**Computational Methods**

FOR MECHANOCHEMICAL BIOLOGICAL MECHANISMS IN ARTERIES

**COMETA**

- Computational-analytical modelling strategies
- Multiscale and multiphysics mechanisms
- Numerical strategies for coupled problems

\[ \nabla \cdot \sigma(C,s) = 0 \]
\[ \frac{\partial c}{\partial t} + \nabla \cdot (-D \nabla c) = R(c,C) \]
\[ \frac{\partial s}{\partial t} + \nabla \cdot (-A \nabla s) = I(s,c) \]

**MArCo**

Interdisciplinary and industrial applications:
- *In silico* medical research
- Computer-aided design of devices

Michele Marino – m.marino@ing.uniroma2.it

Department of Civil Engineering and Computer Science
Cardiovascular diseases (CVDs) are the leading cause of deaths worldwide, causing 3.9 million deaths in Europe, i.e. 45% of all deaths, and over 1.8 million deaths in the European Union (EU), i.e. 37% of all deaths. Nowadays, CVDs are estimated to cost the EU economy €210 billion a year and these costs are prone to increase with the ageing of the population. Therefore, **novel engineering approaches for personalized medicine arise as urgent needs.**

A major role in the aetiology of CVDs is played by the imbalance of cascades of biochemical reactions involved in cell-cell signalling pathways. The imbalance of these pathways leads to non-physiological concentrations of molecules in tissues. In turn, over- or under-production of active molecules, such as growth factors or enzymes, determine non-functional growth and remodelling (G&R) of tissue constituents. Therefore, **chemo-biological** mechanisms highly affect the **mechanics** of cardiovascular tissues in terms of stiffness, strength and anisotropic properties. In turn, tissue stresses and strains pave the way to biochemical reactions, closing the loop of a refined feedback control system.

Computational approaches have reached limited results in the understanding of the aetiology of CVDs diseases, since reliable only in terms of mechanical quantities (i.e., stresses and strains) in biological structures at a given pathological state. As a consequence, **in silico** analyses are nowadays far from being used in medical research and clinical practice. The term “digital twin” in a biomechanical context is indeed abused, since current approaches do not manage to reproduce the living properties of biological structures. In this context, **COMETA** is motivated by the high need for **renewing the perspective of in silico approaches** in biomechanics, which are to-date not effective in accounting for coupled mechano-chemo-biological effects. **COMETA** will contribute in shedding a light on **how arteries evolve in health and disease.**

**Challenges** are related to the need of coupling very different physical mechanisms, as well as length and time scales:

(i) loads affecting the **mechanics** of arteries (millimetres) vary with the cardiac cycle (seconds);

(ii) the **biochemical environment**, determined by inter-cellular molecular diffusion (micrometres), reaches the steady-state within hours;

(iii) **biological mechanisms in G&R** occur within several days and affect arterial geometry (millimetres), histological features (micrometres) and molecular properties (nanometres).
Mechanical-Chemical-Biological Methodological Approach

**Mechanics**
- Displacement field $u$

**Chemical Environment**
- Molecular concentrations

**Biological Mechanisms**
- Growth and remodelling of structural features

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### T1) bioFE

**Analytical Core**
- $J \sigma = -p \mathbf{I} + 2 \mu \frac{\partial \Psi_T}{\partial \mathbf{C}} \mathbf{F}^T$
- $\Psi_T = \alpha_M \Psi_M(C) + \alpha_F \Psi_F(\lambda_m, H)$
- Damage variables

**T2) multiT&G&R**
- Transport problem
  $$\frac{\partial c_q}{\partial t} + \nabla \cdot (-D_q \nabla c_q + \mathbf{v} c_q) = \mathbf{R}_q(c, C)$$
- G&R of structural feature $s_j$
  $$\frac{\partial s_j}{\partial t} - \nabla \cdot [\mathbf{A}_j \nabla (s_j - s_j^0)] = - \left( \frac{s_j}{s_j + \lambda_j(c)} - 1 \right) \frac{s_j}{\nu_j}$$

**Scales**
- mm
- $\mu$m
- nm

### T3) MArCo: simulation tool

**Arterial multiphysics coupled formulation**
- Balance laws
  $$\left( L_u(u, c, s) \right) = 0$$
- Solution strategies:
  - fully vs loosely coupled
  - analytical vs numerical

Pathogenesis
- Parametric campaigns of in silico analyses:
  - micro/nano defects
  - inflammatory states
  - wound healing
  - transvascular alterations

**Medical Devices**
- DIAGNOSIS
  - Radiolabeled imaging
- TREATMENTS
  - Healing pathways

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Michele Marino – m.marino@ing.uniroma2.it

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• Funded by Minister of Education, University and Research

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• Availability of Bachelor and Master Theses projects

• Availability of PhD projects

• International network of research partners:

Michele MARINO
Assistant Professor - Rita Levi Montalcini tenure-track Professorship
Department of Civil Engineering and Computer Science
University of Rome Tor Vergata
Via del Politecnico 1, 00133 Rome, Italy
Tel: +39 (0)6 7259 7045 – Room: 029

ORCID 0000-0002-4323-3061
e-mail: m.marino@ing.uniroma2.it

Michele Marino – m.marino@ing.uniroma2.it