Institut de **M**athématiques et de
Modélisation de **M**ontpellier
UMR 5149 – I3M

YALES2BIO: a general multiscale solver for blood flows

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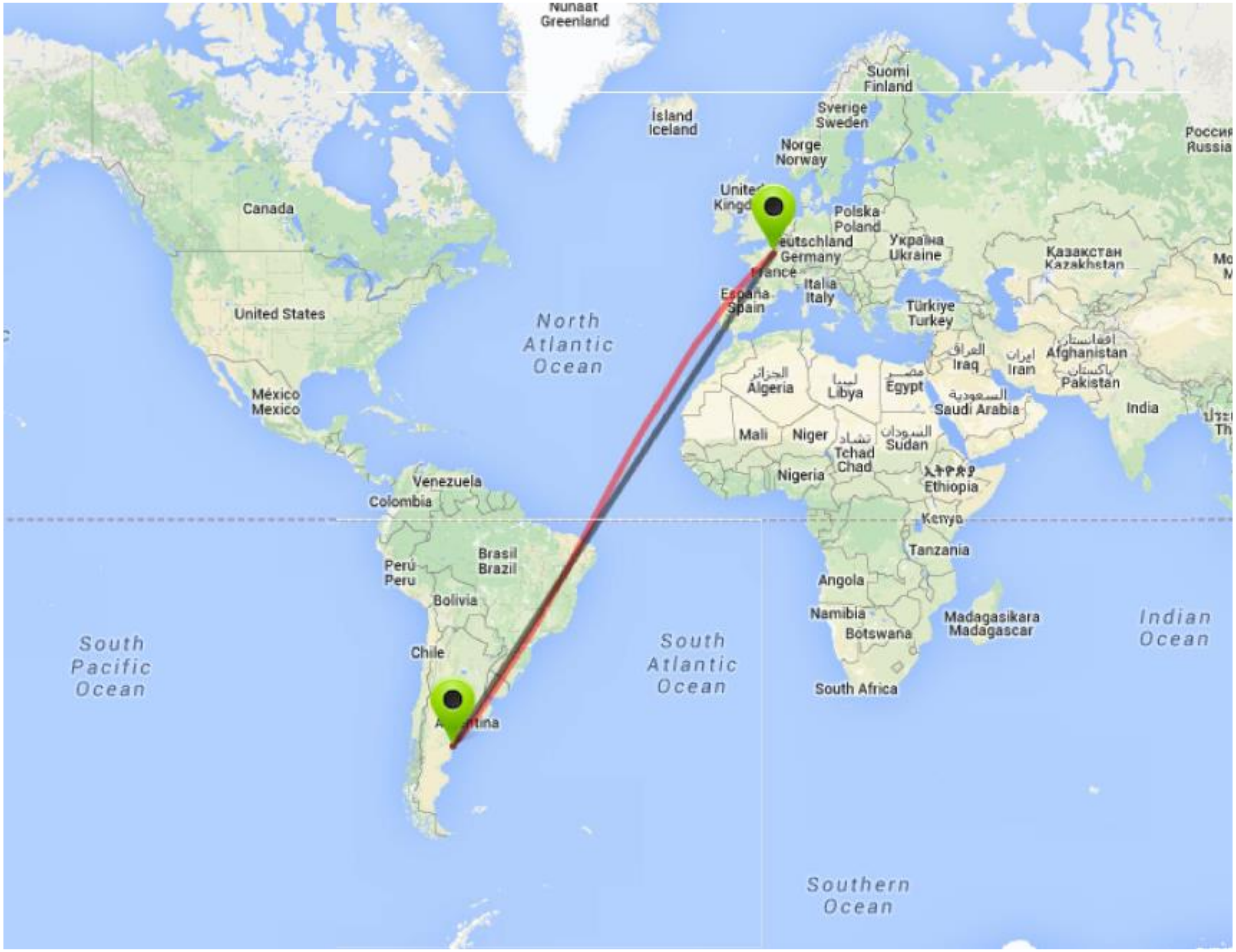
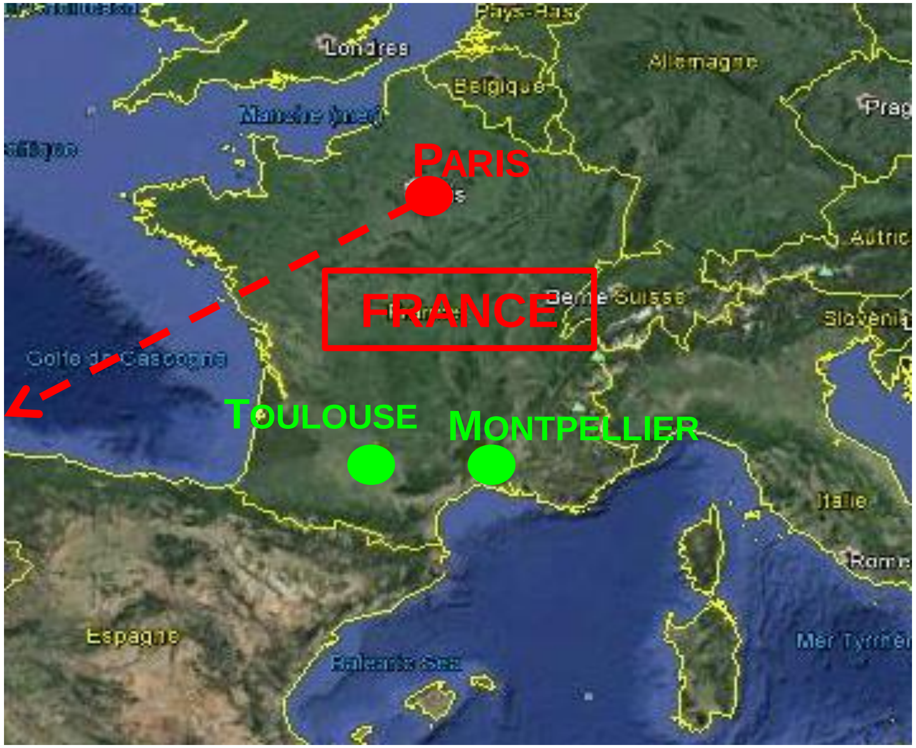
Researcher at CNRS/I3M
Chief architect

*** and the other people from the YALES2BIO team**

WHERE I COME FROM



MY TWO SCIENTIFIC LIFES



IN MONTPELLIER

UNIVERSITÉ MONTPELLIER 2
SCIENCES ET TECHNIQUES

Laboratory of Mathematics and Modelling of Montpellier University

CARDIO-VASCULAR BIOMECHANICS - 1ST TALK

IN TOULOUSE

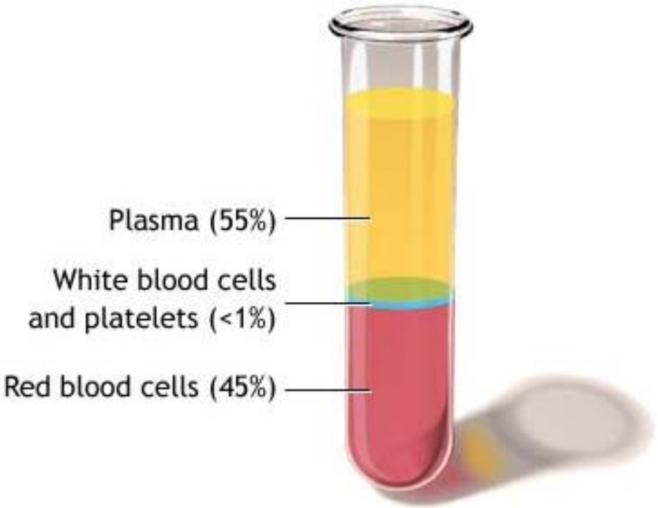
European Center for Research and Advanced Training in Scientific Computing

COMBUSTION INSTABILITIES - 2ND TALK

About Blood

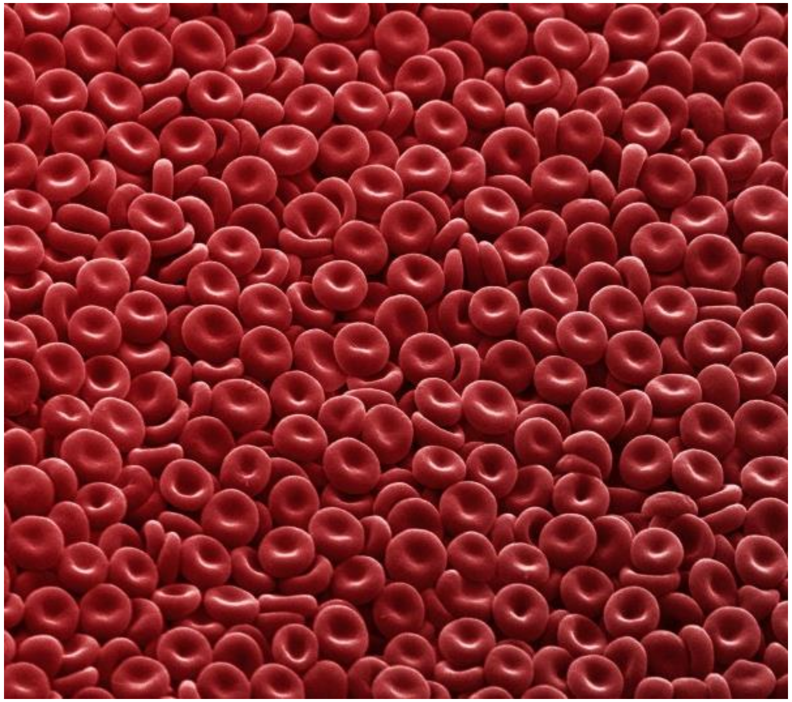
Composition

- Plasma (55%)
- Red Blood Cells (≈44%)
- White Cells
- Platelets

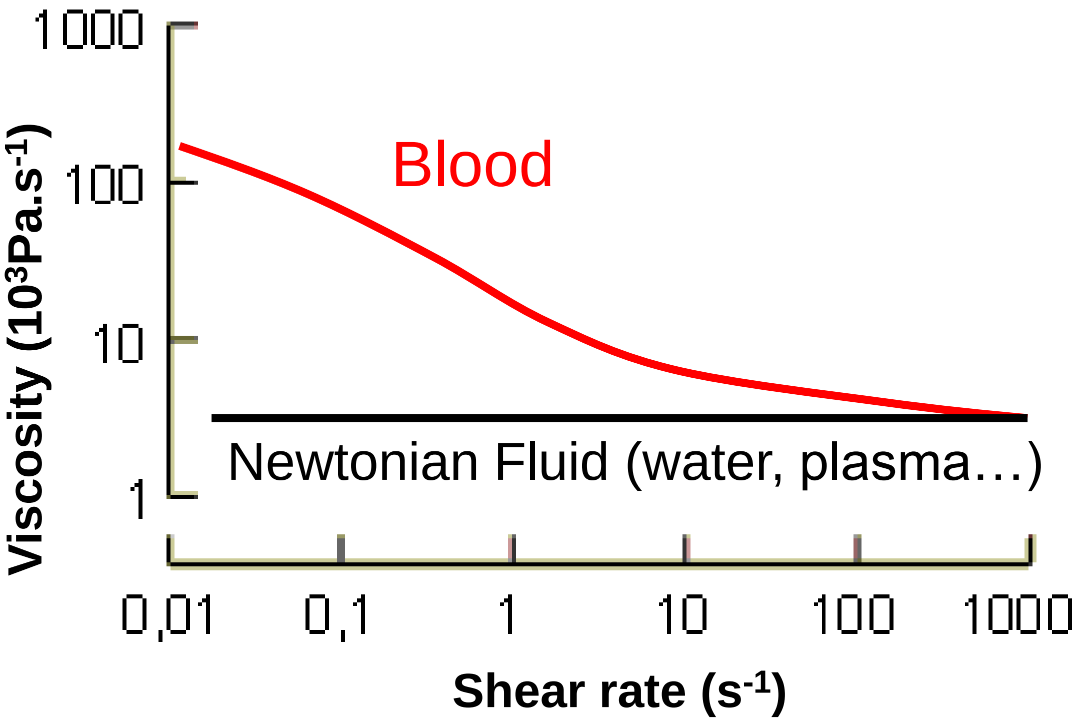


- 4-5 millions of Cells per mm^3 …
- Not a simple fluid: shear-thinning for viscosity …

About Blood

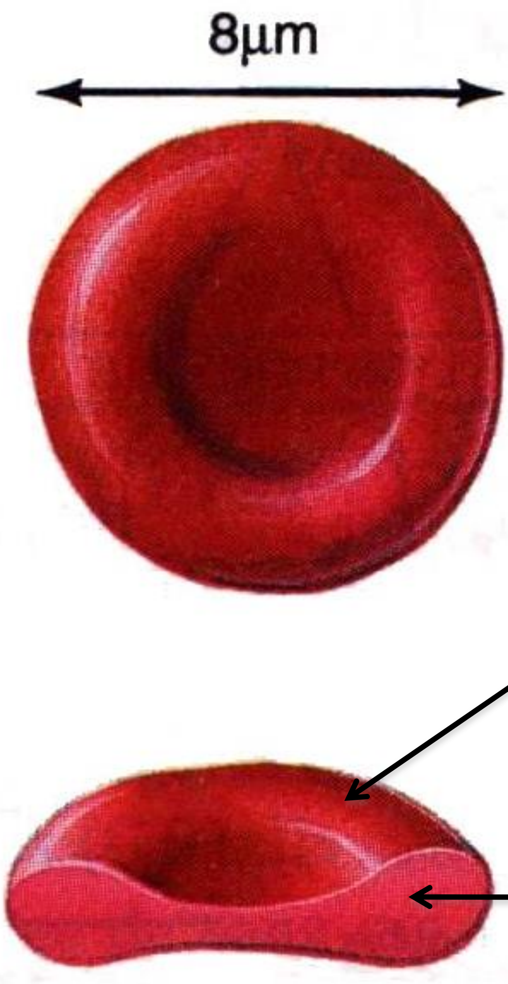


Red Blood cells in a Blood sample



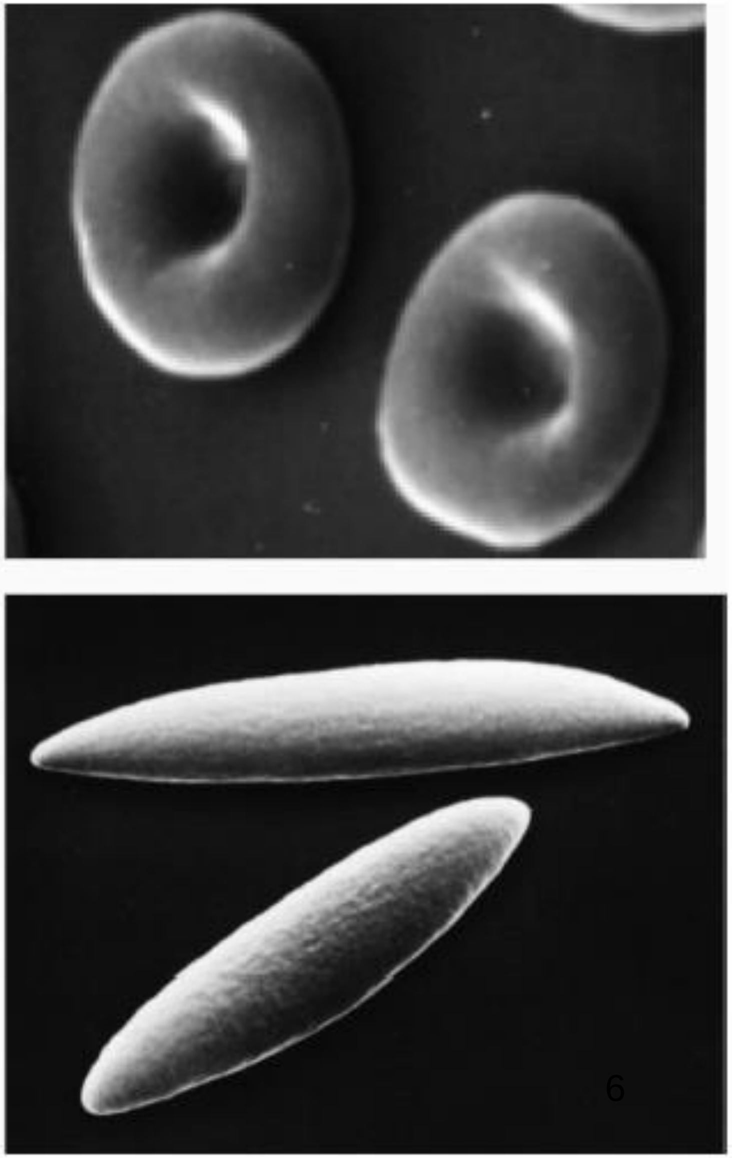
About Red Blood Cells

Mohandas, *Blood*, 2008.



Thin membrane

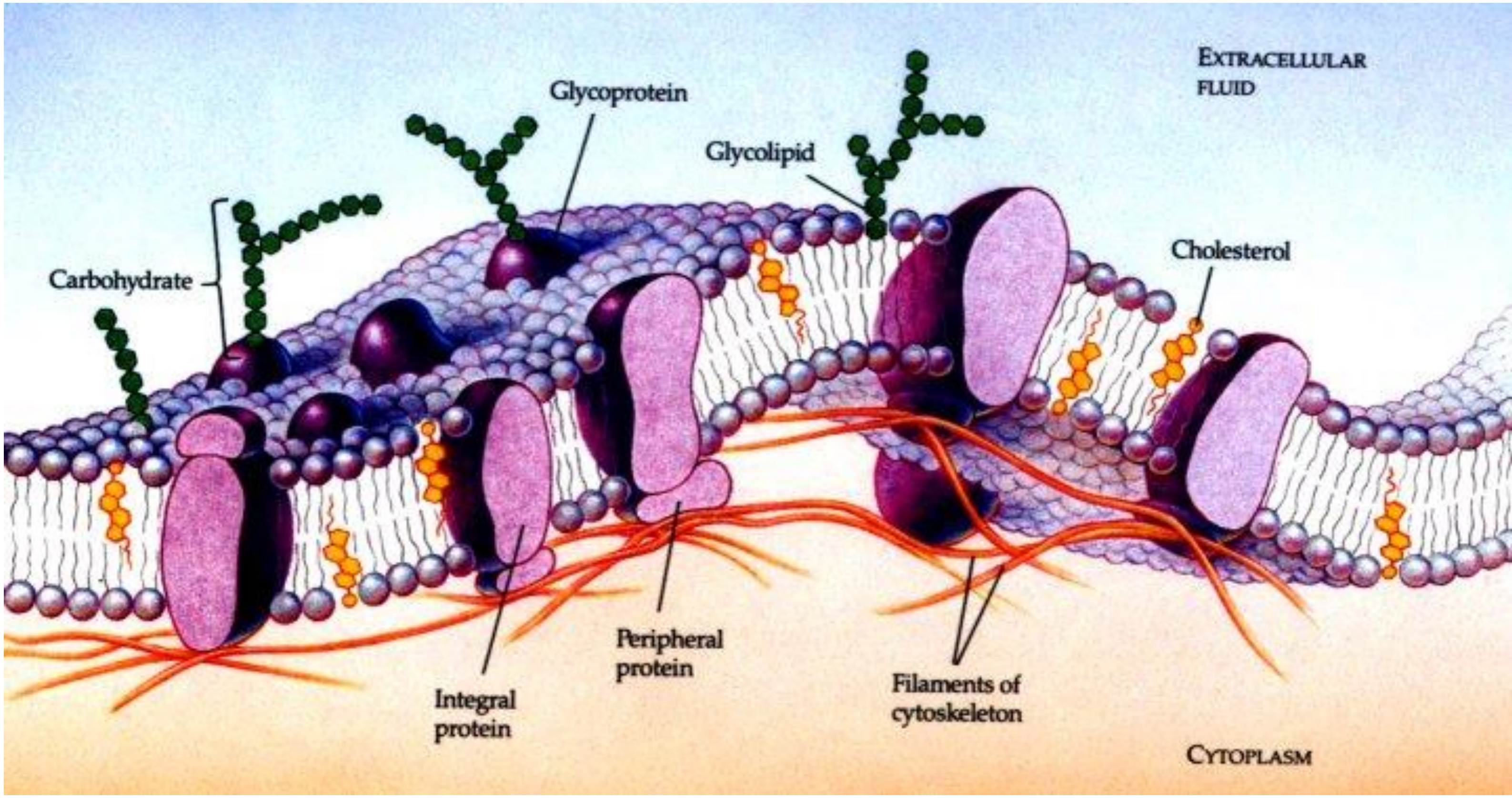
Cytoplasm
(Newtonian fluid)



SIMPLE CELLS, COMPLEX MEMBRANE

Lipid bilayer

Cyto-skeleton



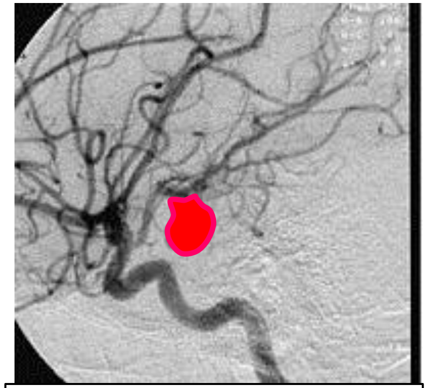
Mechanics : resistance to - Area change

- Bending

- Shear

BLOOD FLOWS RELATED QUESTIONS

- **Fluid mechanics point of view**
  - Blood flow characteristics: how do pressure and velocity components evolve over space and time ?
  - Motion of solid materials (arteries, valves, stent, …) interacting with blood
  - Associated constraints (pressure, viscous)

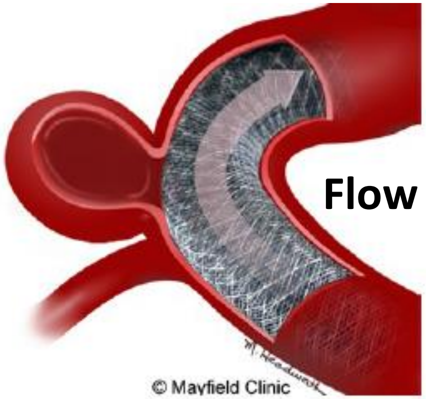

Cerebral Aneurysm

- **Medical point of view**
  - Aneurysm **rupture risk** (leads to (lethal) hemorrhage) ,
  - **Vascularization** of the different parts of the arterial tree
  - **Thrombus** formation (leads to (lethal) emboli)
  - **Hemolysis** rate (destruction of red blood cells, leads to anemia)

Our long-term objective at I3M

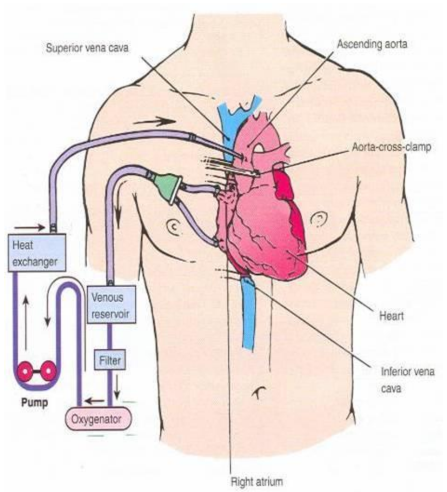
The study of blood flows using numerical simulations, with the application to the optimization of biomedical devices

Ventricular Assist Devices



Flow diverters

Artificial hearts



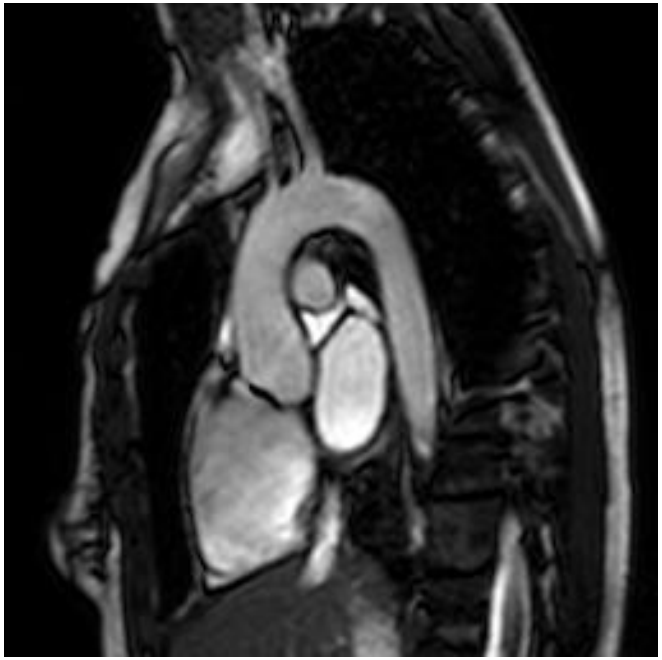
Extracorporeal circulation

Can we optimize the hydrodynamic and thrombogenic performances while minimizing hemolysis ?

SOME BLOOD FLOWS-RELATED CHALLENGES

- **Generally speaking :**
  - multi-scale flows (10 μm – 10 cm)
  - **fluid-structure interactions** [Blood/arteries/valves OR Plasma/cell membranes]
- **Macroscopic scale** :
  - 3D complex geometries ; complex rheology (shear thinning, thixotropic)
  - Pulsated BCs and **transitional** (neither laminar nor turbulent) flow regimes
- **Microscopic scale** :
  - Huge number of cells interacting
  - **Highly deformable cells**
- **Others** : Biochemistry, electric coupling, …

EXAMPLE OF COMPLEX MOVING GEOMETRIES



Heart and Aorta arch over time
Sagittal cut
(CT scan - Moreno – CHU Toulouse)

Heart and Aorta at fixed time
3D view
(CT scan - Moreno – CHU Toulouse)

THE YALES2BIO PROJECT

- In-house solver www.math.univ-montp2.fr/~yales2bio

- **Data structure** inherited from the HPC YALES2 solver (CNRS GIS *SUCCESS*)
  - dedicated to the computation of turbulent reacting flows
  - www.coria-cfd.fr/index.php/YALES2

- **Main features** :
  - Methodologies adapted to micro and macro scale applications
  - fluid-structure interactions (moving meshes; Immersed boundaries)
  - Unstructured meshes (complex geometries)
  - High order, low dissipative schemes (transitional flows)
  - Massively parallel (good scaling up to 10000 cores)

OUTLINE

- **Transitional hemodynamics in a realistic heart**
- Fluid-structure interaction for Micro-scale computations
- Fluid-structure interaction for Macro-scale computations

NAVIER-STOKES EQUATIONS

- The 3D PDE's governing the flow of a constant density (ρ) fluid are:
  - Mass conservation (continuity):

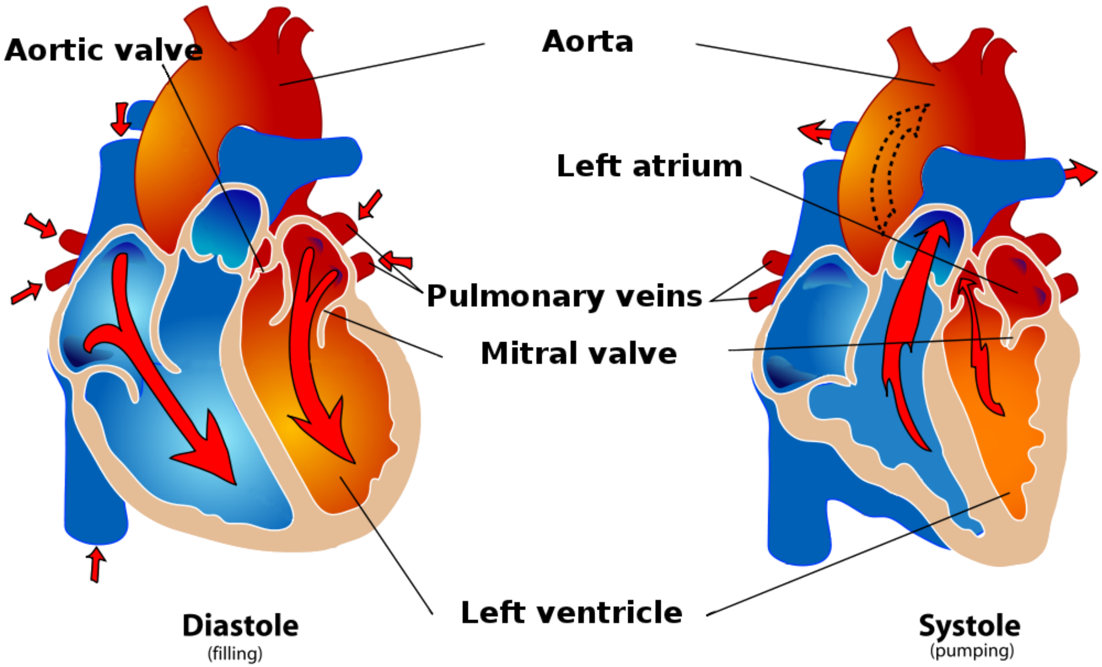
$$\frac{\partial u_i}{\partial x_i} = 0$$

  - Momentum:

$$\frac{\partial u_i}{\partial t} + u_j \frac{\partial u_i}{\partial x_j} = -\frac{1}{\rho}\frac{\partial p}{\partial x_i} + \frac{\partial}{\partial x_j}\left[\nu\left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i}\right)\right], \qquad \text{with} \quad i = 1,2,3$$

- Remarks:
  - p is pressure and ν is the kinematic viscosity (constant if Newtonian fluid)
  - The non-linear term $u_j \frac{\partial u_i}{\partial x_j}$ arises from the inertia effects ; if large enough, it is responsible for **turbulence** generation

Realistic flow in a human left heart

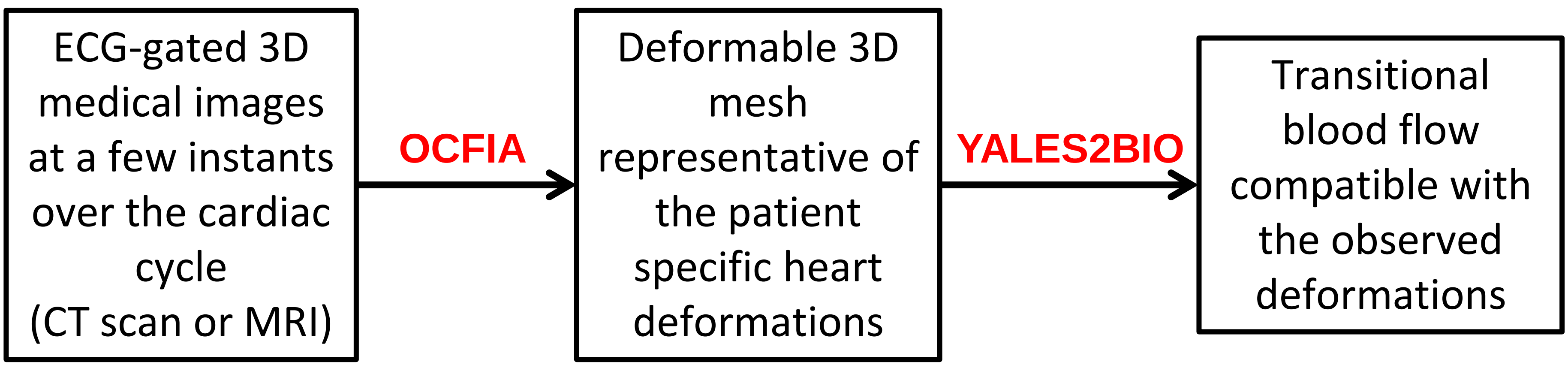


- **Flow characteristics:**
  - Length scale = 1 – 10 cm
  - Reynolds number = 1000 – 5000
  - Flow most probably transitional: neither laminar nor turbulent

$$R_e = \frac{\text{Velocity} \times \text{Length}}{\text{Viscosity}}$$

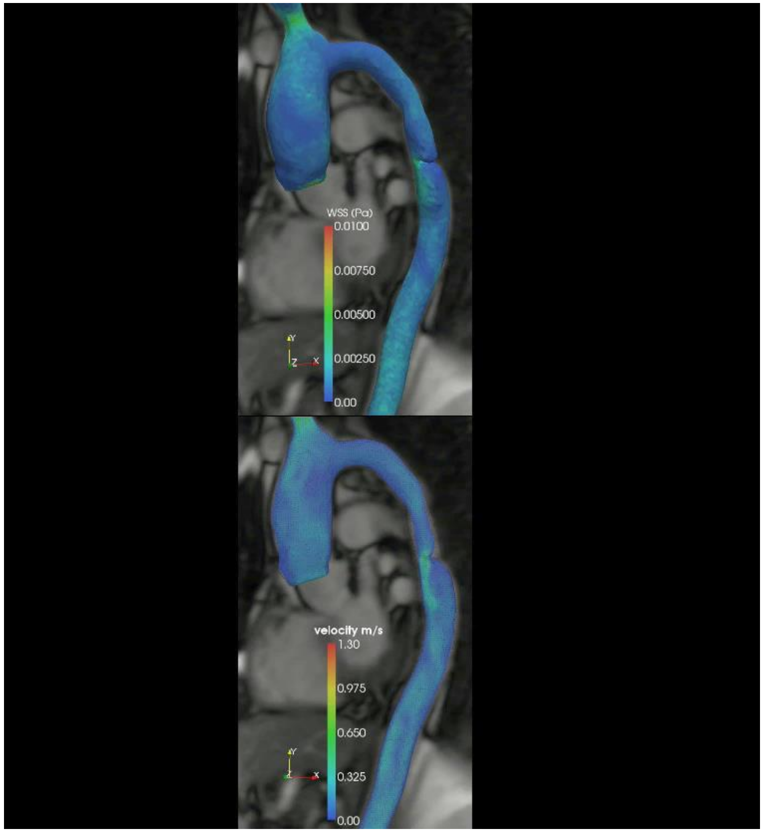
Functional imaging of the heart

- **Only** the intra-cardiac **blood flow** is computed; the motion of the cardiac muscle is deduced from medical imaging.
- Rely on the OCFIA chain developed within a former ANR research project (http://www.ocfia.org/) with University Hospital of Toulouse
- Combining **OCFIA** and the flow solver **YALES2BIO** :

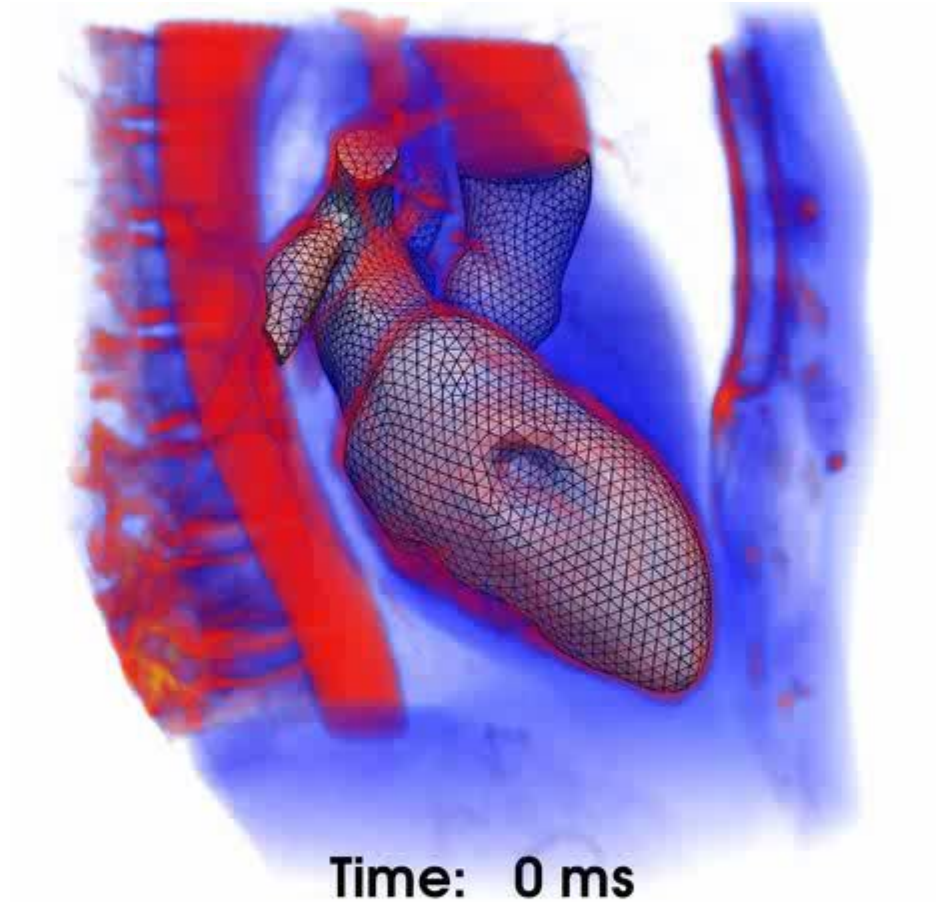


Chnafa et al., Comp. & Fluids, 2014

4D MESH FROM MEDICAL IMAGING



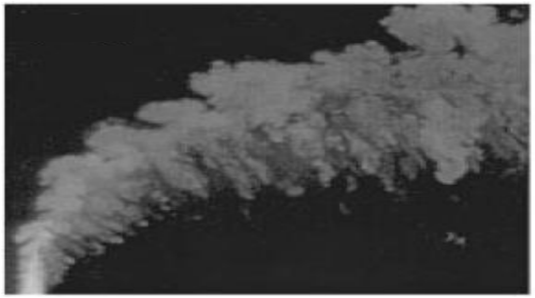
Aorta from CT scan
(Moreno – CHU Toulouse)

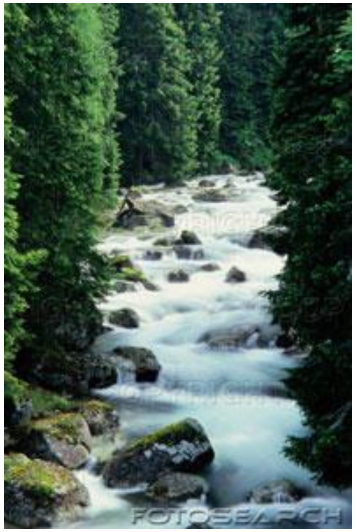


Left heart from CT scan
(Chnafa – I3M Montpellier)

About turbulence

- Turbulence is present in most of the flows met in the everyday life (clouds, shore breaks, wind, airplane wakes, …)





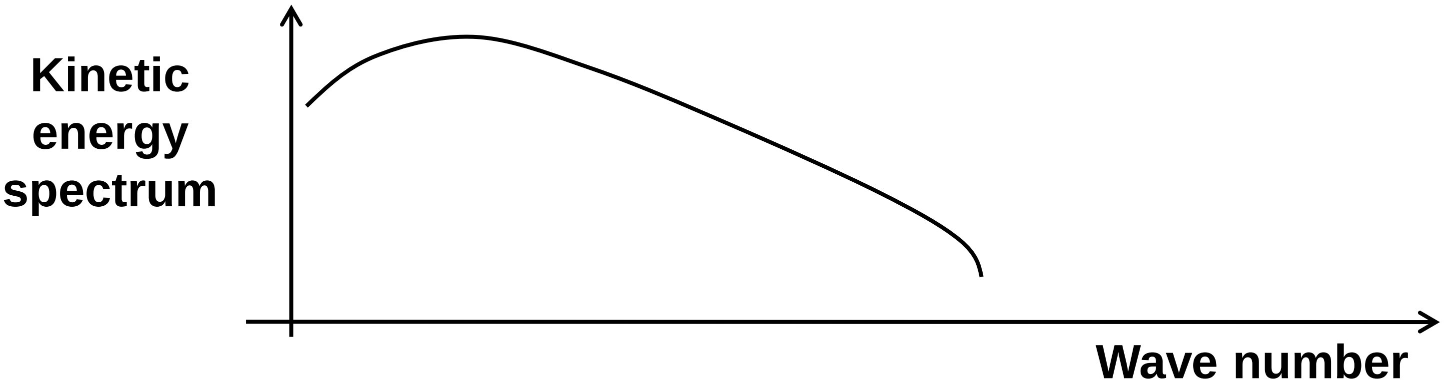
ABOUT TURBULENCE

- Turbulence is present in most of the flows met in the everyday life (clouds, shore breaks, wind, …)

IS TURBULENCE PRESENT IN

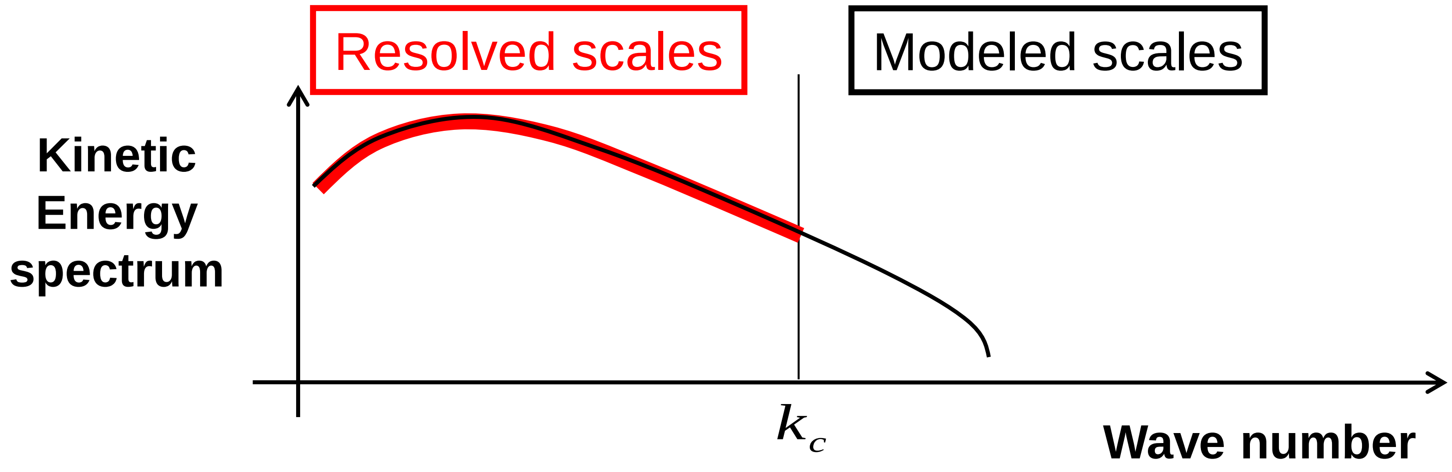
CARDIAC HEMODYNAMICS ??

MODELING TURBULENCE



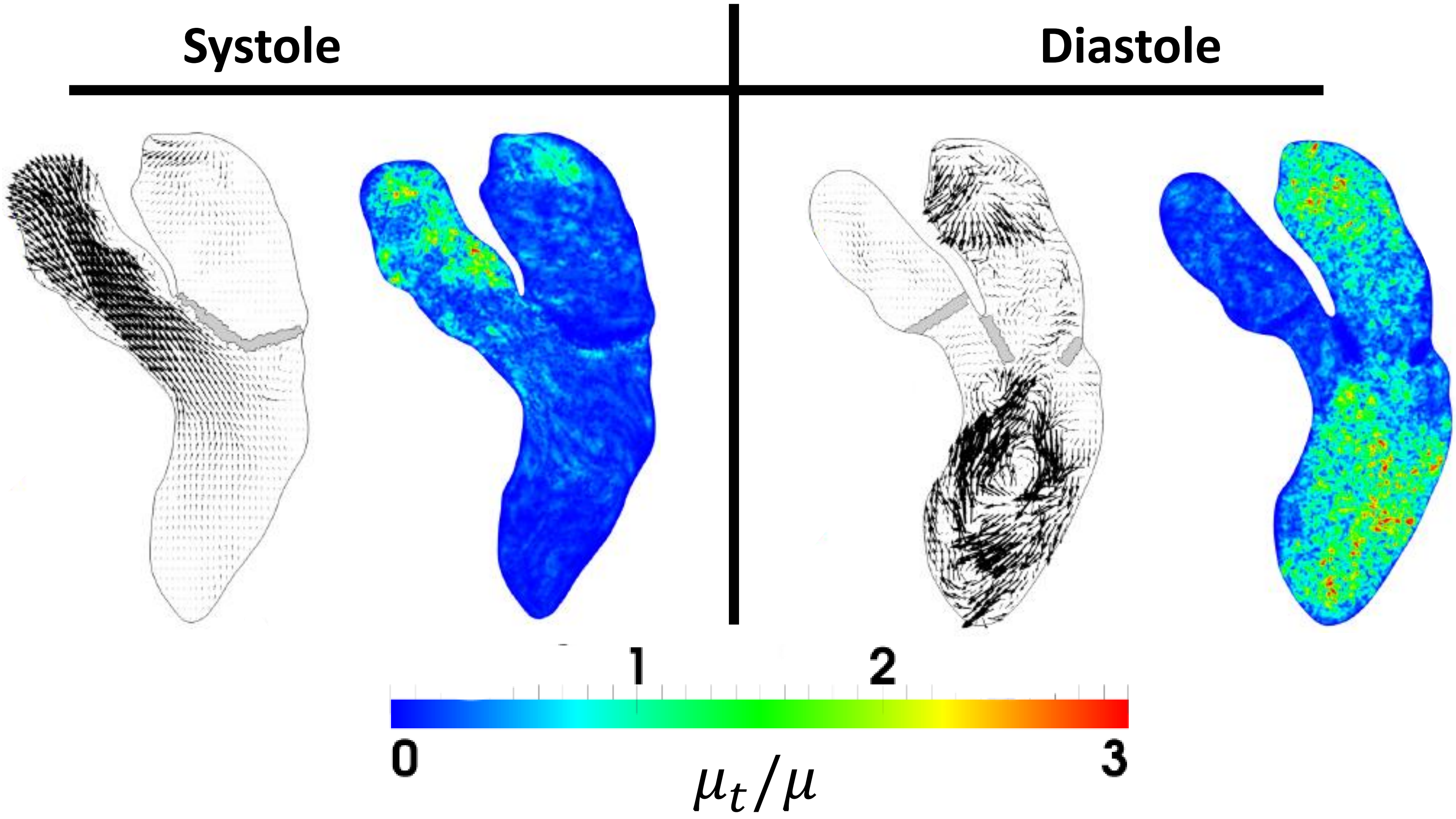
- Direct Numerical Simulation
  - Solve all the scales - No model required
  - complexity increases like (Reynolds number)$^{9/2}$
- Reynolds-Averaged Navier-Stokes
  - Model all the scales (e.g.: k-ε model)
  - Hardly predictive; no suitable for transitional flows
- **Large-Eddy Simulation offers an alternative view**

LARGE-EDDY SIMULATION



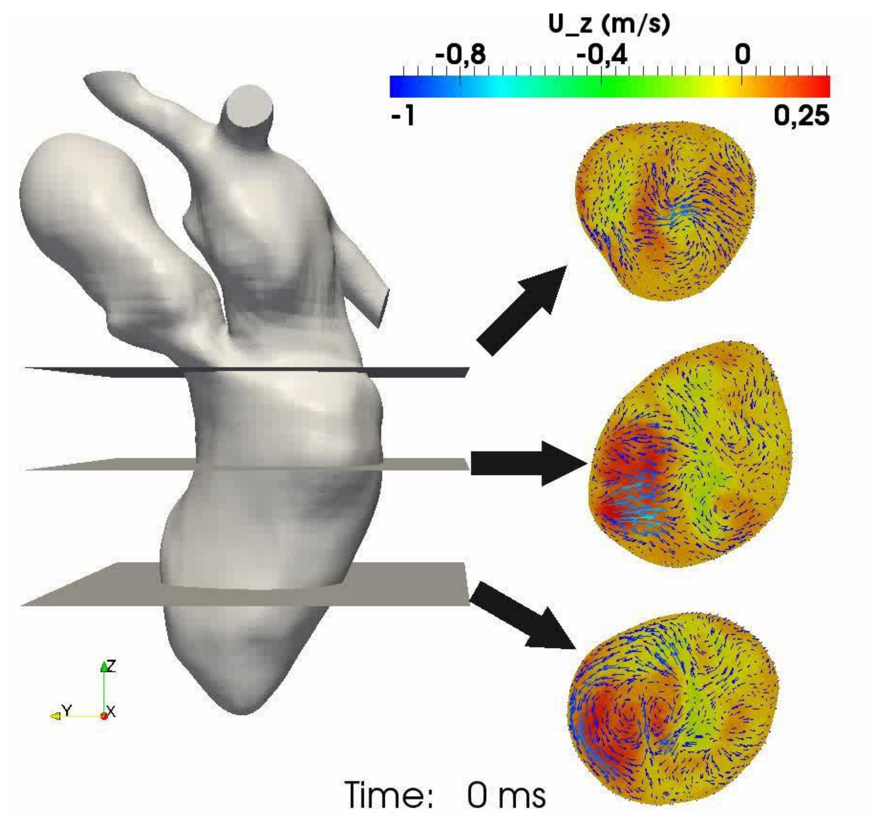
- The filtered Navier-Stokes equations are solved
  - The largest scales are computed directly
  - The smallest scales (subgrid scales) are modeled so that their effect on the largest scales dynamics is accounted for
- Requires an efficient, HPC compatible and low dissipative flow solver.
- YALES2BIO (www.math.univ-montp2.fr/~yales2bio) gathers these properties

SUBGRID SCALE VISCOSITY

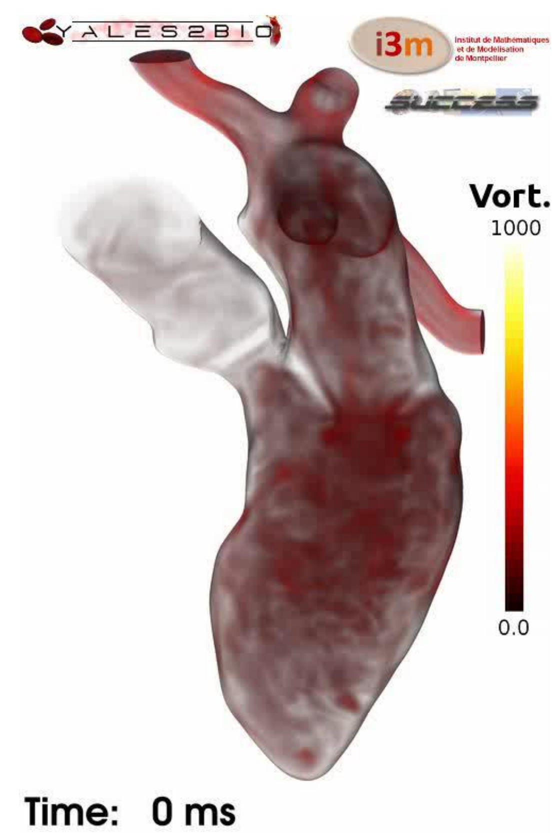


Sigma model (Nicoud et al., 2011)

FLOW VISUALIZATION



In-plane and vertical velocity



Vorticity modulus

Chnafa et al., Comp. & Fluids, 2014; Chnafa et al., Ed. A. Quarteroni, 2014

Flow visualization

The **Q-criterion** allows visualizing vortices in the blood flow. The point of view is also rotation around the heart in the movie.

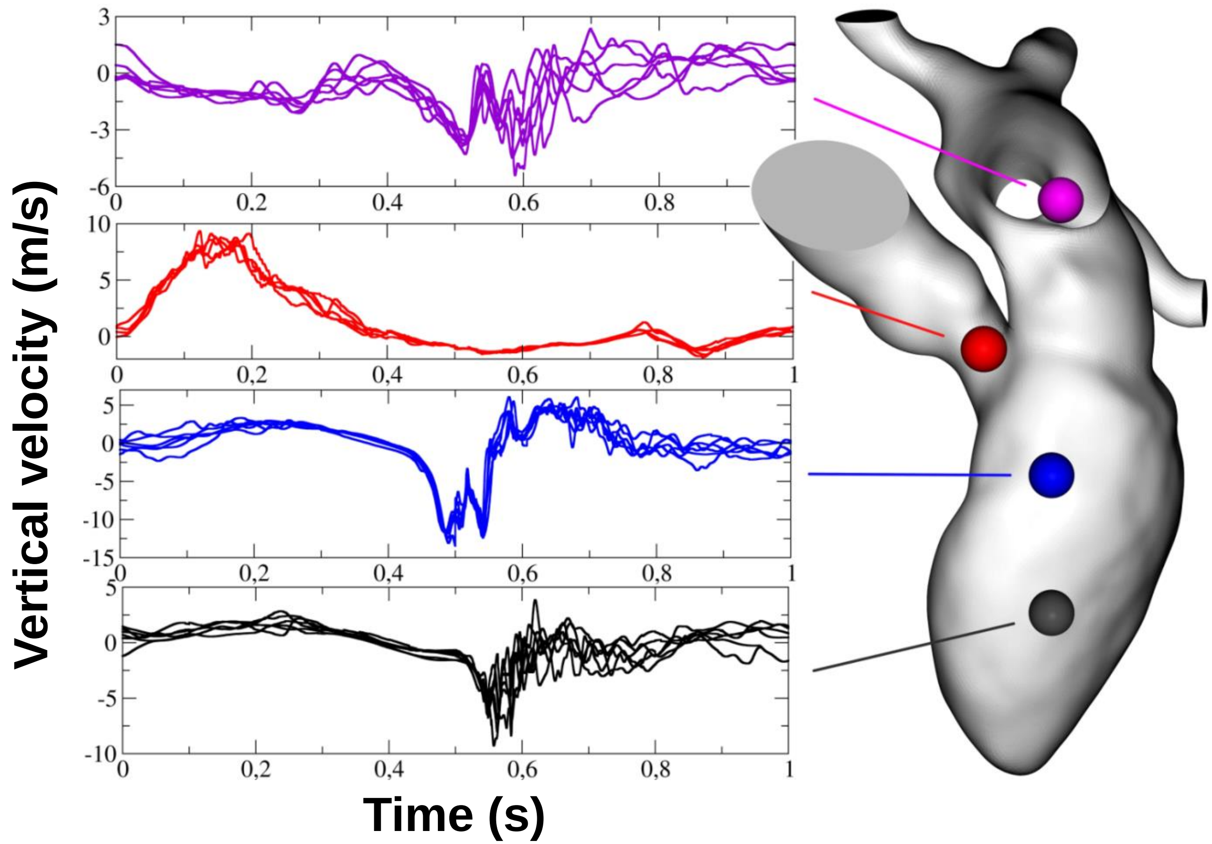
$$Q = \frac{1}{2}(\Omega^2 - S^2)$$

(Jeong & Hussain 1995)

Chnafa et al., TSFP, 2013

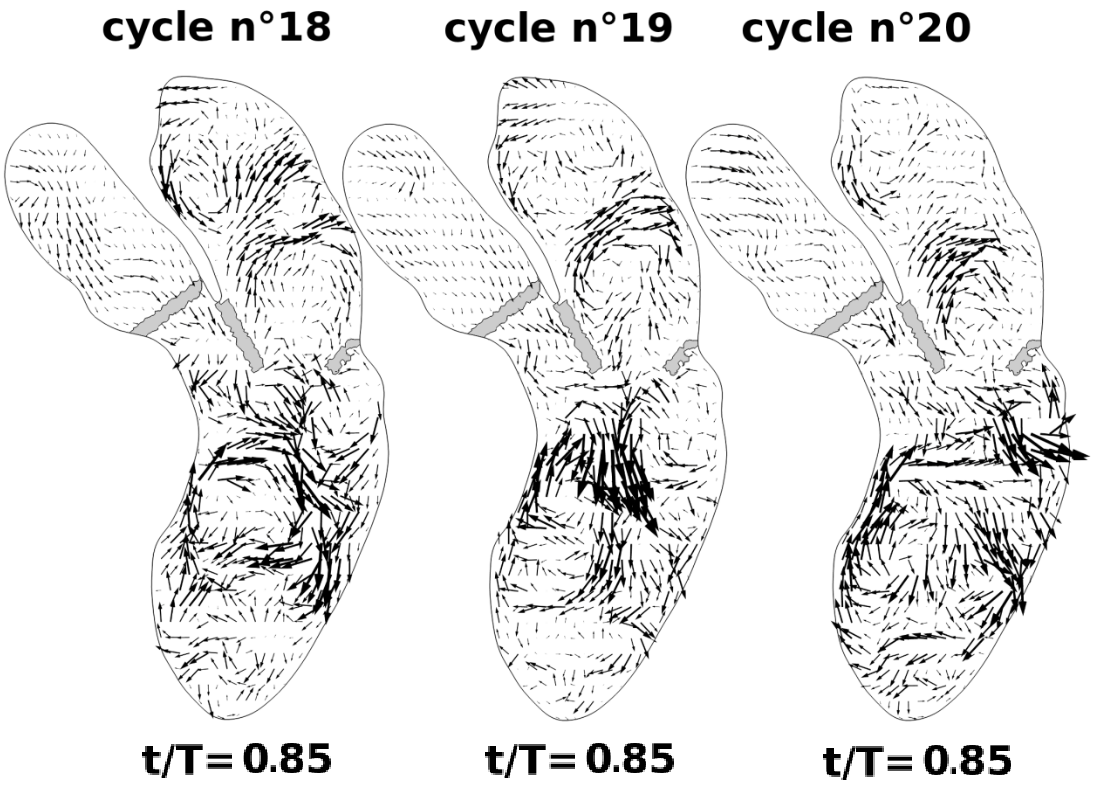
CYCLE TO CYCLE VARIATIONS

- Approx. **50 cycles** were computed
- **Vertical velocity at four probes over 6 cardiac cycles**



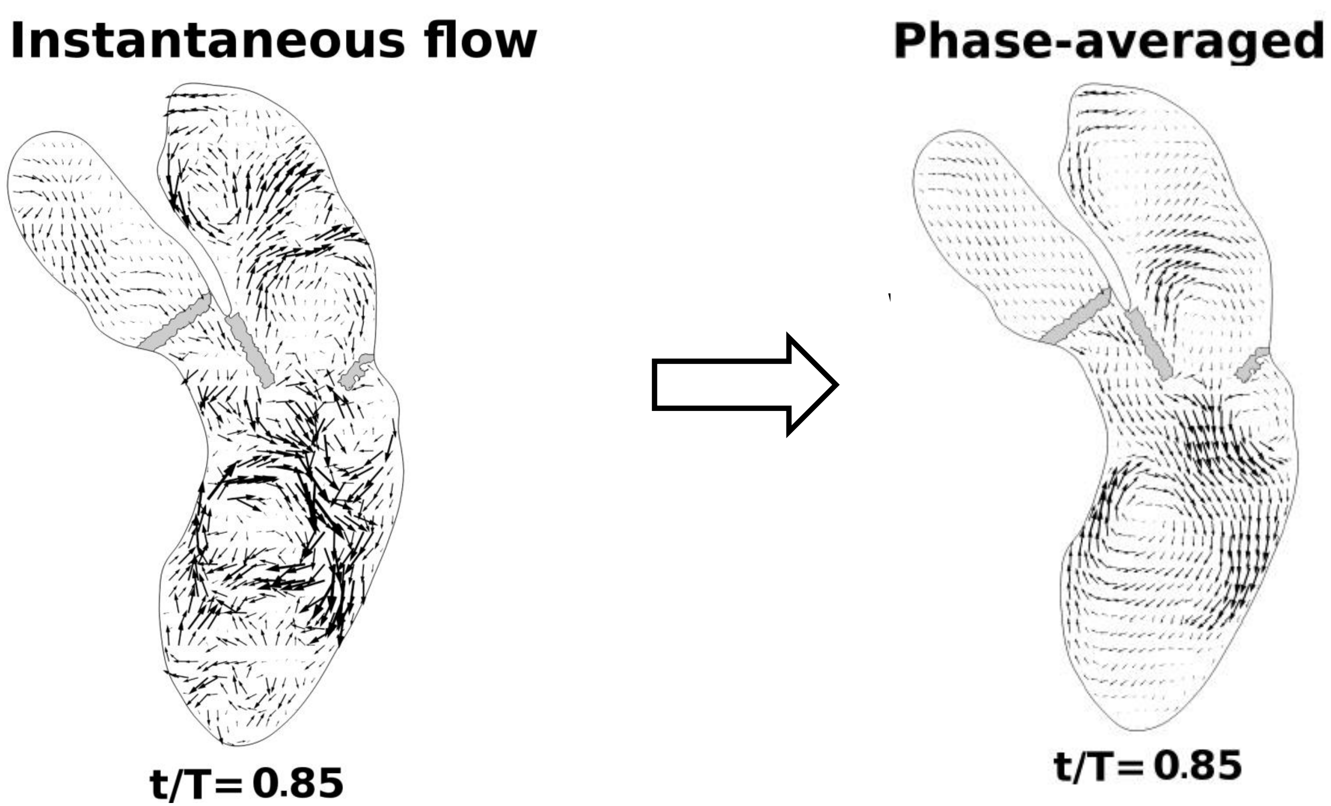
CYCLE TO CYCLE VARIATIONS

- Approx. **50 cycles** were computed
- **Velocity vectors at the same instant at 3 different cycles**



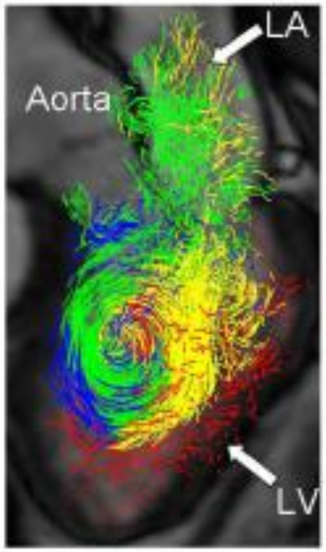
PHASE-AVERAGED FLOW

- Turbulence is not only randomness
- Phase-averaging the numerical results allows retrieving a large recirculation zone within the left ventricle

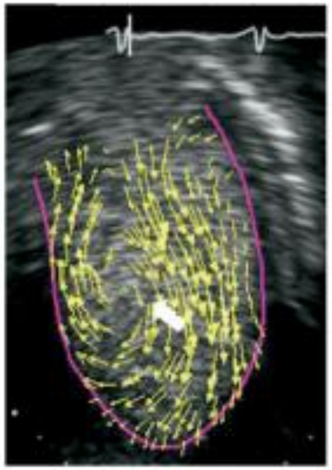


PHASE-AVERAGED FLOW

- Phase-averaging the numerical results allows retrieving a large recirculation zone within the left ventricle
- Coherent with observations from medical images

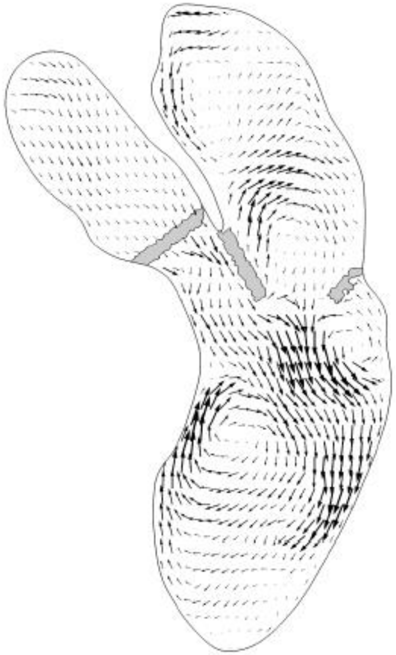


MRI
Eriksson et al.
Eu. Heart J. (2012)



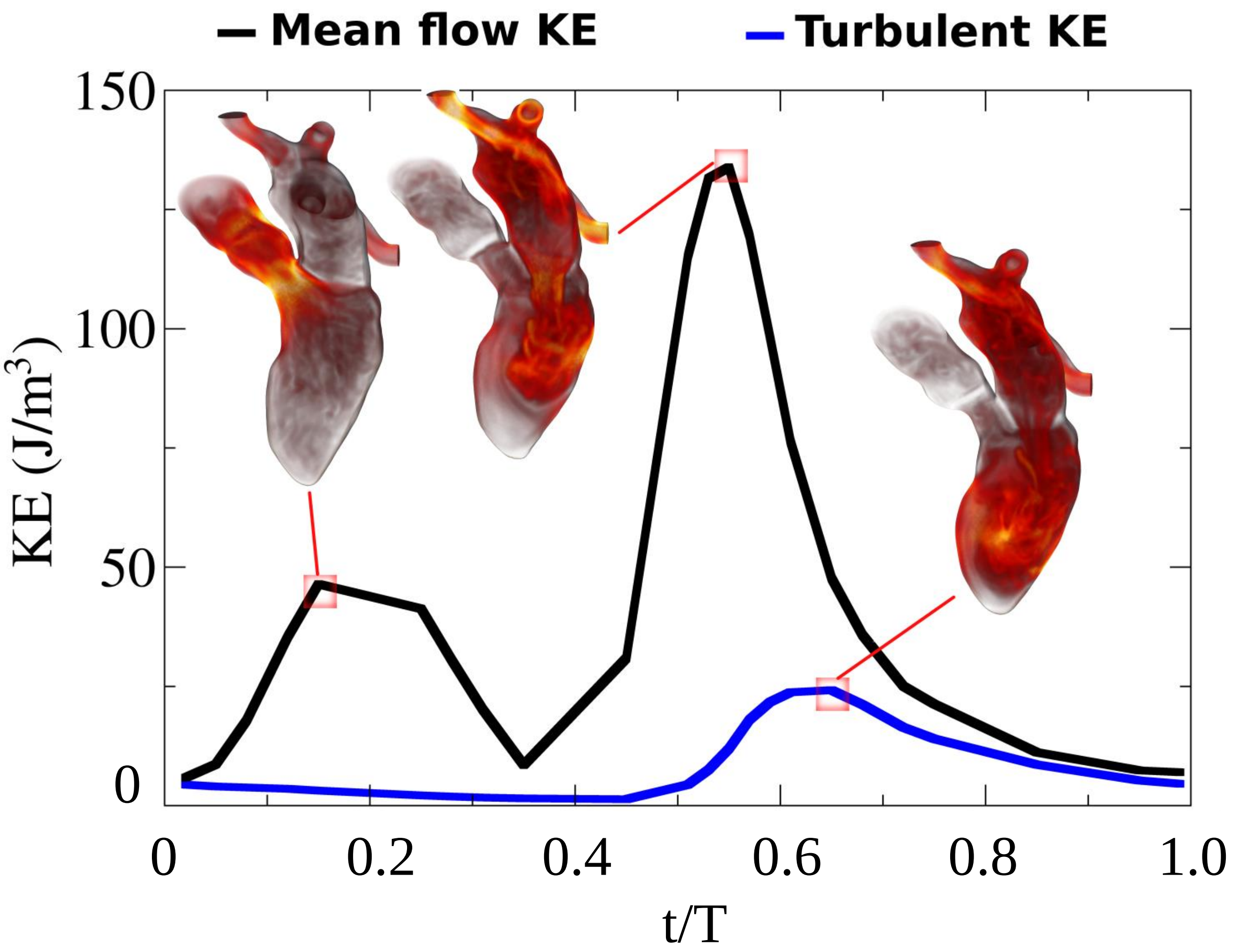
Echocardiography
Hong et al.
Cardio. Imag. (2008)

Phase-averaged



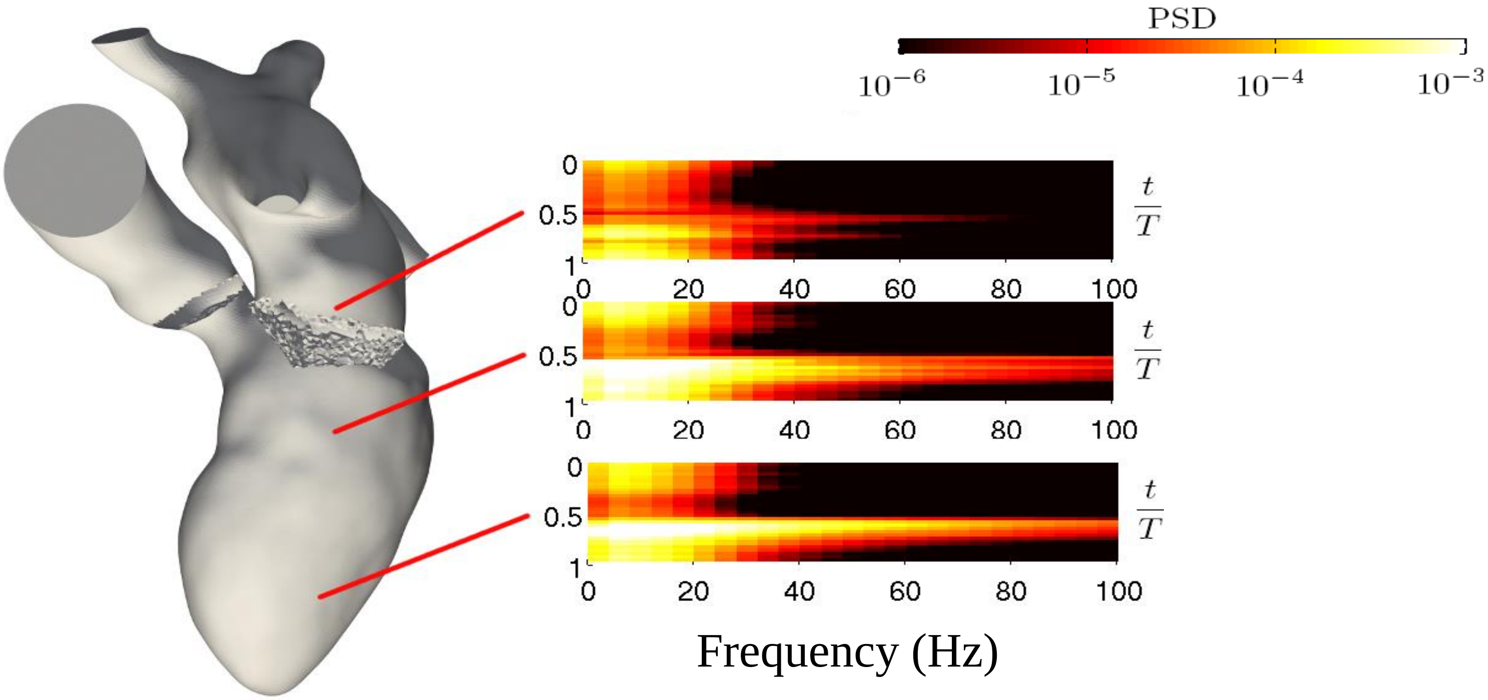
t/T= 0.85

KINETIC ENERGY IN THE VENTRICLE



- **The KE of the mean flow large at early systole and diastole**
- **The KE of the fluctuations large at late diastole**
- **Intensity of the fluctuations of order 30 % at late diastole**

TIME-FREQUENCY ANALYSIS



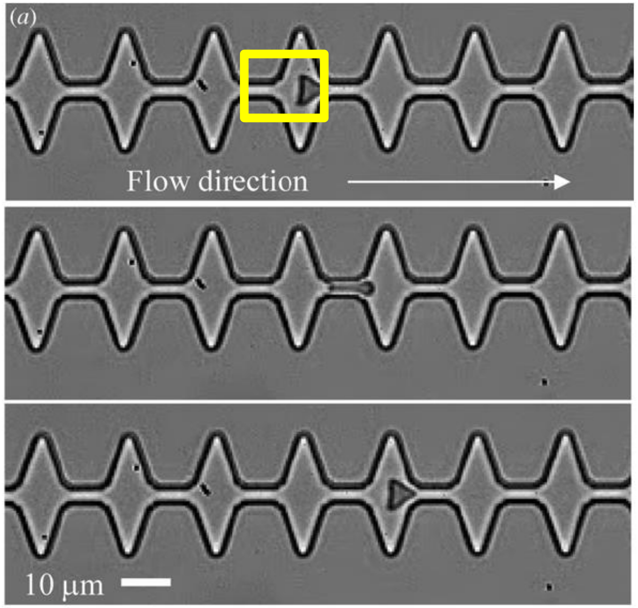
- **The spectra show activity over a much wider frequency range at late diastole**
- **Looks pretty much like intermittent turbulence**
- **Only LES (or DNS but not RANS) can be predictive in this situation**

OUTLINE

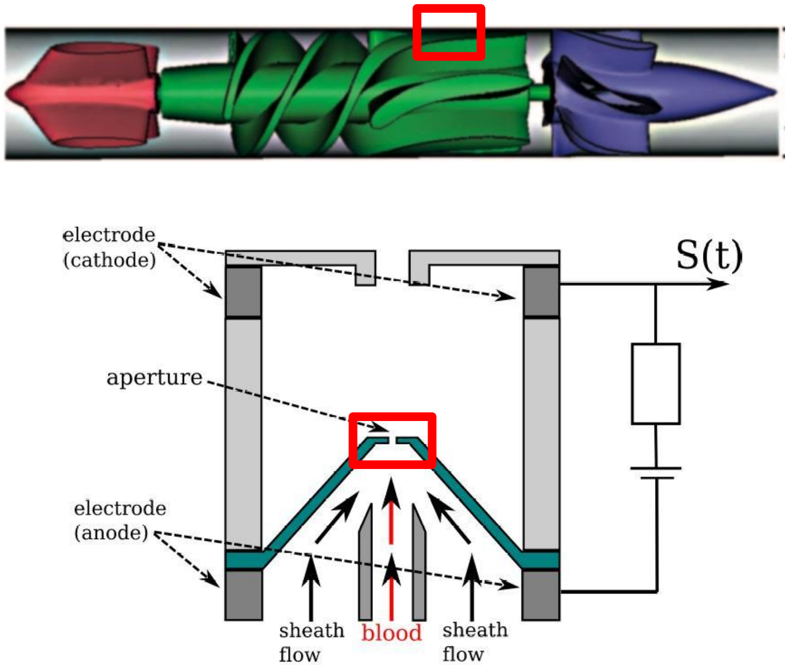
- Transitional hemodynamics in a realistic heart
- **Fluid-structure interaction for Micro-scale computations**
- Fluid-structure interaction for Macro-scale computations

MICRO-SCALE COMPUTATIONS

- **Objective: Red blood cells under flows**
  - in complex domains
  - and at « high » Reynolds number



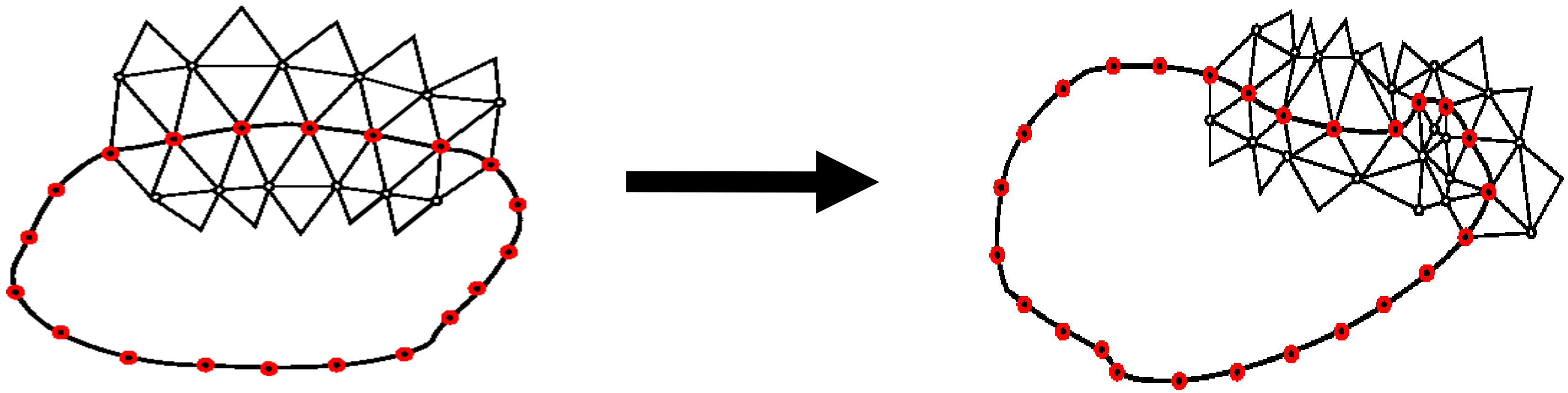
Abkarian et al. BM 2008



Isèbe & Nérin IJNMBE 2013

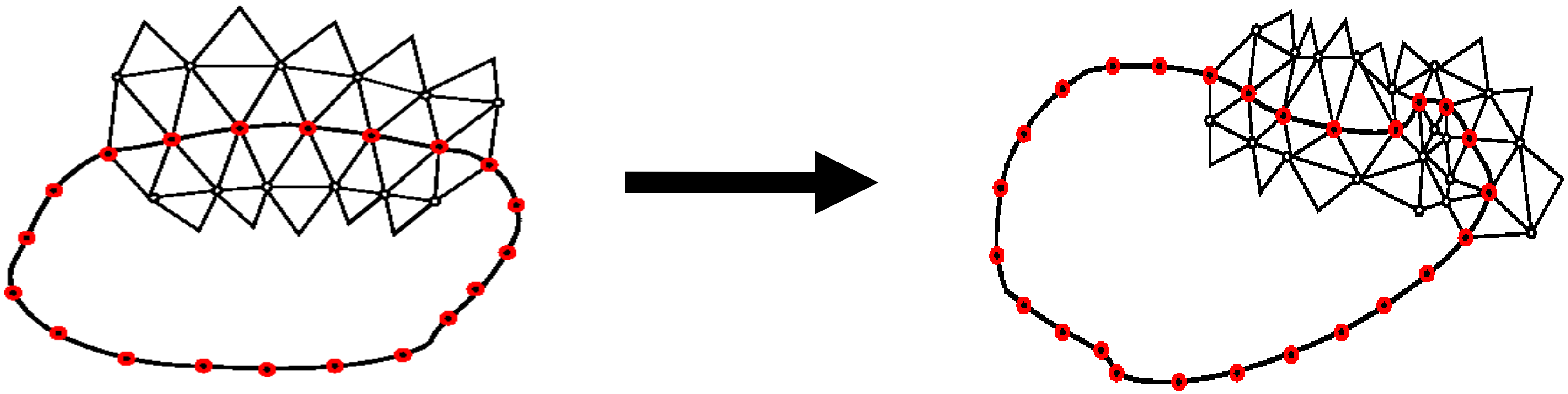
WHICH METHOD ?

t **Conforming mesh method** t + Δt

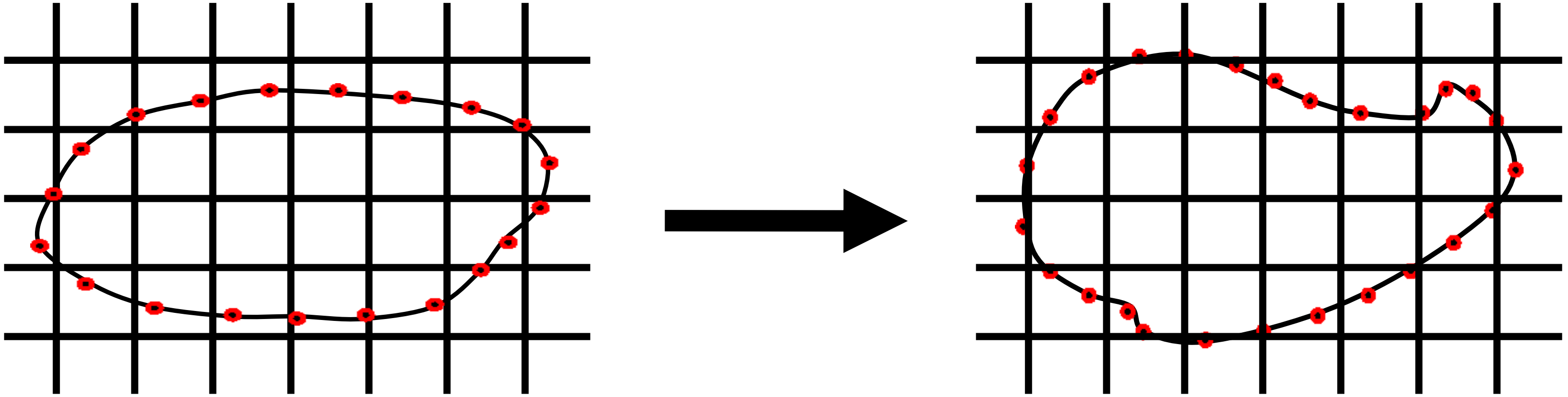


WHICH METHOD ?

t **Conforming mesh method** **t + Δt**



Non-conforming mesh method

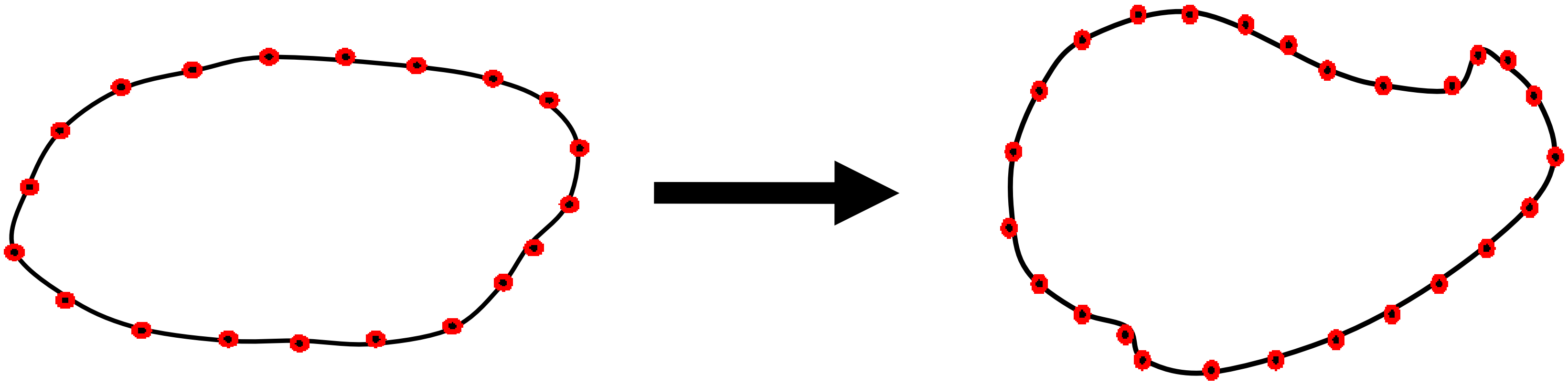


FRONT-TRACKING – IMMERSED BOUNDARIES

- Membrane discretized by Lagrangian markers
  - ✓ massless membrane
  - ✓ convected by the fluid velocity

$$\frac{d\overrightarrow{x_m}}{dt} = \overrightarrow{u_f}$$

- From the membrane position: forces applied on the fluid



Peskin 1972, 2002, Unverdi & Tryggvason 1992, Bagchi et al.

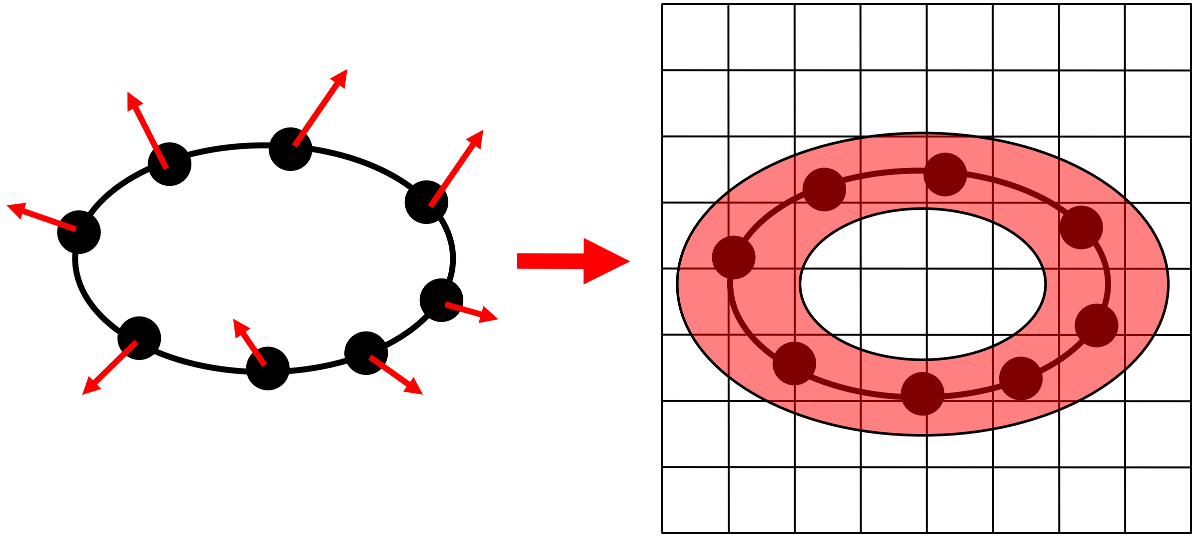
FRONT-TRACKING – IMMERSED BOUNDARIES

- Navier-Stokes forced by the membrane forces

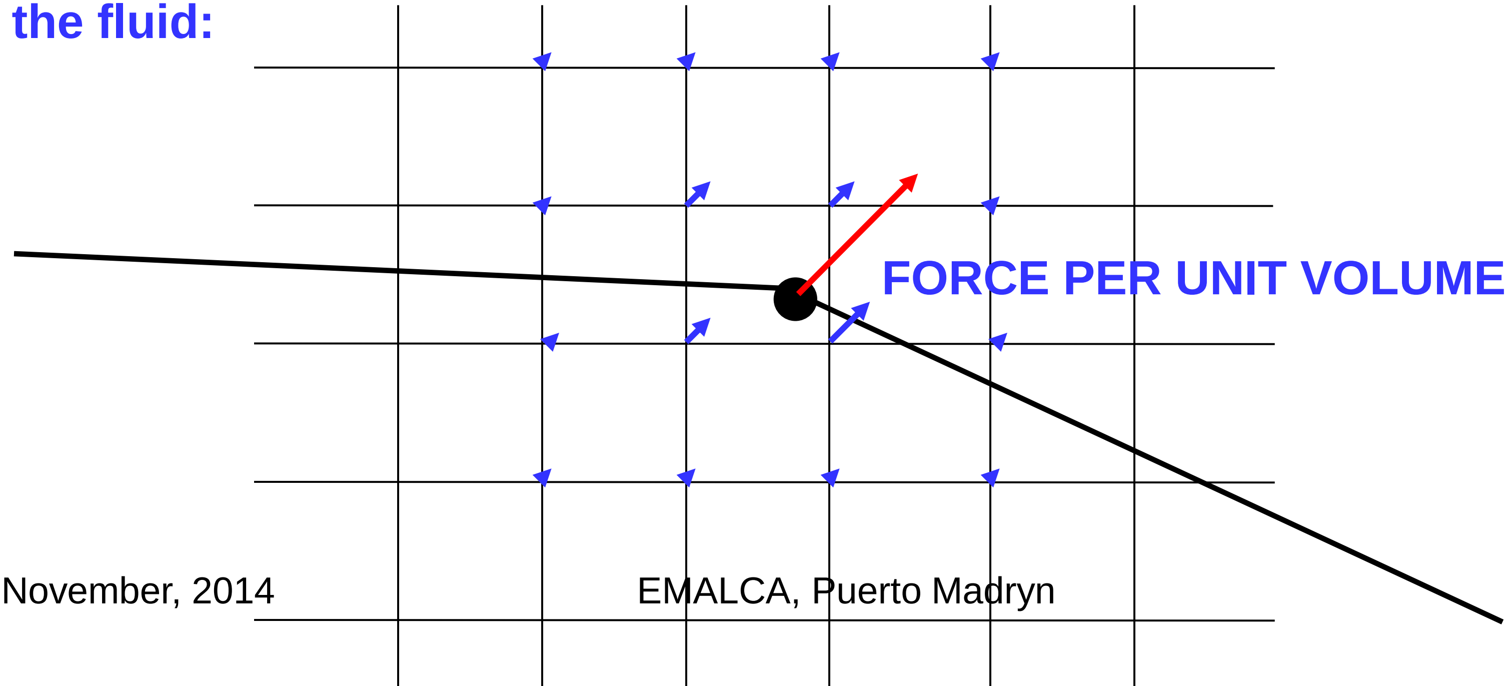
$$\underbrace{\frac{\partial u_i}{\partial t} + u_j \frac{\partial u_i}{\partial x_j} = -\frac{1}{\rho}\frac{\partial p}{\partial x_i} + \frac{\partial}{\partial x_j}\left[\nu\left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i}\right)\right]}_{\text{Navier-Stokes}} + \sum_m f_i^m$$

- To each marker on the membrane corresponds a Dirac force which must be properly accounted for when solving for the fluid

REGULARIZATION



For the fluid:



IMMERSED BOUNDARY METHOD

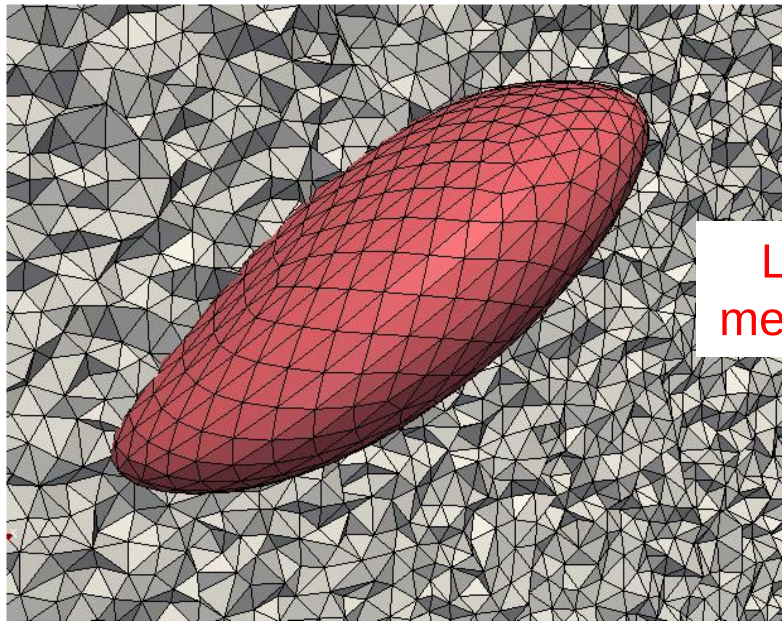
Navier-Stokes eqs
+
Membrane forces

REGULARIZATION

Membrane forces

Finite volumes

Eulerian fluid grid



Lagrangian membrane grid

Finite elements

Fluid velocity

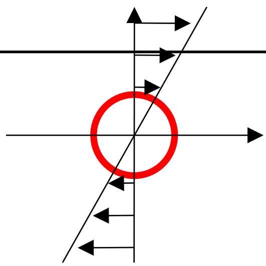
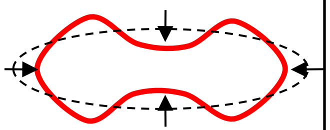
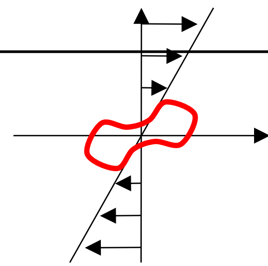
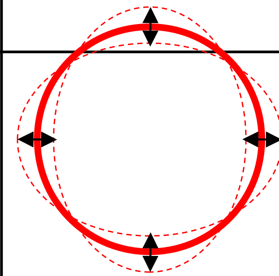
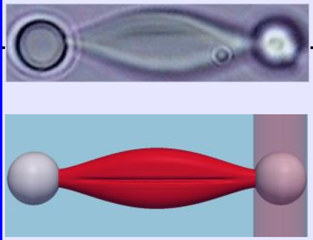
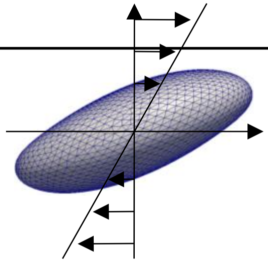
INTERPOLATION

Mechanical laws
+
Membrane displacements

Peskin, AM 2002, Charrier et al. JSA 1993, Eggleton & Poppel PF 1998, Pinelli et al. JCP 2011, Yazdani & Bagchi JFM 2013

VALIDATIONS

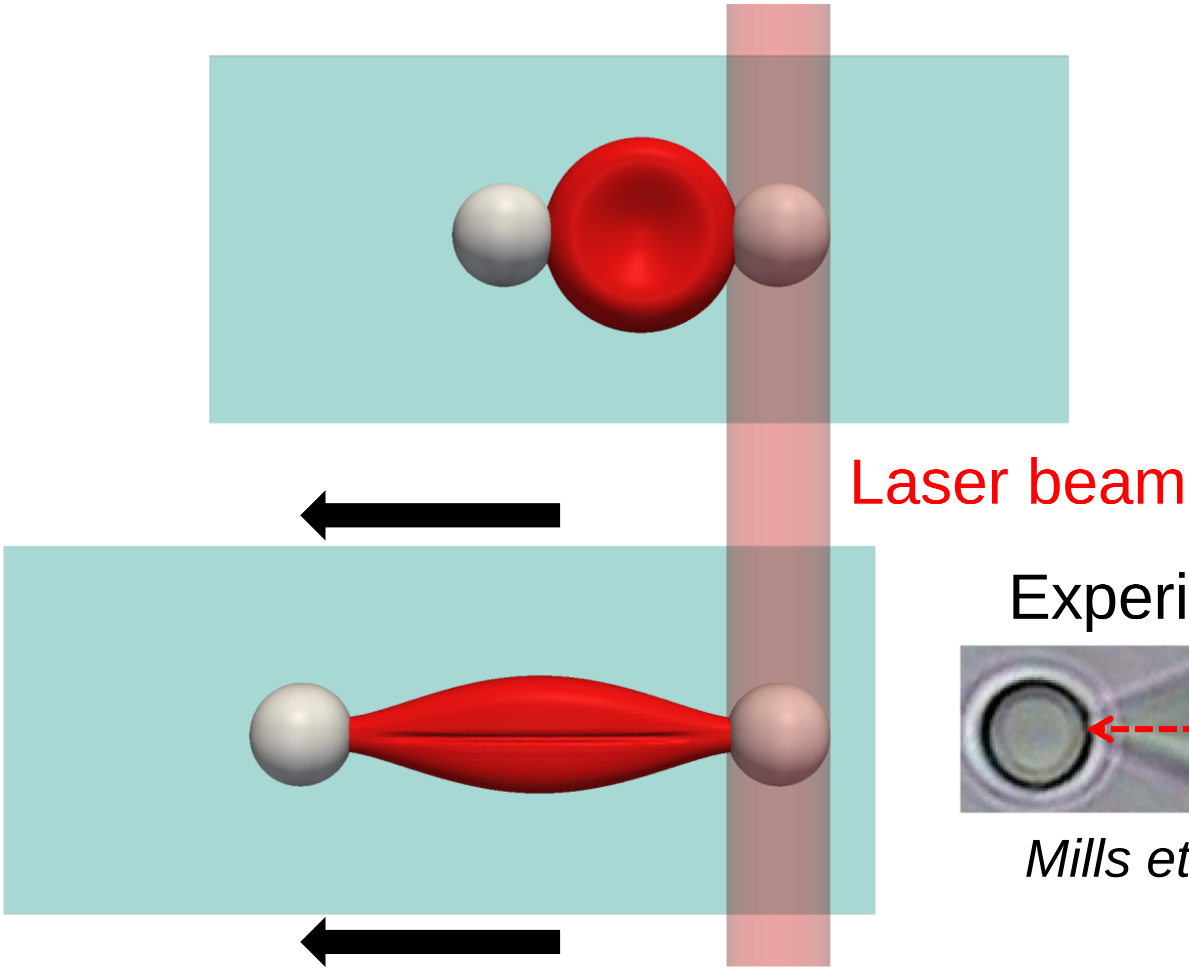
2D | 3D

Capsules in simple shear flow	Equilibrium shapes of vesicles	Vesicles in simple shear flow	Damped oscillations of capsules	Red cells stretched by optical tweezers	Capsules in simple shear flow
					
Breyiannis et al., TCFD 2000, Woolfenden 2010	Veerapaneni et al, JCP 2009, Laadhari 2011	Veerapaneni et al, JCP 2009, Beaucourt et al, PRE 2004 …	Martins Afonso et al, 2014	Dao et al, JMPS 2003 Mills et al MCB 2004	Lac et al JFM 2004, Walter et al IJNME 2010…

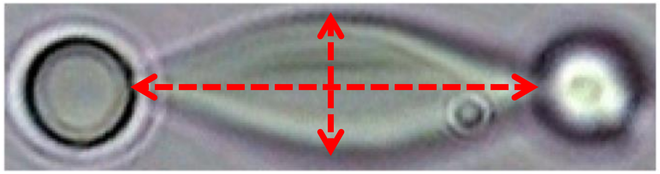
Mendez, Gibaud & Nicoud, J. Comp. Physics, 2014, ; Martins Afonso, Mendez & Nicoud, J. Fluid Mech., 2014

Optical tweezers: principle

Measurement apparatus for cell mechanics



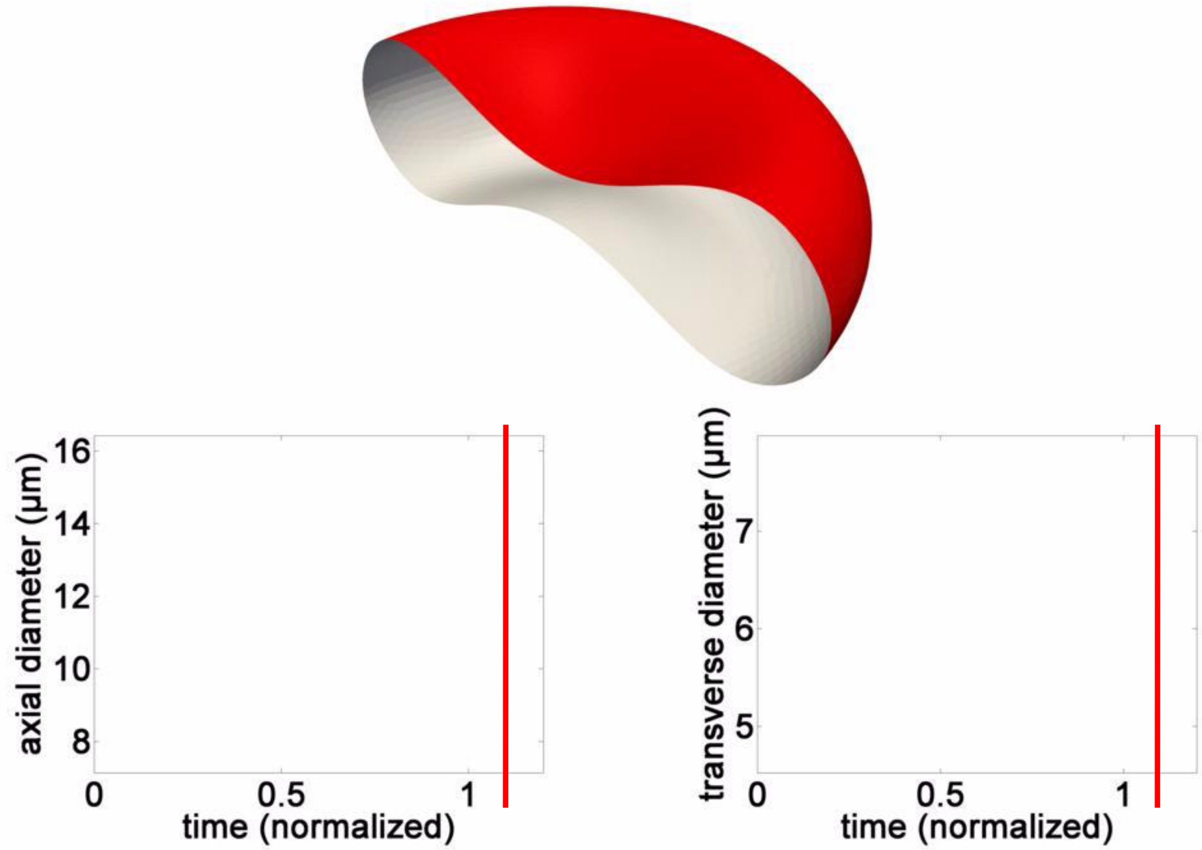
Experimental image



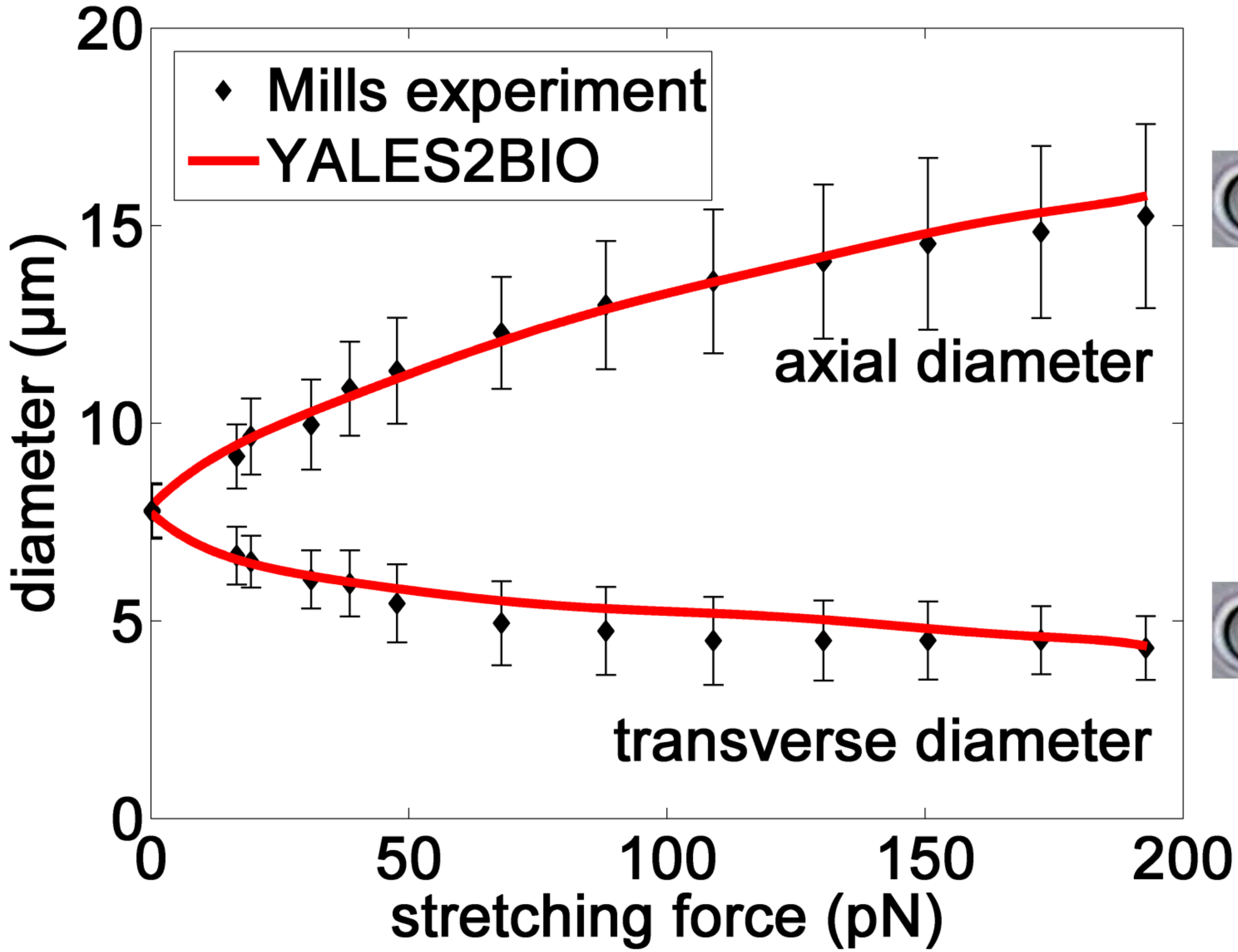
Mills et al MCB (2004)

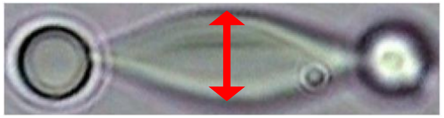
OPTICAL TWEEZERS: SIMULATION

- Biconcave red blood cell
- Mechanical properties modeled with a Skalak law (Es = 3.7 µN/m)

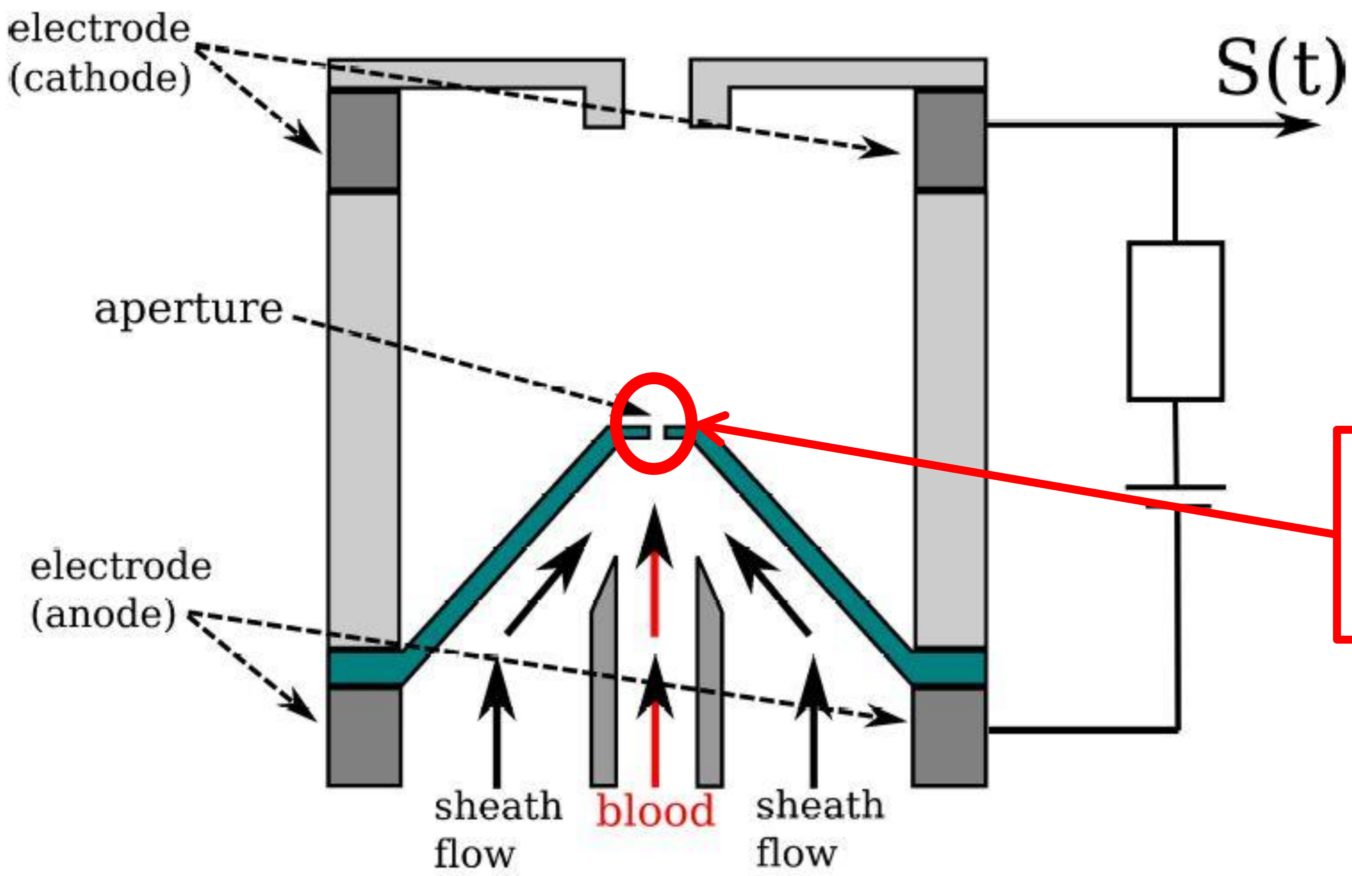


Optical tweezers: results





APPLICATION TO SIZING IN A CYTOMETER

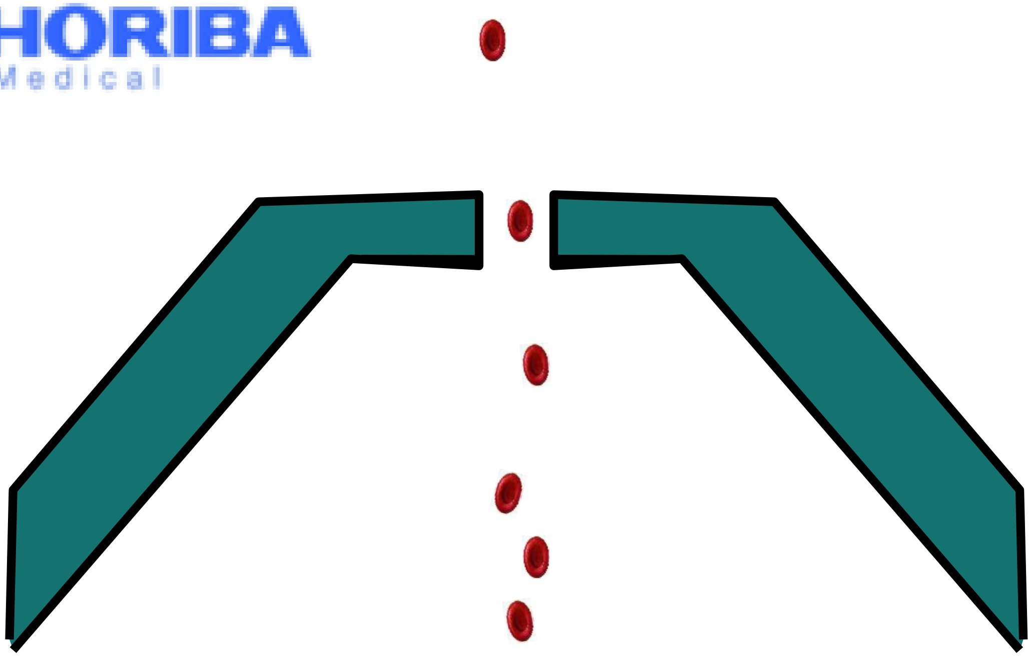


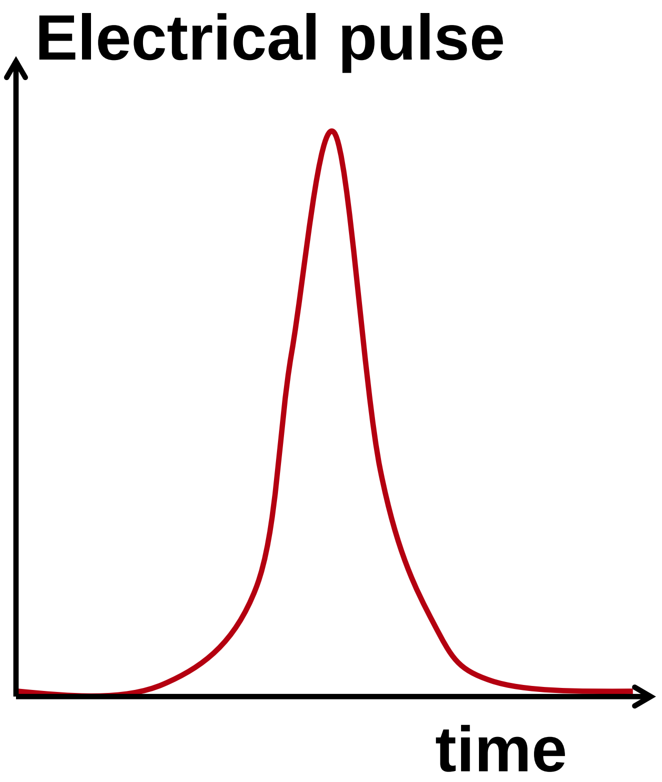
Region of interest

Re ~ 300
in a 50µm aperture

APPLICATION TO SIZING IN A CYTOMETER

HORIBA Medical



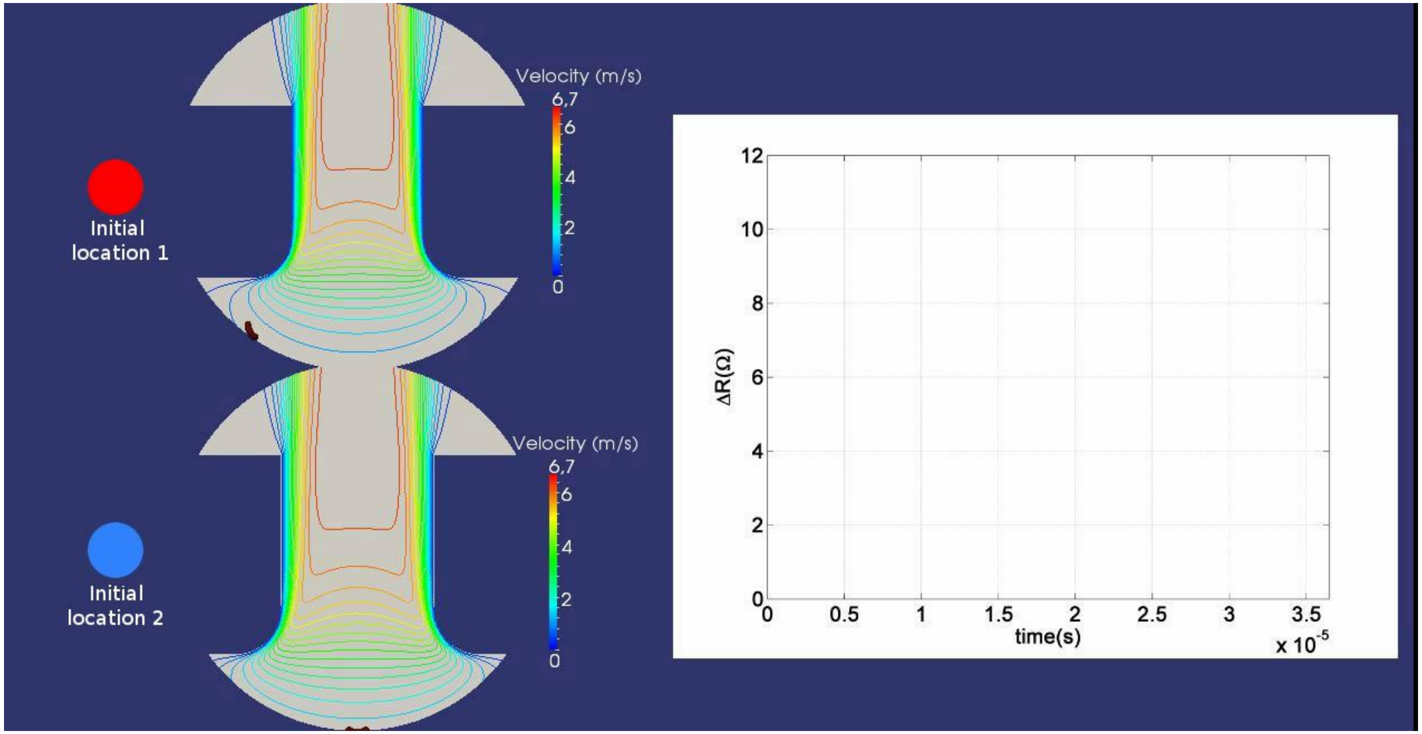


Counting: 1 pulse = 1 red blood cell

Sizing: Pulse size ~ Cell volume

INFLUENCE OF THE CELL TRAJECTORY

2 identical cells at 2 different initial locations



Movie by E. Gibaud (PhD student at I3M)

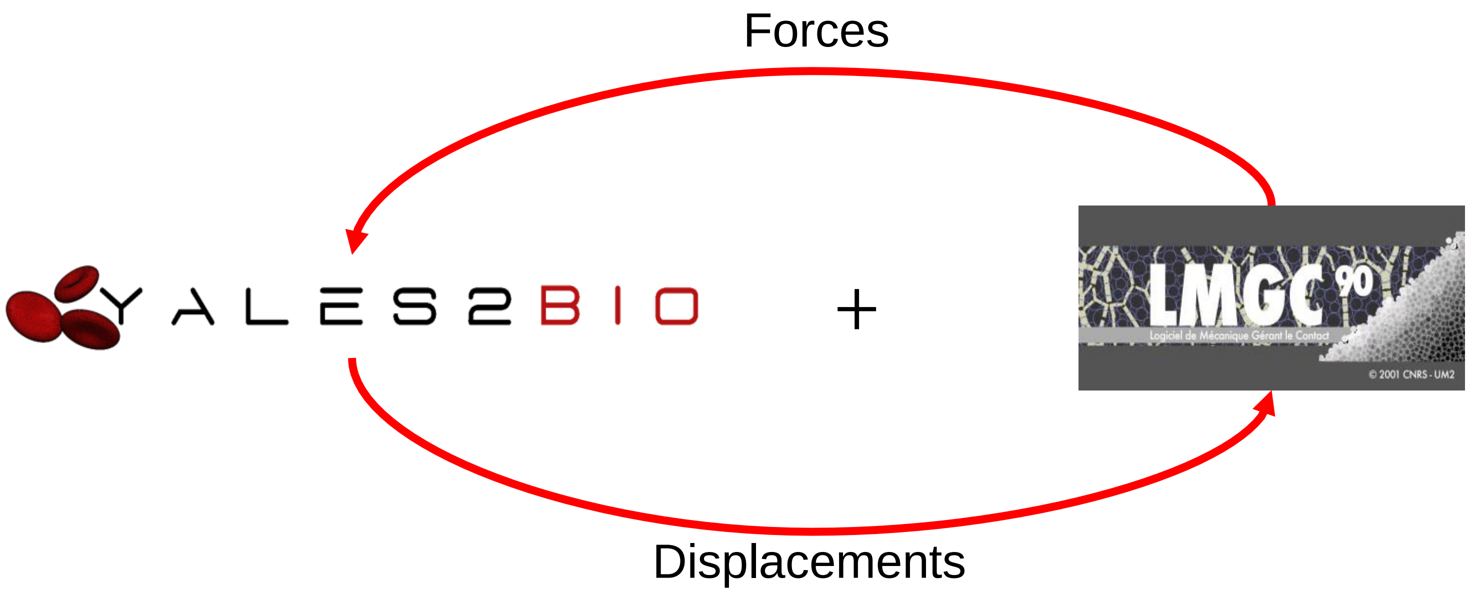
Pulse characteristics are not related only to Cell volume

OUTLINE

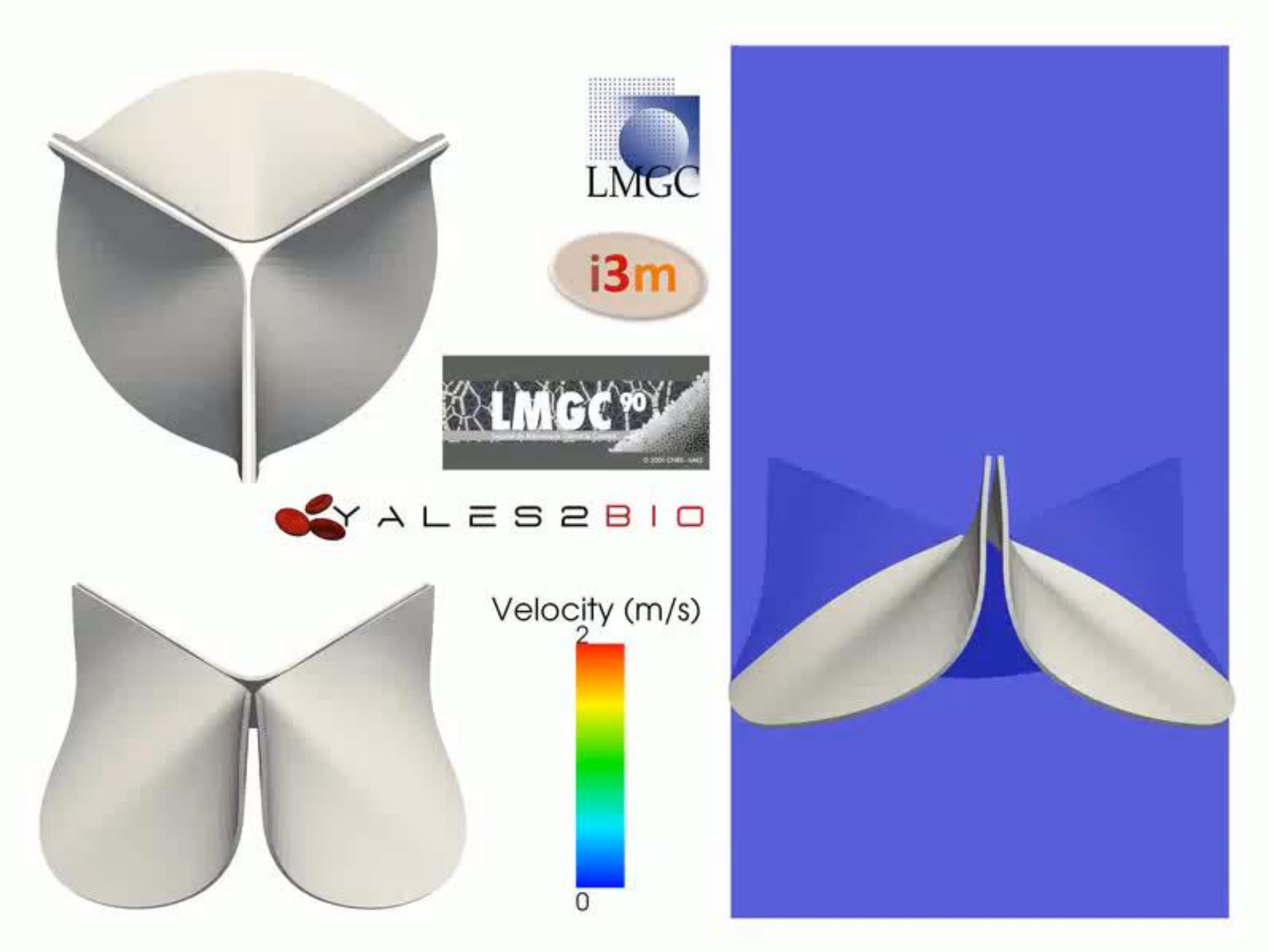
- Transitional hemodynamics in a realistic heart
- Fluid-structure interaction for Micro-scale computations
- **Fluid-structure interaction for Macro-scale computations**

ABOUT ARTIFICIAL ORGANS

- To be able to represent complex thin membranes (viscoelasticity, contact), a dedicated solid mechanics solver should be used
- Keeping the same numerical strategy (FT-IBM), the YALES2BIO fluid solver was coupled to the LMGC90 solver for complex rheology and contact (work with the LMGC lab in Montpellier)



Example with aortic valve



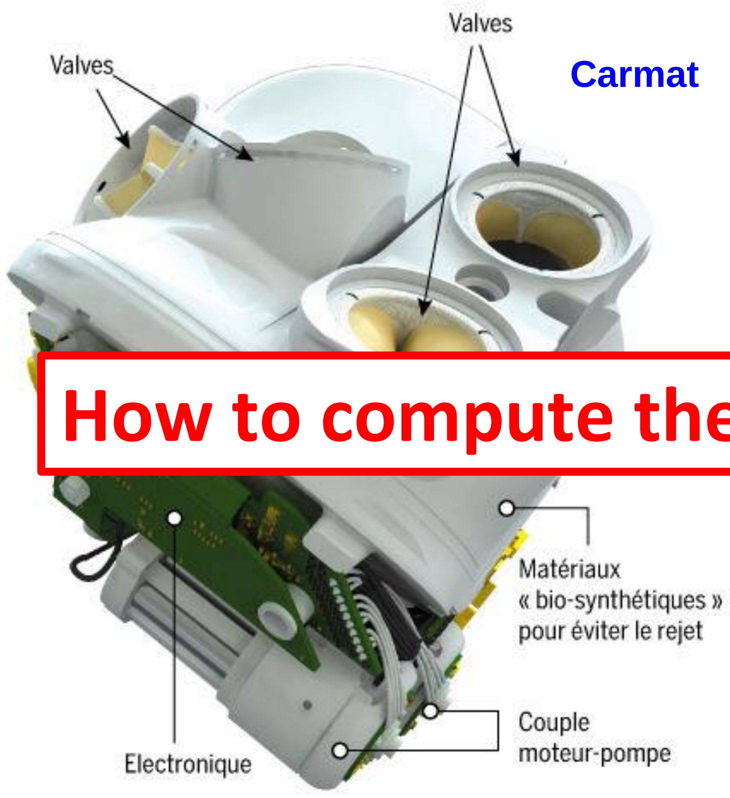
Movie by J. Sigüenza (PhD student at I3M)

AN ARTIFICIAL HEART

Syncardia heart (Slepian et al., J. Biomech. 2013)

Abiocor, Carmat hearts,…

Carmat

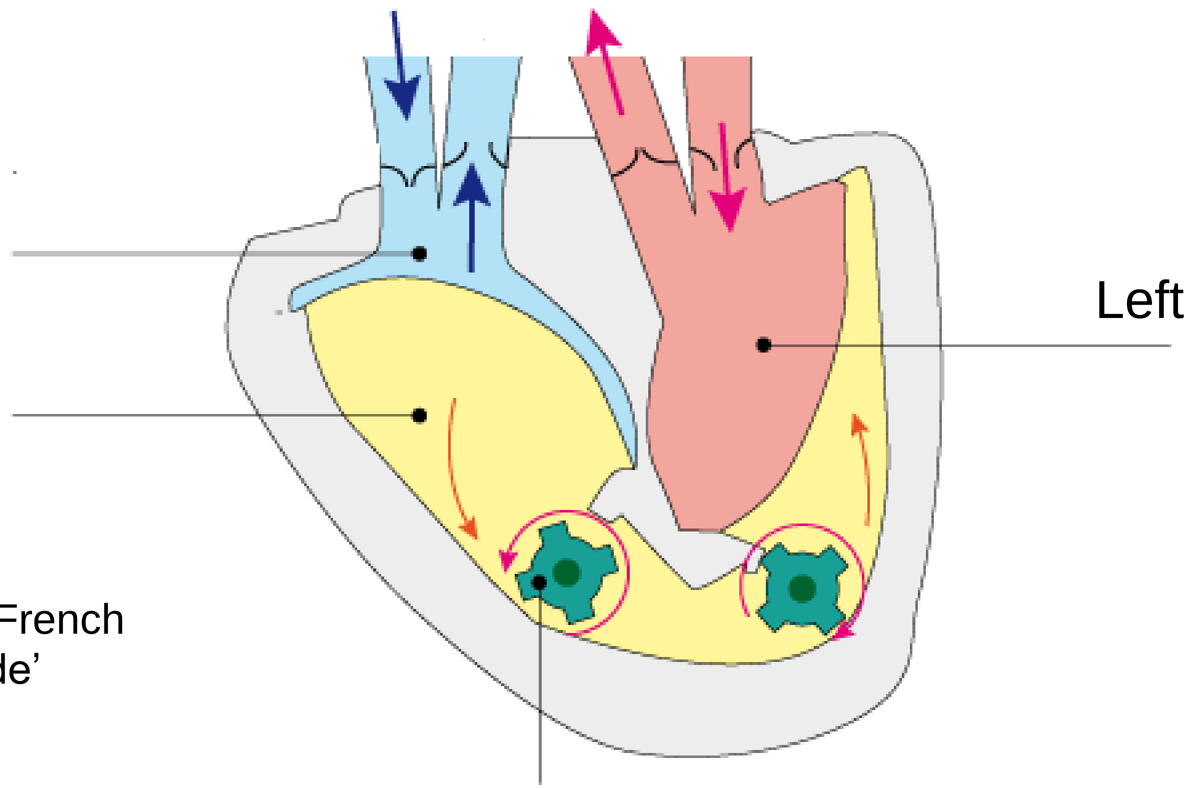


How to compute the flow in these systems?

An artificial heart

Syncardia heart (Slepian et al., J. Biomech. 2013)

Carmat heart

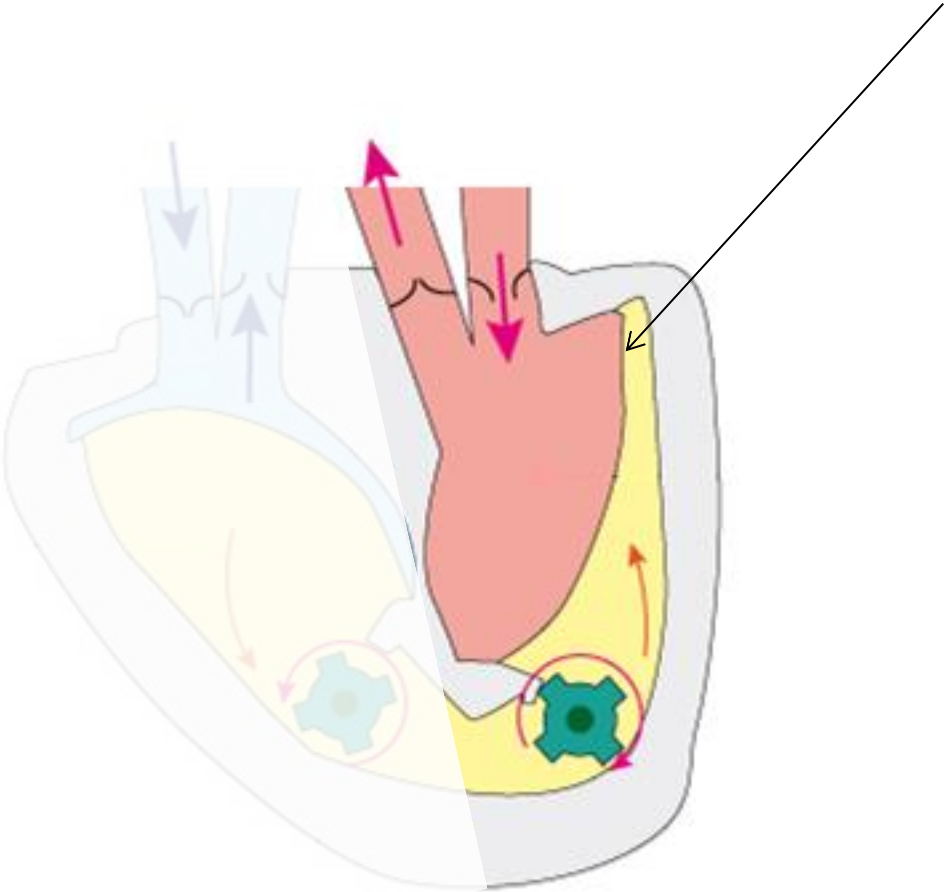


Schematic from the French newspaper 'Le Monde'

INFOGRAPHIE LE MONDE

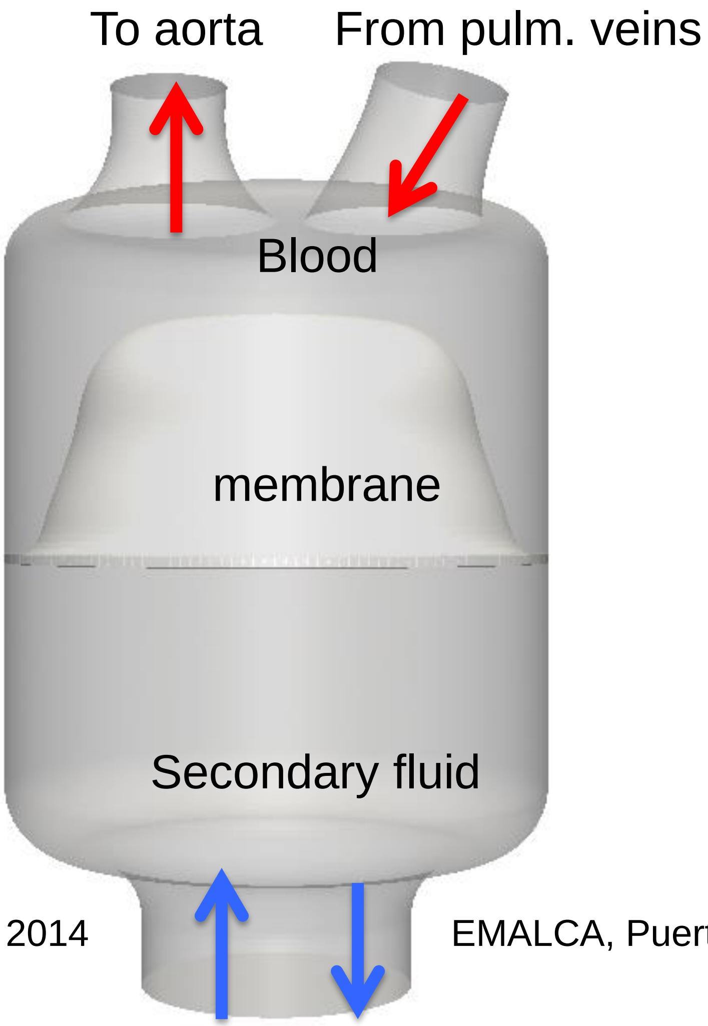
HALF AN ARTIFICIAL HEART

A first attempt in half the system: unstructured LES + flexible membrane



SIMPLIFYING THE GEOMETRY

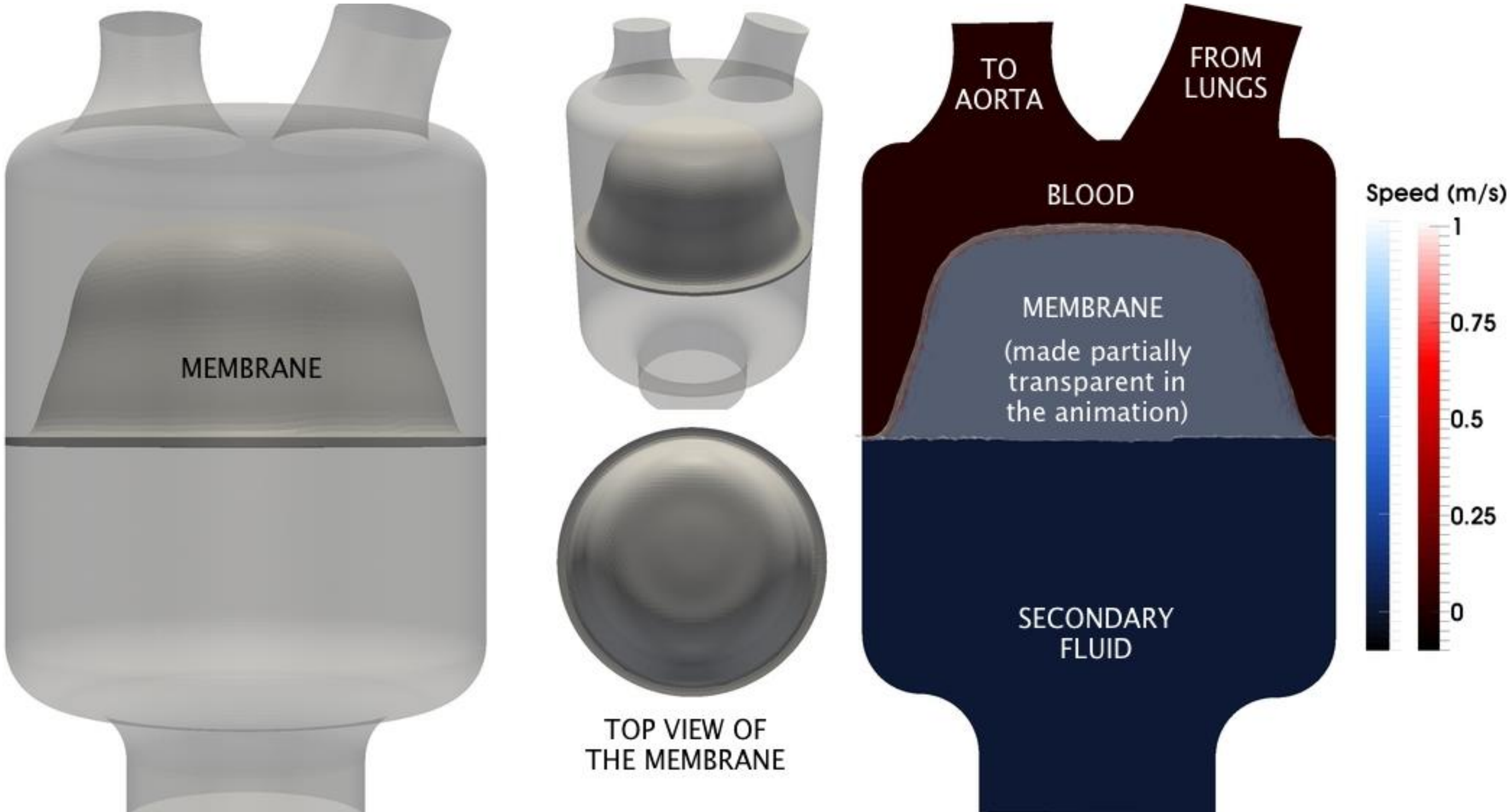
- A domain mimicking the left heart flow (only half of the heart is considered).




Side view


Top view

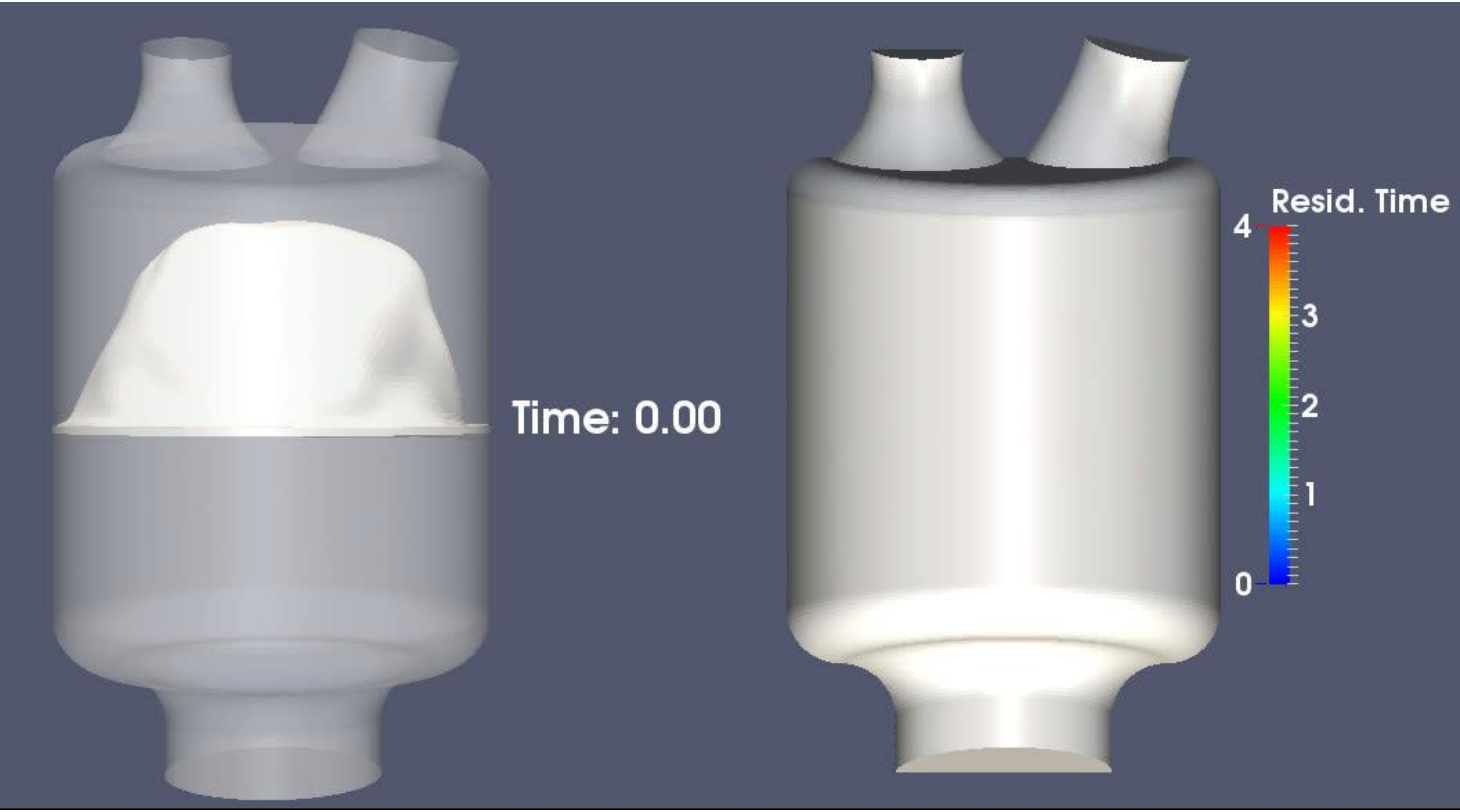
Movie presentation



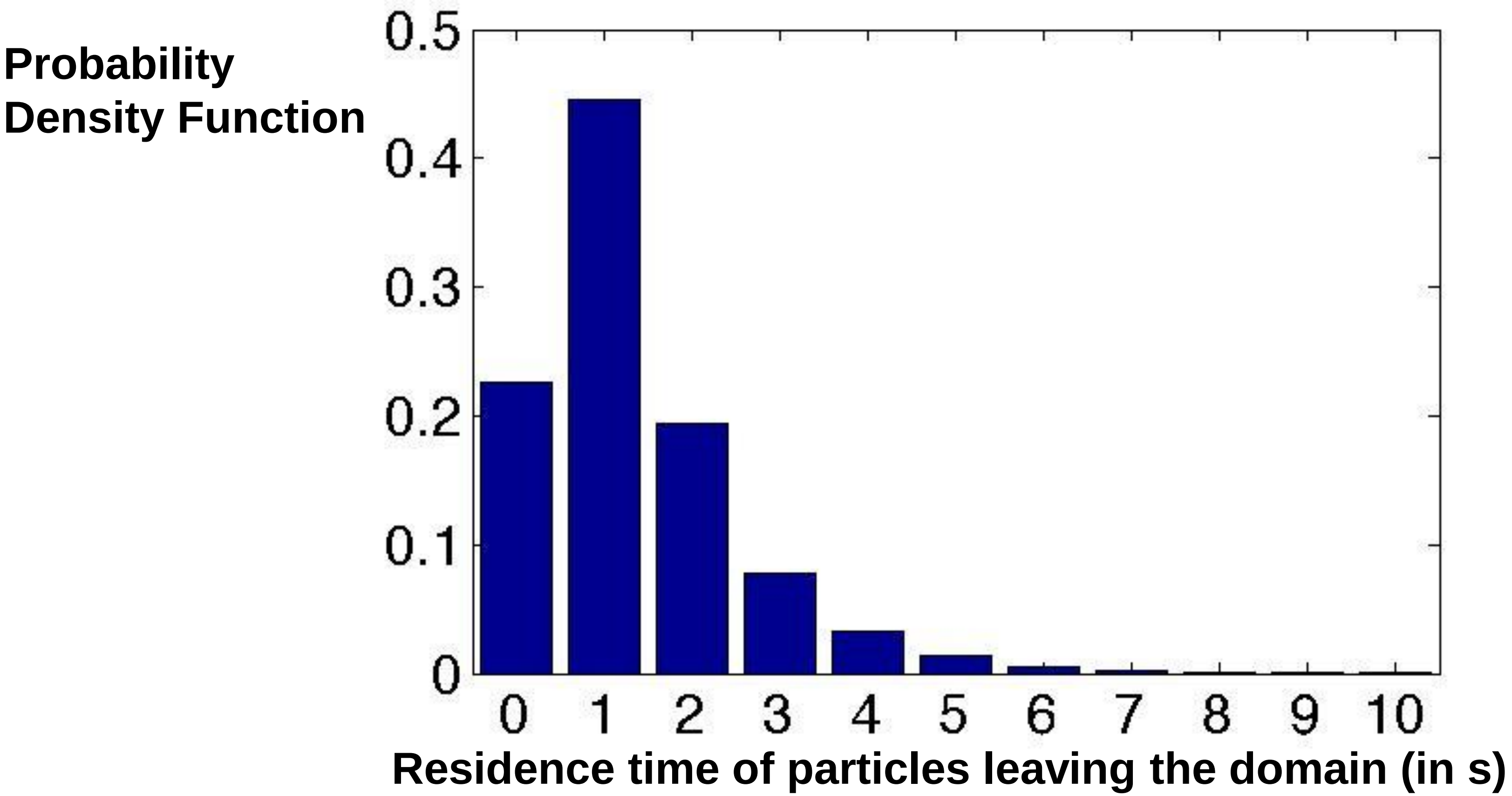
Cutting plane showing velocity field

Movie showing 5 cycles from the start

Time of residence (8 cycles)



Residence time – Statistics



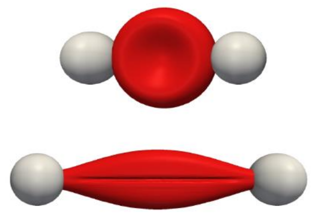
- In this design, 67% of the red blood cells leave the domain after staying less than 1.5 s.
- 5% of the RBCs stay 3.5 seconds and more

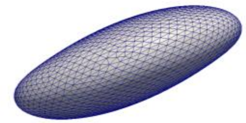
MORE INFORMATION …

- http://www.math.univ-montp2.fr/~yales2bio/
  - Publications
  - People involved
  - Other applications and movies

- **Licensing**:
  - YALES2BIO may be made freely available to any **research** team upon simple request [INSERM & CHU Toulouse, Univ. Avignon]
  - Industrial licenses can be setup on a case-by-case basis [Horiba Medical]

Thank you for your attention





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We thank for financial support: