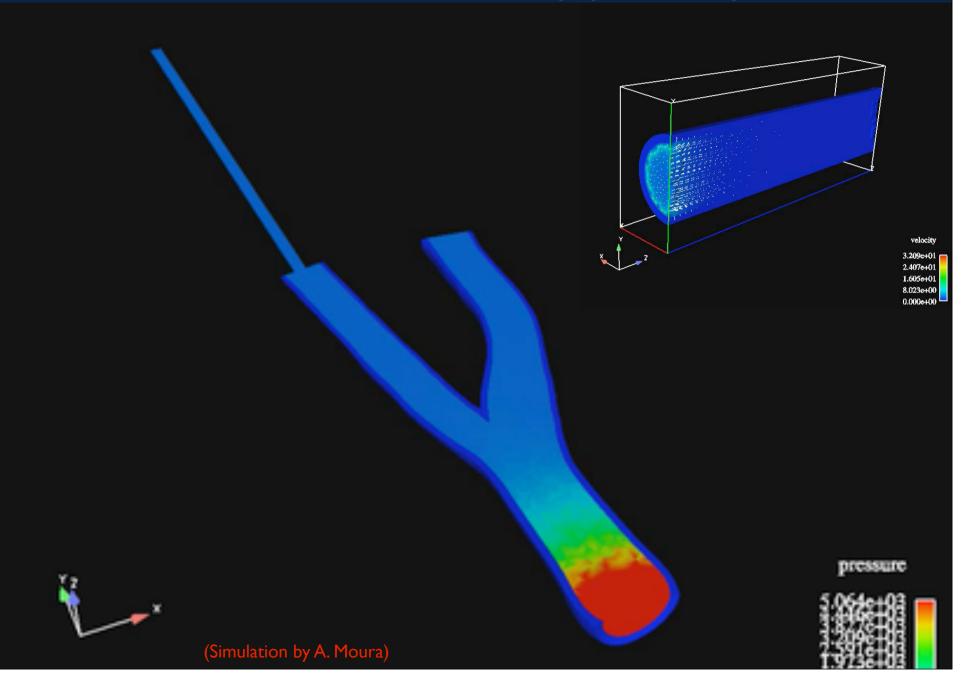
### **LifeV**

Cristiano Malossi @ CMCSLifeV Cristiano Malossi @ CMCS

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### 3D-ID for the carotid artery: pressure pulse



### **Geometric Multiscale - an Instance**

LifeV

Malossi - Crosetto @ CMCS

### **Models:**

- 3-D FSI Aorta & Iliac Artery
- I-D arterial tree
  92 tapered elements
  - viscoelastic wall
- 0-D terminals
   47 Windkessel elements (RCR)

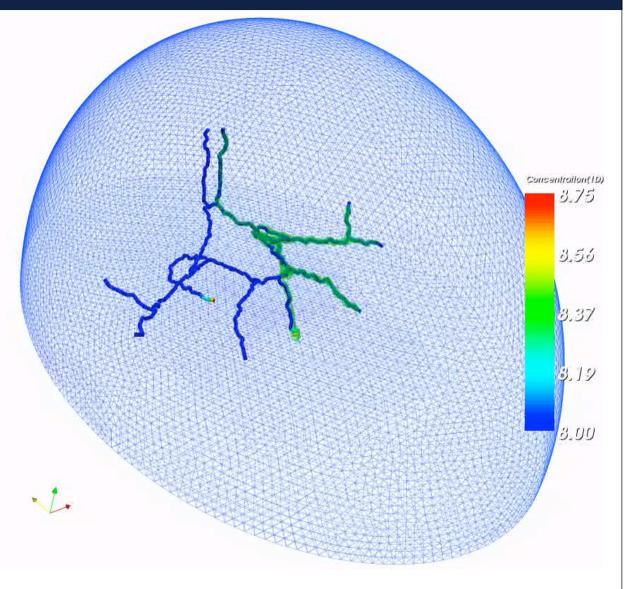
### **Coupling:**

- averaged/integrated quantities at the interfaces (flow rate or normal stress)
- segregated approach for the solution of the coupled problem (Newton, inexact-Newton, or Broyden methods)

### Imbedded ID-3D



Application to oxygen transport in the brain: isosurface of oxygen concentration. Impairment due to left carotid artery occlusion.

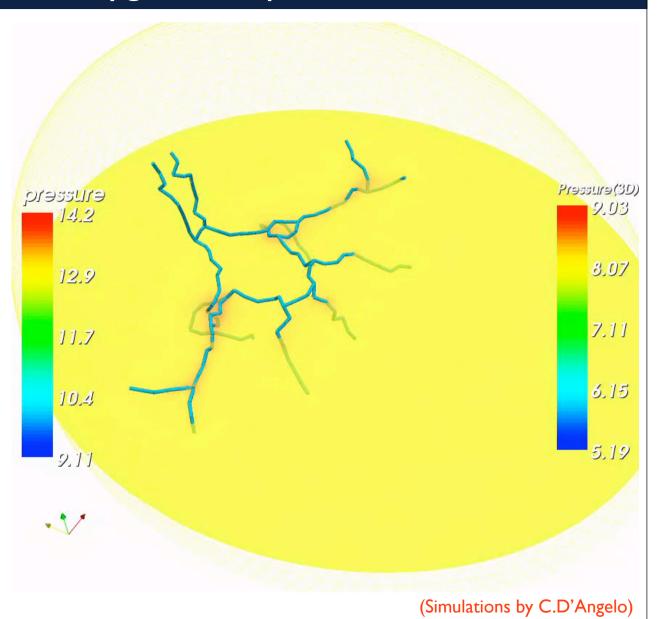


(Simulations by C. D'Angelo)

### Blood Flow and Oxygen Transport in the Brain



ID (vessels) and 3D (brain tissue) blood pressures with pulsatile input blood flow rate and left carotid artery occlusion



### **ID-3D** Perfusion Model

A realistic time-dependent ID-3D model:

$$\begin{pmatrix} C_{t} \frac{\partial}{\partial t} p_{t} + \nabla \cdot (K_{t} \nabla p_{t}) + \alpha p_{t} - \phi(p_{t}, p_{v}) \delta_{\Lambda} = 0 \ t > 0, \ x \in \Omega, \\ \frac{\partial}{\partial t} \begin{bmatrix} p_{v} \\ q_{v} \end{bmatrix} + \begin{bmatrix} 0 & \frac{1}{c} \\ \frac{1}{l} & 0 \end{bmatrix} \frac{\partial}{\partial s} \begin{bmatrix} p_{v} \\ q_{v} \end{bmatrix} + \begin{bmatrix} \frac{1}{c} \phi(p_{t}, p_{v}) \\ rq_{v} \end{bmatrix} = 0, \qquad t > 0, s \in \Lambda,$$

 $p_{t}: \Omega \to \mathbb{R} \text{ blood pressure in the tissue (3D)}$   $p_{V}: \Lambda \to \mathbb{R} \text{ blood pressure in the vessel (ID)}$   $q_{V}: \Lambda \to \mathbb{R} \text{ blood flow rate in the vessel (ID)}$   $\phi: \Lambda \to \mathbb{R} \text{ the exchange term}$ 

### **ID-3D** Perfusion Model

### **Flow model**

$$\begin{cases} C_{\mathsf{t}} \frac{\partial}{\partial t} p_{\mathsf{t}} + \nabla \cdot (K_{\mathsf{t}} \nabla p_{\mathsf{t}}) + \alpha p_{\mathsf{t}} - \phi(p_{\mathsf{t}}, p_{\mathsf{v}}) \delta_{\mathsf{\Lambda}} = 0 \ t > 0, \ \mathbf{x} \in \Omega, \\ \frac{\partial}{\partial t} \begin{bmatrix} p_{\mathsf{v}} \\ q_{\mathsf{v}} \end{bmatrix} + \begin{bmatrix} 0 & \frac{1}{c} \\ \frac{1}{l} & 0 \end{bmatrix} \frac{\partial}{\partial s} \begin{bmatrix} p_{\mathsf{v}} \\ q_{\mathsf{v}} \end{bmatrix} + \begin{bmatrix} \frac{1}{c} \phi(p_{\mathsf{t}}, p_{\mathsf{v}}) \\ r q_{\mathsf{v}} \end{bmatrix} = \mathbf{0}, \qquad t > 0, s \in \mathsf{\Lambda}, \end{cases}$$

Venous transmission coefficients [range: 10<sup>-3</sup> kPa<sup>-1</sup> s<sup>-1</sup>]

Capillary compliance [10<sup>-3</sup> kPa<sup>-1</sup>]

Tissue conductivity [0.05 mm<sup>2</sup> kPa<sup>-1</sup> s<sup>-1</sup>]

Vessel Windkessel parameters

### **ID-3D** Perfusion Model

### **ID-3D** mass transport and diffusion models:

$$\begin{cases} \frac{\partial}{\partial t} u_{t} - D_{t} \Delta u_{t} + v \cdot \nabla u_{t} - \theta(u_{t}, u_{v}) \delta_{\Lambda} = f, \ t > 0, \ x \in \Omega, \\ A_{0} \frac{\partial}{\partial t} u_{v} - A_{0} D_{v} \frac{\partial^{2} u_{v}}{\partial s^{2}} + q_{v} \frac{\partial}{\partial s} u_{v} = 0, \qquad t > 0, s \in \Lambda, \end{cases}$$

$$u_{t} : \Omega \to \mathbb{R} \text{ mass concentration in the tissue (3D)}$$

$$u_{v} : \Lambda \to \mathbb{R} \text{ mass concentration in the vessel (1D)}$$

$$\theta = \frac{1}{\epsilon} (u_{v} - \overline{u}_{t}) \text{ is a penalization term.}$$

$$- \text{ Same form as } \phi$$

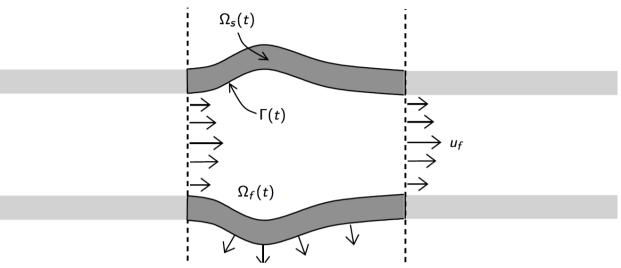
$$- \text{ Enforces} \qquad u_{v} = \overline{u}_{t}$$

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Computing -Complexity

FSI algorithms

### The Coupled FS system in compact form



### • FS system

With variables  $(u_f, d_f, d_s)$  for the fluid solution and displacements of the fluid and structure domain respectively, the fluid-structure interaction problem is

$$F(u_f, d_s, d_f) = 0,$$
  

$$S(u_f, d_s) = 0,$$
  

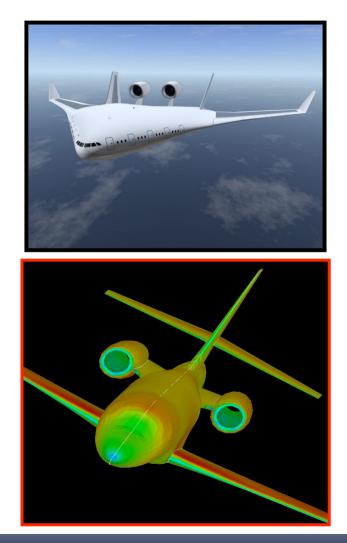
$$G(d_s, d_f) = 0$$

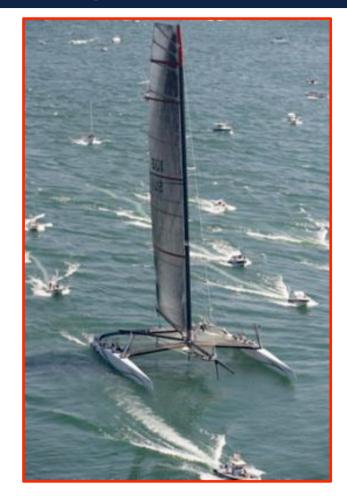
fluid subproblem structure subproblem geometry subproblem.

## Fluid structure Interaction (FSI) - Not only blood flow

#### Aerodynamics

## Aircrafts, Flying Bodies





Wing Multihulls
 Wind-sail interaction

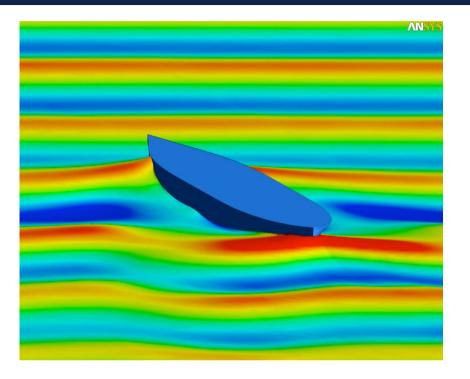
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## Fluid structure Interaction (FSI)

#### **Rowing and sea-keeping**



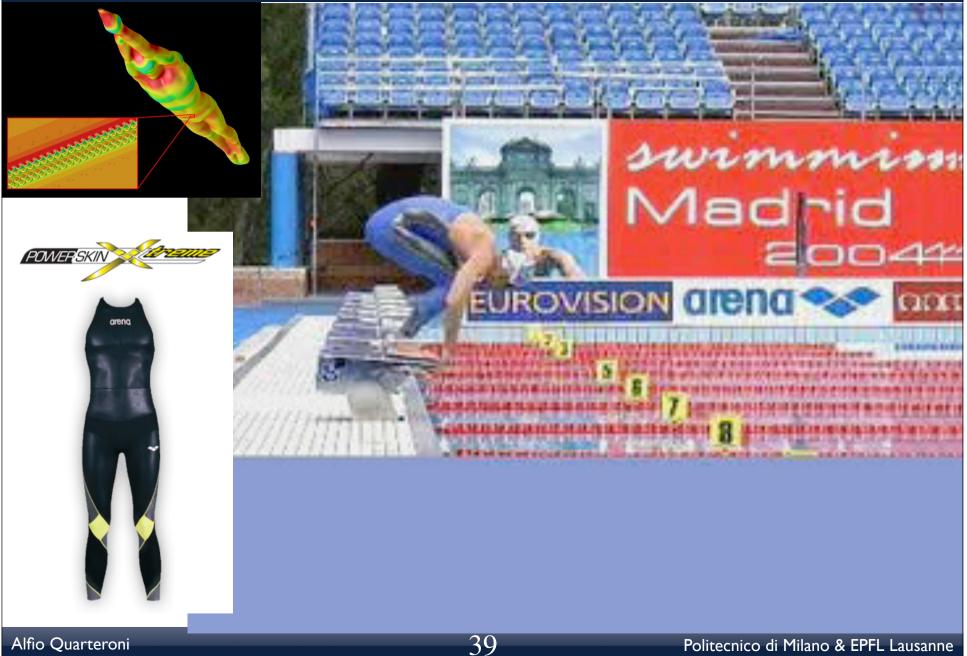






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#### Swinsuits optimization (A.Veneziani, N.Parolini)



## Fluid structure Interaction (FSI)

#### Wind/sails interaction





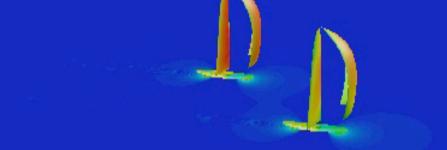
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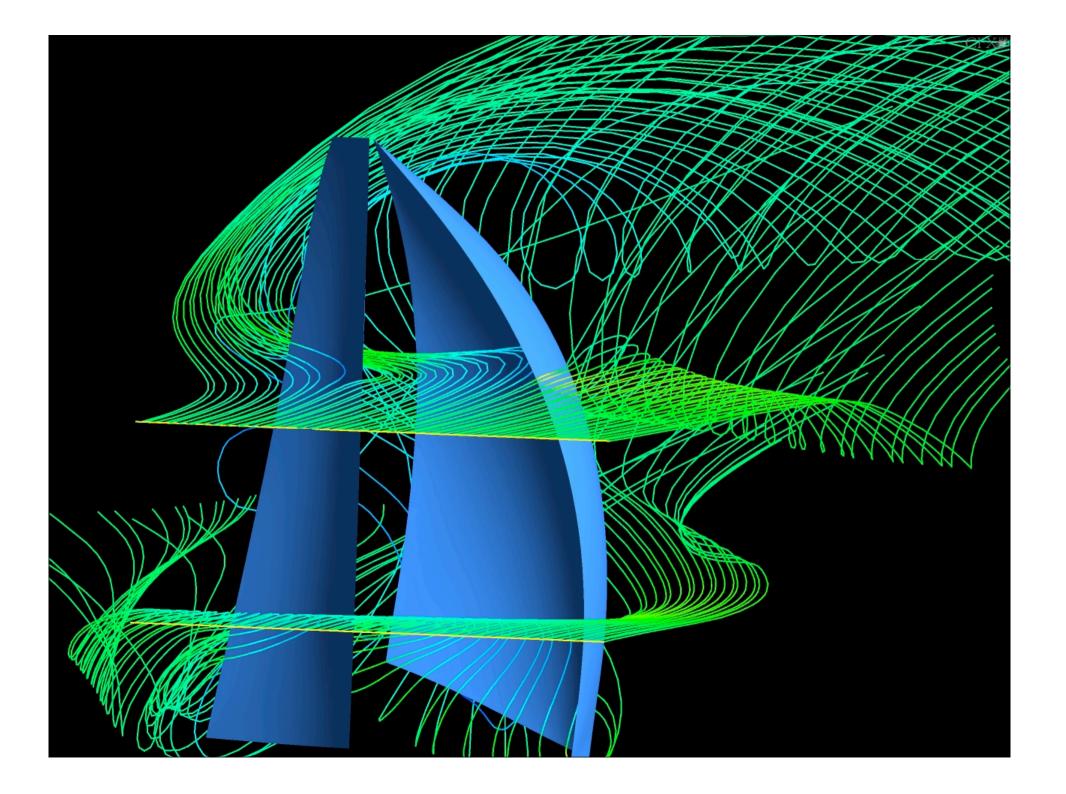


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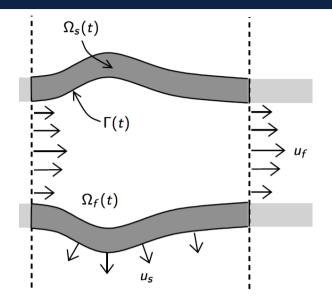
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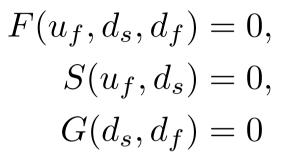






## FSI - Numerical Algorithms





#### Solution approach: FEM in space, FD in time, then:

Segregated / Monolithic / Hybrid

- Newton linearization
- Krylov iterative methods
- Domain Decomposition preconditioners

based on blockwise parallel Schwarz preconditioners

(P.Crosetto, S.Deparis, G.Fourestey, A.Q, Parallel Algorithms for Fluid Structure Interaction Problems in Haemodynamics, SIAM J. Sci. Comp., 2011)

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#### Reduction to the interface problem



#### Goal: eliminate fluid, structure and geometric variables

Let us define The Steklov-Poincaré operators for the fluid and structure subdomains as

$$S_{f}: H^{1/2}(\Gamma)^{3} \rightarrow H^{-1/2}(\Gamma)^{3}$$

$$\lambda = \mathbf{d}_{s\Gamma} \quad \mapsto \quad \boldsymbol{\sigma}_{f}^{o}|_{\Gamma}$$

$$S_{s}: H^{1/2}(\Gamma)^{3} \rightarrow H^{-1/2}(\Gamma)^{3}$$

$$\lambda = \mathbf{d}_{s\Gamma} \quad \mapsto \quad \boldsymbol{\sigma}_{s}|_{\Gamma}$$

$$(17)$$

that map the trace space of displacements on the interface  $\Gamma$  to the dual space of the normal stresses exerted on  $\Gamma$ .

#### **Applications**

# Understanding Physiology

## Subdomain partition for lumen and wall

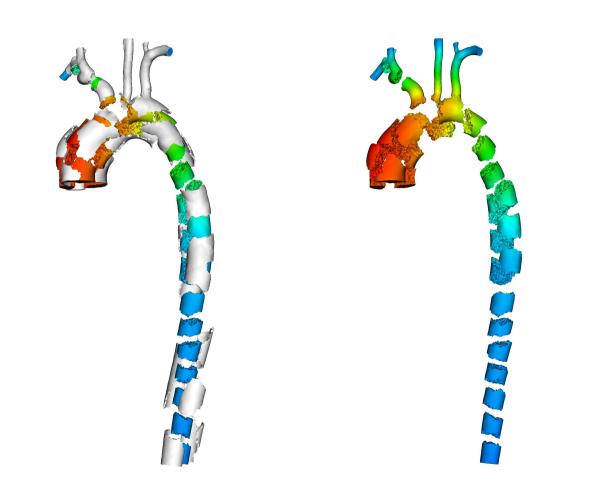
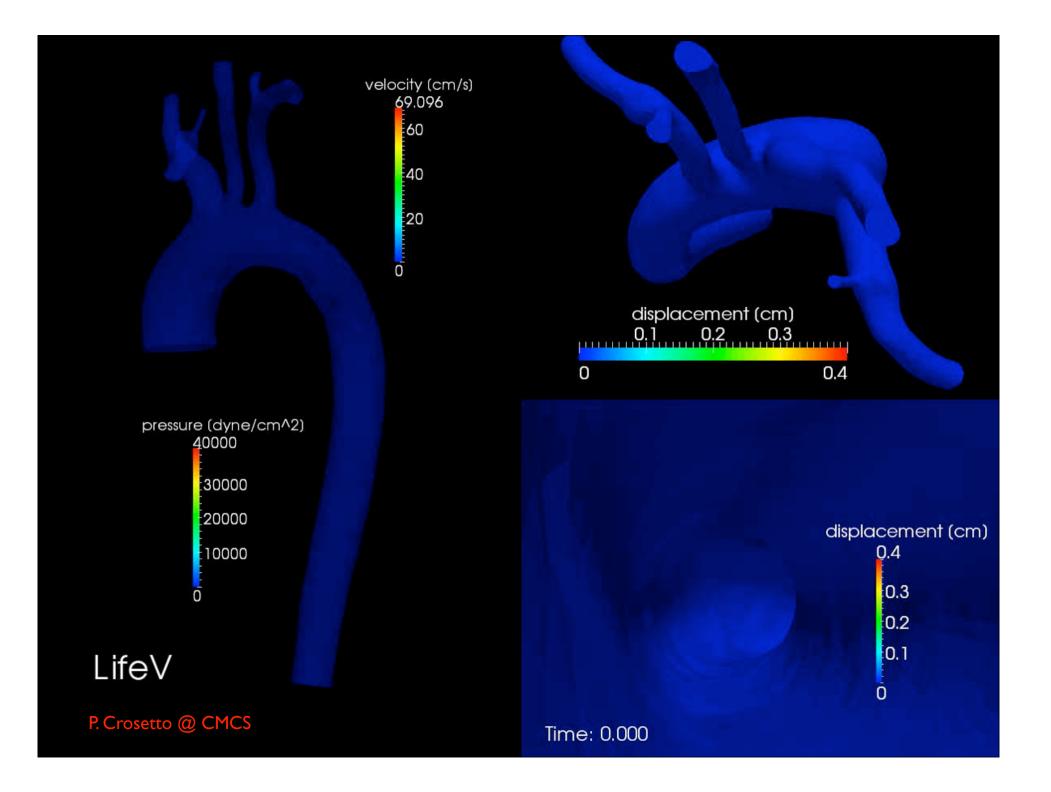


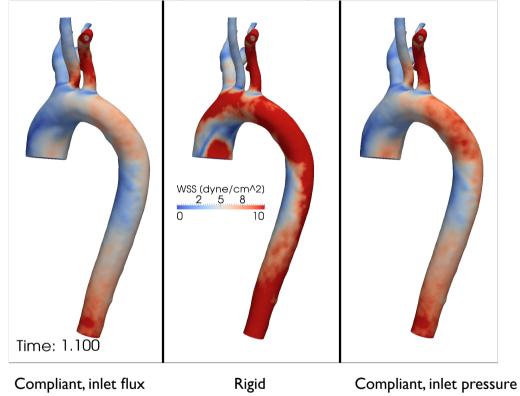
FIGURE: The fluid and the solid meshes are partitioned in  $2\times32$  subdomains. 380'690 tetrahedra and 324'000 dofs



#### FSI in the aortic arch: WSS comparisons

#### **Compliant versus rigid walls: WSS pattern at systole**

The rigid walls simulation (middle) shows important differences in WSS



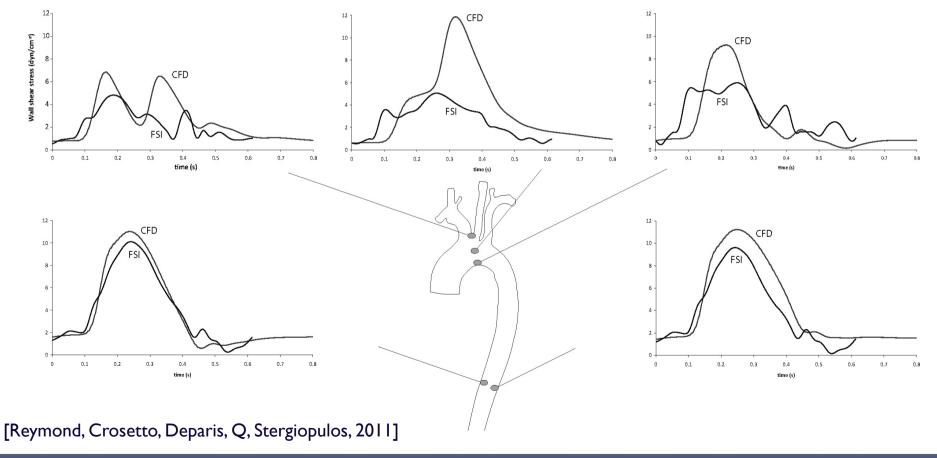
Patient-specific geometry and boundary conditions. Simulation run for 3 heartbeats, timings: about 30s per timestep, 6.6h per heartbeat (800 timesteps), using 128 processors on Cray XT6 cluster HECToR (www.hector.ac.uk)

(Crosetto, Reymond, Deparis, Kontaxakis, Stergiopulos, AQ, submitted, 2011)

## FSI in the aortic arch: WSS comparisons

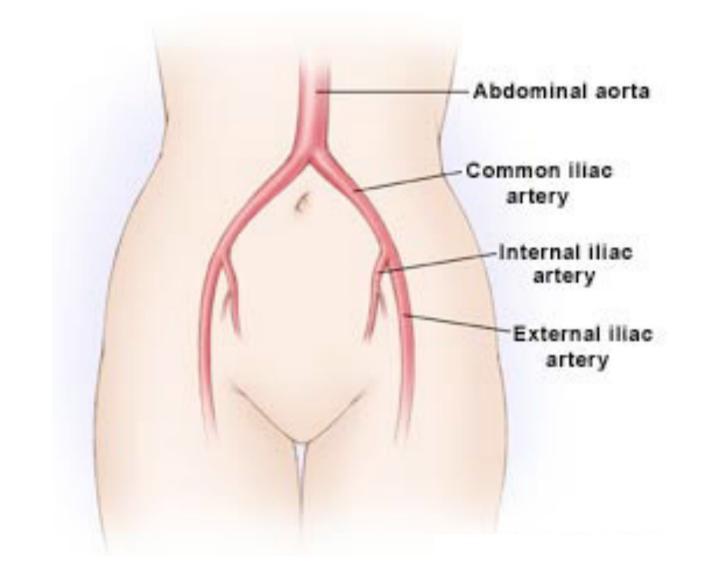
#### **Compliant versus rigid walls:** history of space averages at different locations

WSS mainly overestimated by the rigid wall simulation, differences in magnitude and waveform

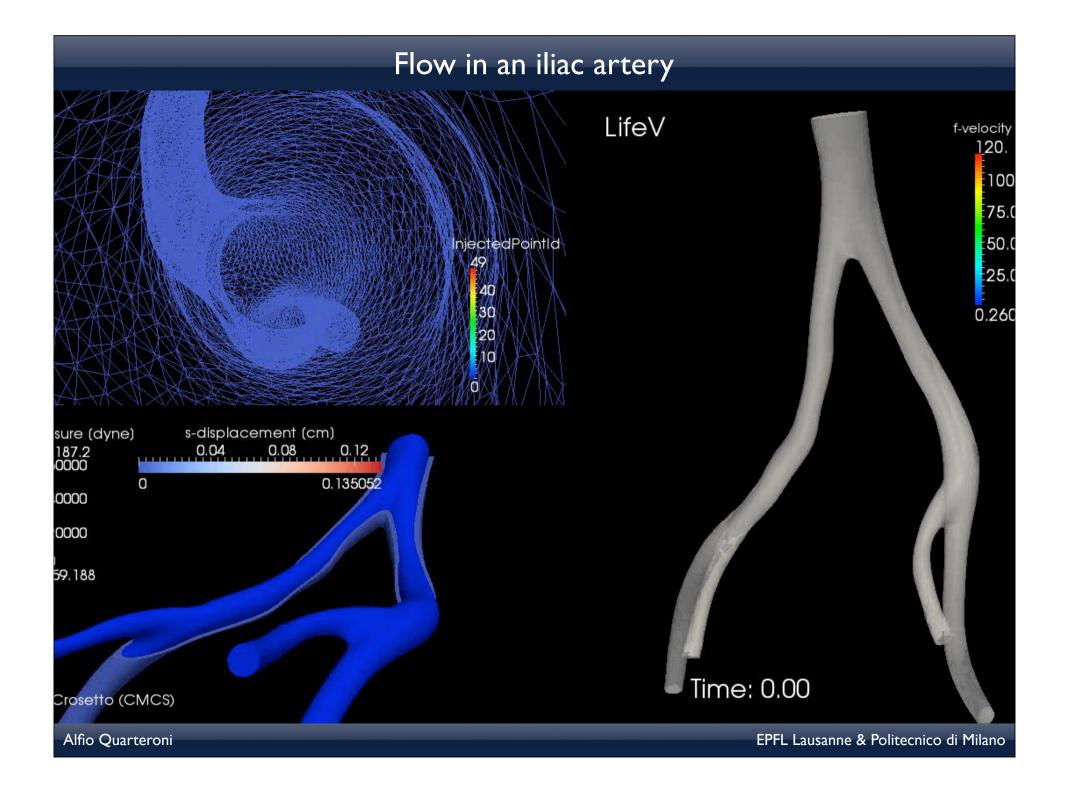


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## Flow in the iliac artery

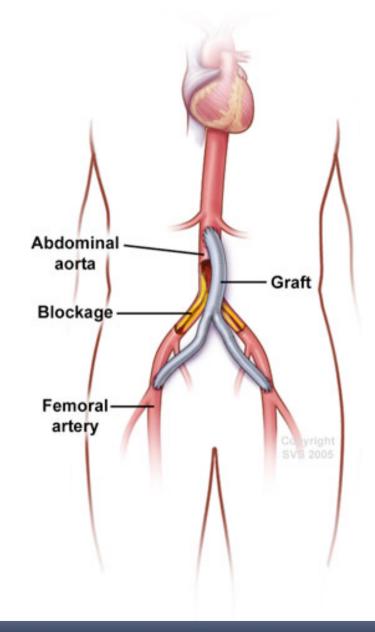


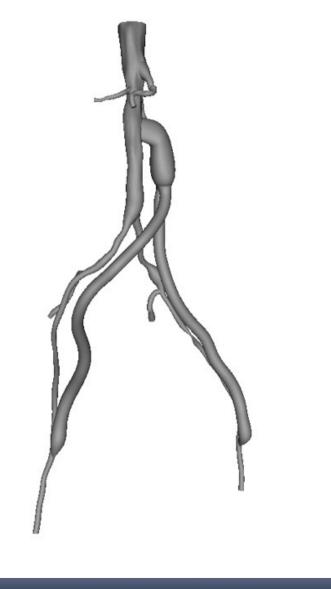
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# Applications Surgical Planning

## Bypass graft in abdominal artery



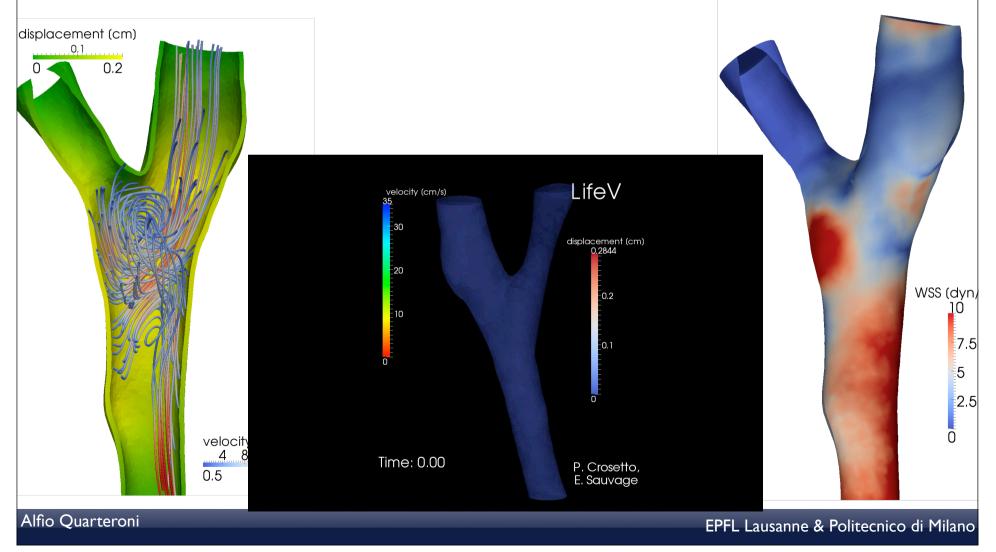


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## FSI in a femoral bypass

#### **WSS and streamlines at systole**

Recirculation zone at the bypass anastomosis (left) produces modification in the WSS pattern (right)



## Flow in Cerebral Aneurysms

Cerebral aneurysms: deformations of cerebral arteries, mostly placed on vessels belonging to or connected to the Circle of Willis.

#### EPIDEMIOLOGICAL STATISTICS

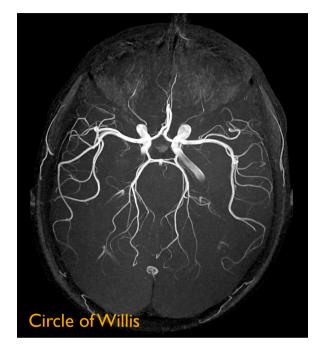
• Incidence rate of cerebral aneurysms:

I/20 people

- Incidence rate of ruptured cerebral aneurysms per year: I/10000 people per year
- Mortality due to a ruptured aneurysm:
  > 50%:

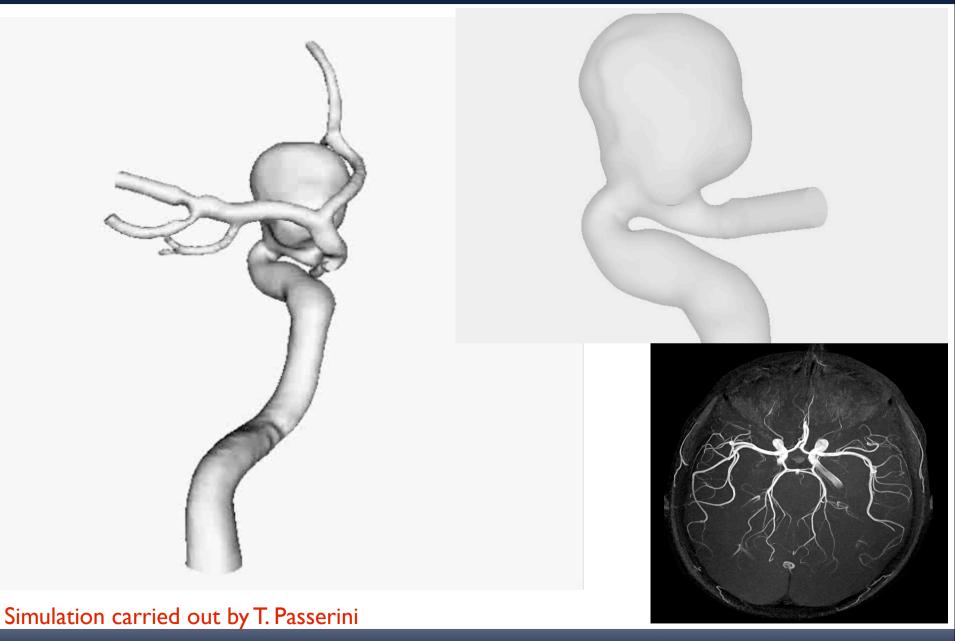
Out of 9 patients with a ruptured aneurysm:

- 3 are expected to die before arriving at the hospital
- 2 to die after having arrived at the hospital
- 2 to survive with permanent cerebral damages
- 2 to survive without permanent cerebral damages



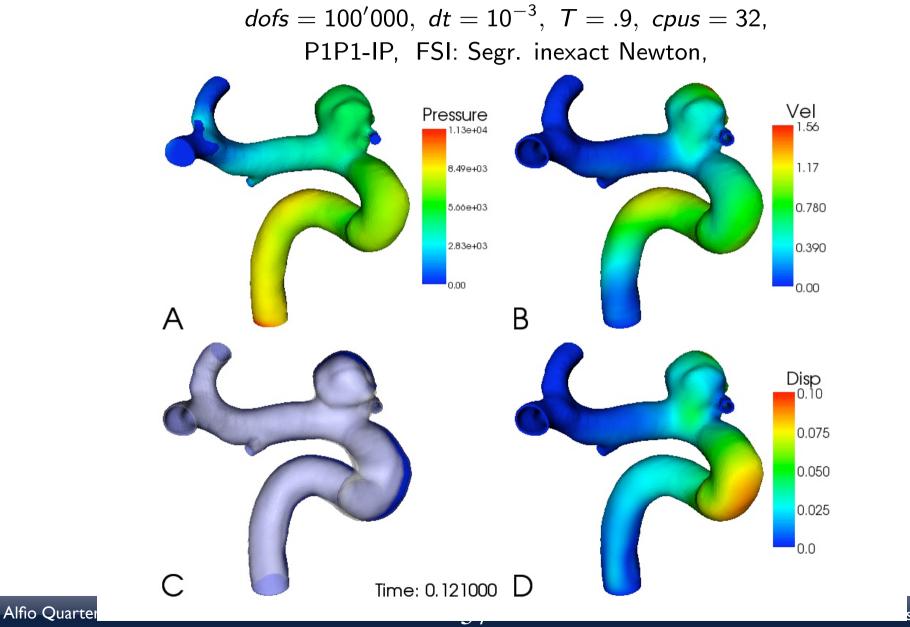


#### Flow in a cerebral aneurysm during a full cardiac pulse

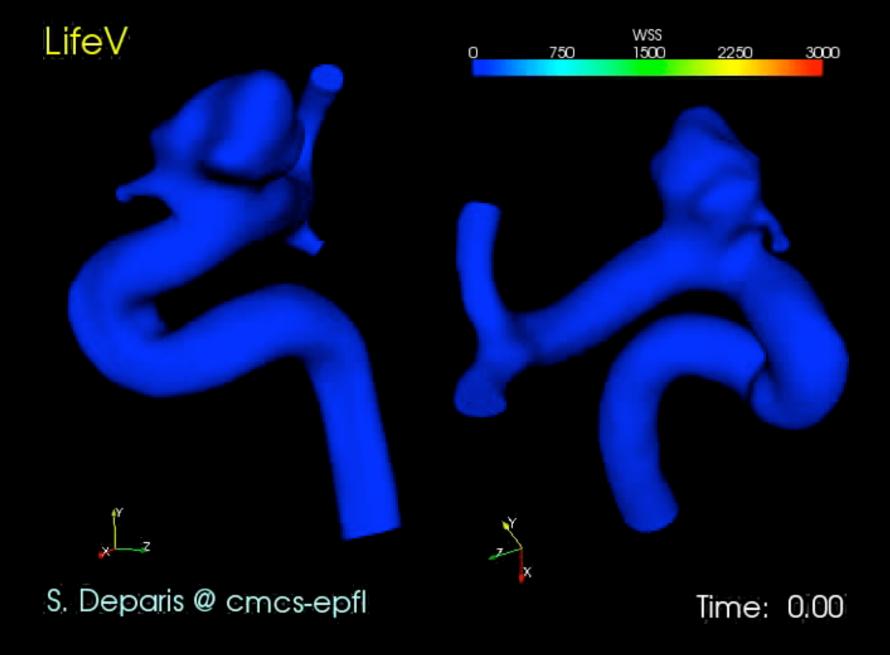


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## Pressure, velocity and wall displacement



## WSS - Wall Shear Stress



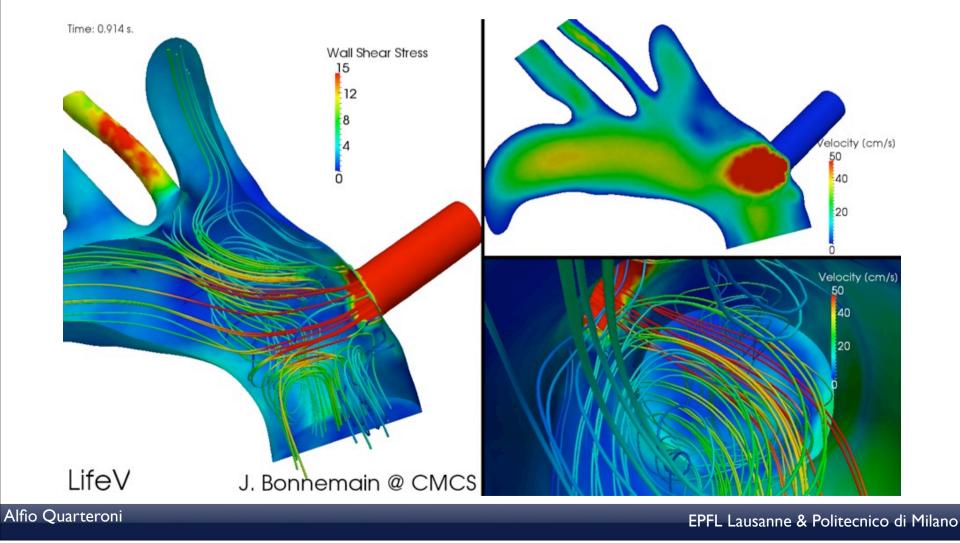
## Applications Prosthetic Devices

## Cannula of a Ventricular Assisted Device (VAD)

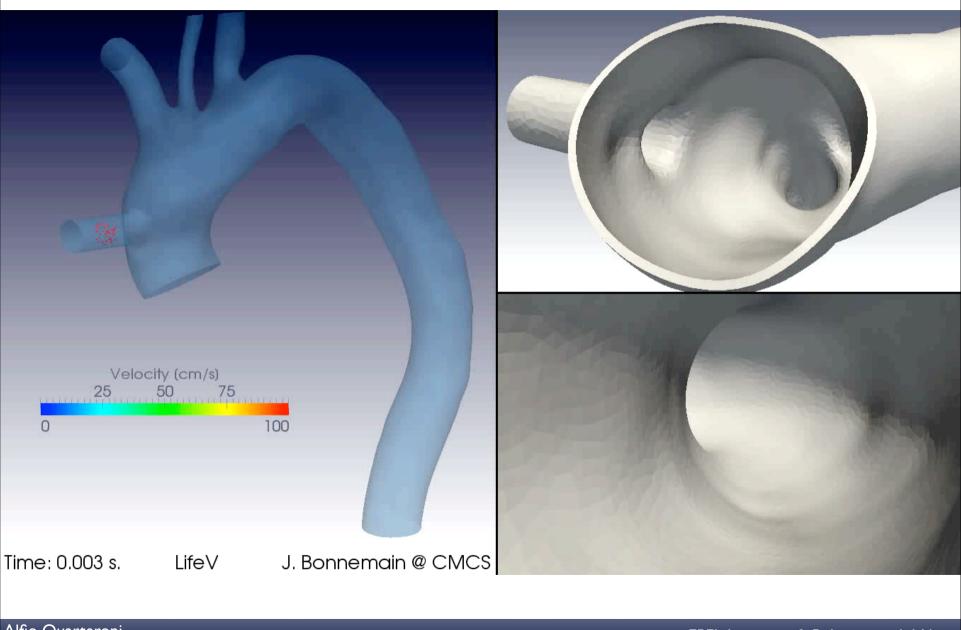
#### **VAD connection to an Aorta** (6 lt/min blood supply)

#### WSS and streamlines (steady state simulation)

Recirculation and secondary flows (left/lower right) velocity magnitude (upper right)

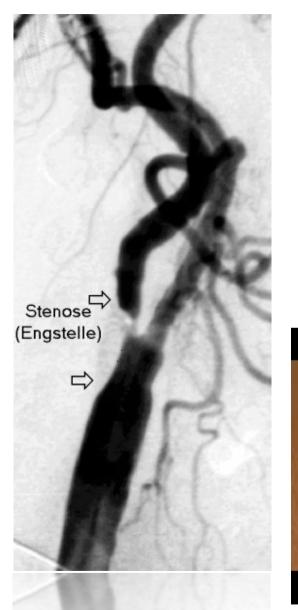


## Cannula of a Ventricular Assisted Device to Aorta

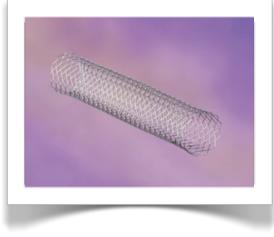


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## Drug release from Stents



# Angiography after stent placement

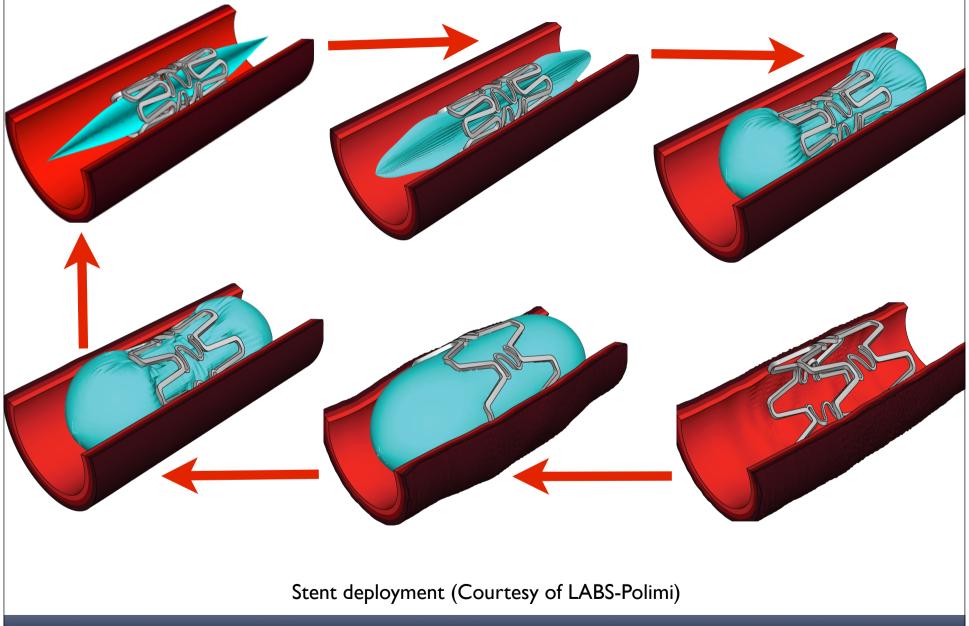






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## Drug release from Stents

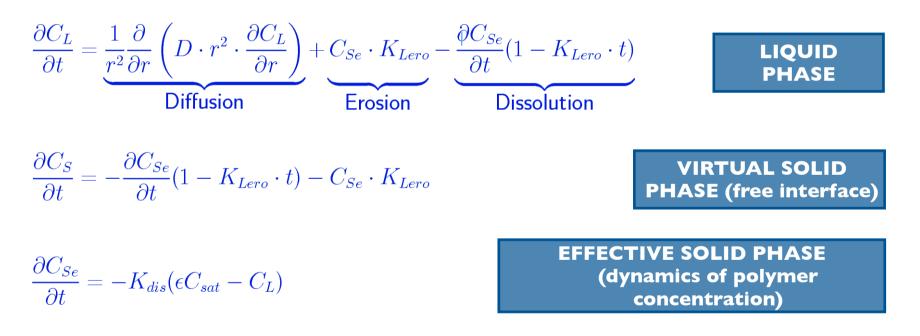


#### A Multi-Domain/Multi-Phase Problem

Macroscale, mm (in the arterial wall)

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

Macroscale, µm (in the coating matrix)

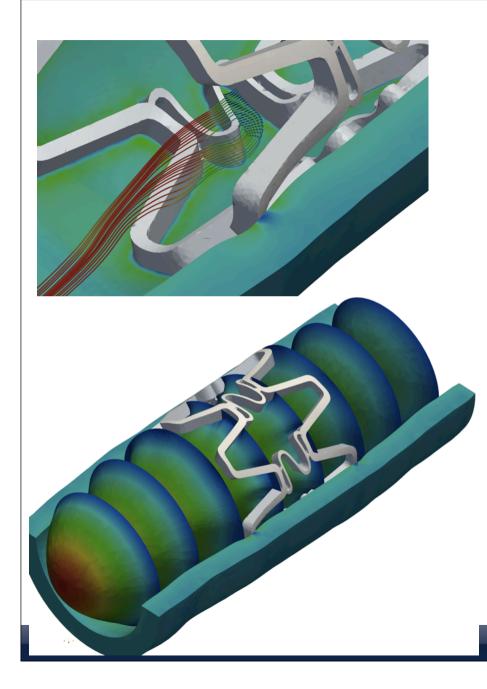


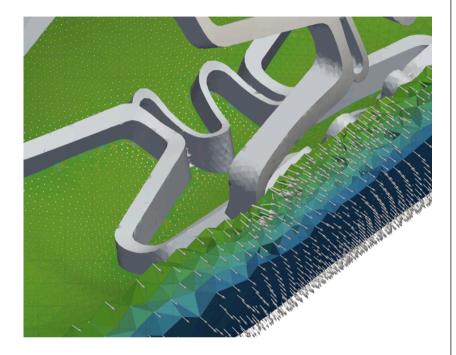
 $K_{dis}, K_{Lero}, D$ 

Depend on polymer characteristics (porosity, tortuosity,...) Determined by stochastic models

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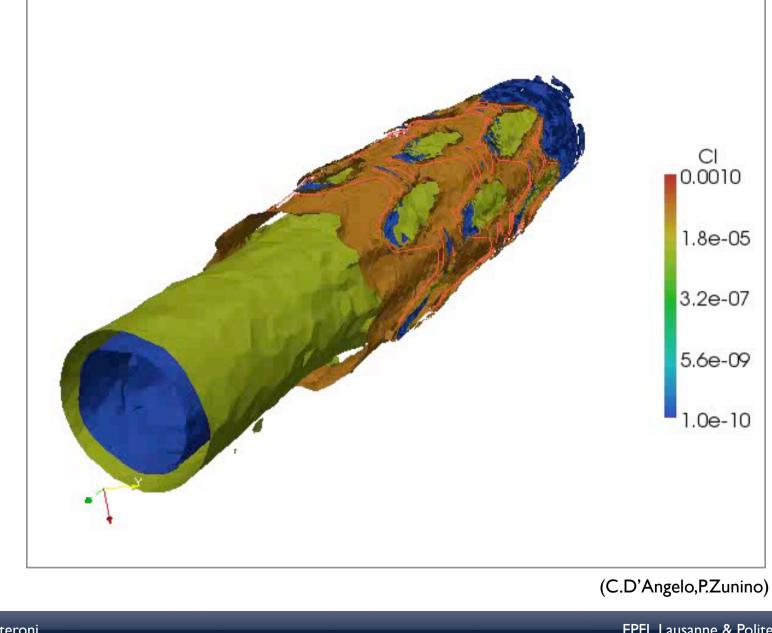
## Flow Field Around a Stent: Numerical Simulation





- Simulations by C.D'Angelo,
- P.Zunino, MOX in collaboration
- with LABS, PoliMi

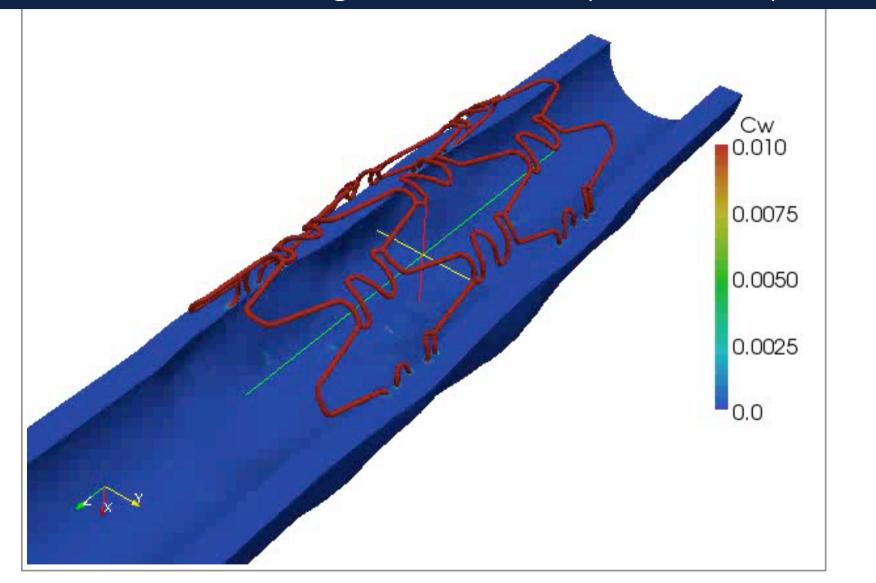
## Isosurfaces of drug concentration (lumen)



EPFL Lausanne & Politecnico di Milano

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## Isosurfaces of drug concentration (arterial wall)



(C.D'Angelo, P.Zunino)

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