INTRODUCTION to CARDIOVASCULAR MATHEMATICS - 06
Blood is a suspension of red cells, leukocytes and platelets on a liquid suspension called plasma.
Representation Framework: Neither Lagrangian...
... nor Eulerian...
... ALE!

ALE (Arbitrary Lagrangian Eulerian) Representation

\[ \Omega(t) \]

with inflow and outflow boundaries fixed
ALE framework: an abstract setting

The moving control domain

\[ \hat{w} = \frac{\partial \hat{A}_t}{\partial t} \]
Fluid equations

Assumptions on the fluid (in large arteries):

- Homogeneous
- Newtonian ($\mu = \text{constant}$)

\[ \sigma_f(u_f, P) = -PI + 2\mu \epsilon(u_f) \]

Cauchy stress tensor

\[ \epsilon(u_f) = \frac{1}{2} (\nabla u_f + (\nabla u_f)^T) \]

Strain rate tensors

Incompressible Navier-Stokes equations in ALE conservation form:

\[ \frac{\rho_f}{J_A} \frac{\partial J_A u_f}{\partial t} + \text{div} (\rho_f u_f \otimes (u_f - w) - \sigma_f(u_f, P)) = 0, \text{ in } \Omega_f(t) \]

\[ \text{div} u_f = 0, \text{ in } \Omega_f(t) \]

\[ u_f = u_{f,D}, \text{ on } \Gamma_{f,D} \]

\[ \sigma_f(u_f, P)n_f = g_{f,N}, \text{ on } \Gamma_{f,N} \]

\[ u_f = u_{\Gamma}, \text{ on } \Gamma(t) \]
Velocity profiles in carotid bifurcation (rigid boundaries, Newtonian)
WSS (Wall Shear Stress) - an indicator of atherosclerosis

\[ WSS = \mu \left( \frac{\partial u}{\partial n} \cdot \tau \right) \bigg|_{\text{wall}} \]

- \( u \): velocity field
- \( n, \tau \): 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

**Rouleaux 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

\[ \sigma_f(u_f, P) = -P I + 2\mu \varepsilon(u_f) \]  
Cauchy stress tensor

**Generalized Newtonian model:**

\[ \mu = \mu(\dot{\gamma}) \quad \dot{\gamma} = \sqrt{2\text{tr}(\varepsilon^2)} \]  
(\dot{\gamma} \text{ Rate of deformation, or shear rate})

**POWER LAW model:**

\[ \mu(\dot{\gamma}) = k \dot{\gamma}^{n-1} \]

Shear thinning if \( n < 1 \), \( \mu \) is a decreasing function of \( \dot{\gamma} \)

[Graph showing \( \mu \) vs. \( \dot{\gamma} \) for different sets of \( (n, k) \) values]
PROBLEM
Analysis of the cardiovascular system

Experimental Model
- In Vivo
- In Vitro
- Literature benchmark

Mathematical Model
- Geometry
- PDE’S and analysis
- Numerical methods
- Computer simulation

Post-processing
- 3D visualization of results

Feedback

Patient’s real data
- uncertainty
- sensitivity

Comparison with experiments, validation
**Some Generalized Non-Newtonians Models**

\[
\mu_0 = \lim_{\dot{\gamma} \to 0} \mu(\dot{\gamma}) = 0.056 \text{ Pa s}
\]

\[
\mu_\infty = \lim_{\dot{\gamma} \to \infty} \mu(\dot{\gamma}) = 0.00345 \text{ Pa s}
\]

<table>
<thead>
<tr>
<th>MODEL</th>
<th>(\frac{\mu(\dot{\gamma}) - \mu_\infty}{\mu_0 - \mu_\infty})</th>
<th>MATERIAL CONSTANTS FOR BLOOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Powell-Eyring</td>
<td>(\frac{\sinh^{-1}(\lambda \dot{\gamma})}{\lambda \dot{\gamma}})</td>
<td>(\lambda = 5.383 \text{ s})</td>
</tr>
<tr>
<td>Cross</td>
<td>((1 + (\lambda \dot{\gamma})^m)^{-1})</td>
<td>(\lambda = 1.007 \text{ s}, m = 1.028)</td>
</tr>
<tr>
<td>Modified Cross</td>
<td>((1 + (\lambda \dot{\gamma})^m)^{-a})</td>
<td>(\lambda = 3.736 \text{ s}, m = 2.406, a = 0.254)</td>
</tr>
<tr>
<td>Carreau</td>
<td>((1 + (\lambda \dot{\gamma})^2)^{(n-1)/2})</td>
<td>(\lambda = 3.313 \text{ s}, n = 0.3568)</td>
</tr>
<tr>
<td>Carreau-Yasuda</td>
<td>((1 + (\lambda \dot{\gamma})^a)^{(n-1)/a})</td>
<td>(\lambda = 1.902 \text{ s}, n = 0.22, a = 1.25)</td>
</tr>
</tbody>
</table>

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)

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

where:

- $\hat{F}_s$: deformation gradient
- $\tilde{J}_s = \det \hat{F}_s$: Jacobian
- $\hat{\Sigma} = \hat{F}_s^{-1} \hat{\Pi}_{\sigma s} = \tilde{J}_s \hat{F}_s^{-1} \hat{\sigma}_s \hat{F}_s^{-T}$: second Piola-Kirchhoff tensor
- $\hat{\rho}_{s,0} = \hat{\rho}_s \tilde{J}_s$: density in reference configuration
Solid wall equations

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

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

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

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

Equilibrium of a hyper-elastic solid:

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

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

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

$$\hat{F}_s \Sigma \hat{n}_s = \hat{J}_s \hat{F}_s^T \hat{n}_s \hat{g}_{\Gamma}, \text{ on } \hat{\Gamma}$$
The coupled fluid-structure problem

Equations for the geometry:

\[ \hat{\eta}_f = \text{Ext}(\hat{\eta}_s|\hat{\Gamma}), \quad \hat{w} = \frac{\partial \hat{\eta}_f}{\partial t}, \quad \Omega_f(t) = (I + \hat{\eta}_f)(\hat{\Omega}_f) \]

Equations for the fluid:

\[ \frac{\rho_f}{J_A} \frac{\partial J_A}{\partial t} \mathbf{u}_f + \text{div}(\rho_f \mathbf{u}_f \otimes (\mathbf{u}_f - \hat{w}) - \sigma_f(\mathbf{u}_f, P)) = 0, \quad \text{in } \Omega_f(t) \]
\[ \text{div}\mathbf{u}_f = 0, \quad \text{in } \Omega_f(t) \]
\[ \mathbf{u}_f = \mathbf{u}_D, \quad \text{on } \Gamma_{f,D} \]
\[ \sigma_f(\mathbf{u}_f, P)\mathbf{n}_f = \mathbf{g}_{f,N}, \quad \text{on } \Gamma_{f,N} \]
\[ \mathbf{u}_f = \hat{w}, \quad \text{on } \Gamma(t) \]

Equations for the structure:

\[ \hat{\rho}_s,0 \frac{\partial^2 \hat{\eta}_s}{\partial t^2} - \text{div}_\hat{x}(\hat{F}_s \hat{\Sigma}) = 0, \quad \text{in } \hat{\Omega}_s \]
\[ \hat{\eta}_s = 0 \quad \text{on } \hat{\Gamma}_{s,D} \]
\[ \hat{F}_s \hat{\Sigma} \hat{n}_s = \hat{J}_s|\hat{F}_s^{-T} \hat{n}_s|\hat{g}_{s,N}, \quad \text{on } \hat{\Gamma}_{s,N} \]
\[ \hat{F}_s \hat{\Sigma} \hat{n}_s = \hat{J}_s \hat{\sigma}_f(\mathbf{u}_f, P)\hat{F}_s^{-T} \hat{n}_s, \quad \text{on } \hat{\Gamma} \]
**Energy balance**

For homogeneous boundary data (isolated system):

\[
\begin{align*}
\mathbf{u}_f &= 0 \quad \text{on} \quad \partial \Omega_f(t) \setminus \Gamma(t) \\
\mathbf{F}_s \hat{\Sigma} \hat{n}_s &= 0 \quad \text{on} \quad \partial \hat{\Omega}_s \setminus \hat{\Gamma} \\
\frac{d}{dt} [EK(\mathbf{u}_f, \mathbf{u}_s) + EP(\hat{E})] + \text{Diss}(\mathbf{u}_f) &= 0
\end{align*}
\]

with \( \mathbf{u}_s = \frac{\partial \hat{n}_s}{\partial t} \)

\[
EK(\mathbf{u}_f, \mathbf{u}_s) = \int_{\Omega_f(t)} \frac{\rho_f}{2} |\mathbf{u}_f|^2 dx + \int_{\hat{\Omega}_s} \frac{\hat{\rho}_s,0}{2} |\mathbf{u}_s|^2 d\hat{x}
\]

\( EK(\mathbf{u}_f, \mathbf{u}_s) \) \text{ Kinetic energy}

\[
EP(\hat{E}) = \int_{\hat{\Omega}_s} \hat{W}(\hat{E}) d\hat{x}
\]

\( EP(\hat{E}) \) \text{ Elastic potential energy}

\[
\text{Diss}(\mathbf{u}_f) = \int_{\Omega_f(t)} 2\mu |\varepsilon(\mathbf{u}_f)|^2 dx
\]

\( \text{Diss}(\mathbf{u}_f) \) \text{ 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

\[ \Omega_f(t) \]

\[ \Omega_s(t) \]

\[ \Gamma(t) \]

Interface

Fluid
Steklov-Poincare’ equation

\[ SP_f(\lambda) + SP_s(\lambda) = 0 \]

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

\[ \lambda \rightarrow (\overline{u}, p) = Res_f(\overline{\lambda}) \rightarrow SP_f(\overline{\lambda}) = \sigma_f(\overline{u}, p) \cdot \overline{n}_f \]

\[ \lambda \rightarrow (\overline{u}, p) = Res_s(\overline{\lambda}) \rightarrow SP_s(\overline{\lambda}) = \sigma_s(\overline{u}, p) \cdot \overline{n}_s \]
DD Formulation, II: Preconditioned Iterations

\[ SP_f(\lambda) + SP_s(\lambda) = 0 \]

1. Compute the residual stress from a given displacement

\[ \sigma^k = -(SP_f(\lambda^k) + SP_s(\lambda^k)) \]

2. Apply the inverse of the preconditioner to the stress

\[ \mu^k = P^{-1}\sigma^k \]

⇒ recover displacement

3. Update displacement

\[ \lambda^{k+1} = \lambda^k + \omega^k\mu^k \]

\[ P^{-1} = \alpha^k_f(SP_f(\lambda^k))^{-1} + \alpha^k_s(SP_s(\lambda^k))^{-1} \]

(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
Spurious reflections with free-stress outflow conditions
Geometric Multiscale
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

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

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 (level 1):
3D flow model

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

Global (level 3):
0D capillary network
Dimensional reduction by geometric multiscale

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

1D
- 1D Euler (F) +
- Algebraic pressure law

0D
- 0D lumped parameters
  (system of linear ODEs)
MATHEMATICAL MODEL

Geometric multiscale models

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

\[
\rho_f \left[ \partial_t u + (u - w) \cdot \nabla u \right] - \mu \Delta u + \nabla p = 0 \quad \text{in } \Omega_f
\]

\[
\text{div } u = 0 \quad \text{in } \Omega_f
\]

\[
\partial_{tt} \eta - \text{div } \sigma(\eta) = f(\eta) \quad \text{in } \Omega_w
\]

\[
\sigma(\eta) \cdot n = T(u, p) \cdot n \quad \text{on } \Gamma
\]

\[
u = \partial_t \eta \quad \text{on } \Gamma
\]

Assume that:

- \(u_z \gg u_x, u_y\)
- \(u_z\) has a prescribed steady profile
- average over axial sections
- static equilibrium for the vessel

Then we obtain a 1D problem.
Geometric multiscale model

1D Euler(F) + Algebraic pressure law

\[
\begin{align*}
\frac{\partial_t A}{A} + \frac{\partial_x Q}{Q} &= 0, \\
\frac{\partial_t Q}{Q} + \frac{\partial_x \left( \frac{\alpha Q}{A} \right)}{A} + \frac{A}{\rho} \frac{\partial_x P}{P} &= -K_T \frac{Q}{A}, \\
\beta \frac{\sqrt(A)}{A_0} - \sqrt(A_0) &= P(A)
\end{align*}
\]

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

<table>
<thead>
<tr>
<th>Fluid dynamics</th>
<th>Electrical circuits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure</td>
<td>Voltage</td>
</tr>
<tr>
<td>Flow rate</td>
<td>Current</td>
</tr>
<tr>
<td>Blood viscosity</td>
<td>Resistance R</td>
</tr>
<tr>
<td>Blood inertia</td>
<td>Inductance L</td>
</tr>
<tr>
<td>Wall compliance</td>
<td>Capacitance C</td>
</tr>
</tbody>
</table>

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

One-dimensional models

Stenosed artery  Junction of three arteries (stented abdominal aorta)  Network of 55 arteries
Continuity of fluxes and pressure yields the DAE system:
\[
\begin{align*}
\frac{dy}{dt} &= B(y, z, t) \quad t \in (0, T] \\
\frac{dt}{dt} &= G(y, z) = 0
\end{align*}
\]
A full geometric multiscale model: 0D-1D-2D (or 3D) coupling
MATHEMATICAL MODEL

3D - 1D - 0D

time = 0.2 ms
MATHEMATICAL MODEL

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

3D model (spurious reflections)  3D-1D coupled model

(A. Moura)
3D-1D for the carotid: velocity field
3D-1D for the carotid: pressure pulse
Some references on the 1D system

L. Euler, Principia pro motu sanguinis per arteria determinando, 1775
Existence of local-in-time regular solution for in the half-space for 1D: S. Canic, E.H. Kim, 2003, S. Canic and A. Mikelić, 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
(by either Lagrange multipliers or optimal control)
A Global Scenario: An Outlook

- Respiratory system
- Heart model
- Irrorated compartments
- Nervous system

- Flow Rate
- Arterial Concentration
- Pressures

- Metabolism
- Venous Concentrations
- Systemic Resistance

- Chemoreflex

- Baroreflex
Building the surface $S$ from sample points

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

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

Two possible choices:  \hspace{1cm} \varphi(r) = r \quad \text{or} \quad \varphi(r) = r^3

Extracting information from the surface:

$$H_h(x) = \frac{H(x)}{||\nabla \phi(x)||}, \quad x \in S$$  \text{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
1 - Cavo-pulmonary shunt
2 - Cerebral aneurysms
3 - Stents
1 - Cavopulmonary Shunt

LABS, Politecnico of Milan
Cariplio Foundation
Great Ormond Street Hospital, London
APPLICATION 1: CAVOPULMONARY SHUNT

Shunt for restoring heart-pulmonary circulation

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

INN  LCA  LSA  AoA  RPA  COR  LPA  AoD
CS

ICM 2006
APPLICATION 1: CAVOPULMONARY SHUNT

Central Shunt (CS)

LCA LSA

Flow (%)

80

60

40

20

0

PULMONARY

UPPER BODY

CORONARY

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
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
Generating a computational mesh

Constrained optimization procedures are needed to maximize a suitable measure of the grid quality (to avoid triangle distortion) 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
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

Stenosis in the carotid bifurcation

Angiography after stent placement
APPLICATION 3: DRUG ELUTING STENTS

Stent deployment
Four commercial coronary stents

<table>
<thead>
<tr>
<th>CORDIS</th>
<th>JOSTENT</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="CORDIS Diagram" /></td>
<td><img src="image2" alt="JOSTENT Diagram" /></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>SORIN</th>
<th>PALMAZ</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image3" alt="SORIN Diagram" /></td>
<td><img src="image4" alt="PALMAZ Diagram" /></td>
</tr>
</tbody>
</table>

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 μm

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

\[
\frac{\partial c}{\partial t} = D \Delta c + u \nabla c
\]
Macroscale, mm (in the arterial wall)

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

\[
\frac{\partial C_s}{\partial t} = -\frac{\partial C_{Se}}{\partial t} (1 - K_{Lero} \cdot t) - C_{Se} \cdot K_{Lero}
\]

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

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

Macroscale, \(\mu m\) (in the coating matrix)

LIQUID PHASE
VIRTUAL SOLID PHASE (free interface)
EFFECTIVE SOLID PHASE (dynamics of polymer concentration)
APPLICATION 3: DRUG ELUTING STENTS

Numerical strategy

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

Coating as a 3D domain

Grid around the stent

<table>
<thead>
<tr>
<th>in stent coating</th>
<th>in the wall</th>
</tr>
</thead>
<tbody>
<tr>
<td>#Elements</td>
<td>965.081</td>
</tr>
<tr>
<td></td>
<td>1.018.475</td>
</tr>
<tr>
<td>(many more for realistic geometries)</td>
<td></td>
</tr>
</tbody>
</table>

ICM 2006
GEOMETRIC PRE-PROCESSING

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.
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 uprisings (clinical diagnosis)
- Tool for therapeutic/surgical planning (optimization)

NEW MATHEMATICAL DEVELOPMENTS
ACKNOWLEDGMENTS


C. D’Angelo, G. Fourestey, C. Vergara

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