ACCOUNTING FOR BLOOD COMPLEXITIES IN **HEMODYNAMICS**: ISSUES AND APPLICATIONS

Franck NICOUD*

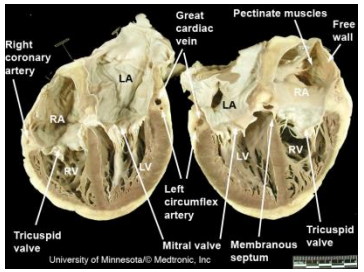
University of Montpellier – IMAG - CNRS UMR 5149

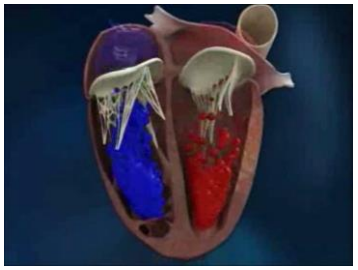
* with **C. Chnafa, E. Gibaud, S. Mendez, J. Siguenza**

CHALLENGES IN MACROSCOPIC BLOOD FLOWS

- HIGHLY COMPLEX AND MULTI-SCALE GEOMETRY
- PULSED BOUNDARY CONDITIONS
- TIME DEPENDENT FLOW DOMAIN / FSI
- TRANSITIONAL REGIME, NEITHER LAMINAR NOR TURBULENT

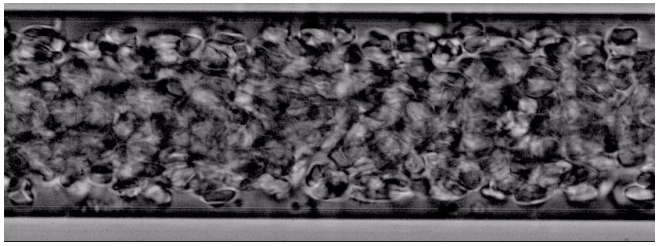
FLOW





- COMPLEX AND MOSTLY UNKNOWN RHEOLOGY (SHEAR THINNING, SUSPENSION-LIKE COMPLEX EFFECTS LIKE WEISSENBERG, FREE CELL LAYER, ...
- THROMBOSIS, HEMOLYSIS, BIOCHEMISTRY, ...

BLOOD



- MULTIPHYSICS
- UNCERTAINTIES IN GEOMETRY AND MATERIALS
- ...

WHO WE ARE

IMAG
INSTITUT MONTPELLIERAIN
ALEXANDER GROTHENDIECK

MONTPELLIER INSTITUTE
ALEXANDER GROTHENDIECK

YALES2BIO

www.math.univ-montp2.fr/~yales2bio

- Software dedicated to the simulation of blood flows
- Developed since 2010 by a team of 6-8 people
- **Objective**: Reliable enough to support the **optimization** of blood-wetted devices
- Methods for both **macroscopic** (TAH, valves, …) and **microscopic** (cytometry) applications

OUTLINE OF THE TALK

- **NUMERICAL STRATEGY FOR FLUID-STRUCTURE INTERACTION**
- MACROSCOPIC HEMODYNAMICS
  - Aortic valve dynamics
  - Human left heart
- SINGLE CELL FLOW
  - Red blood cell modelling
  - Application to cell counting and sizing

FRONT TRACKING IMMERSED BOUNDARY METHOD

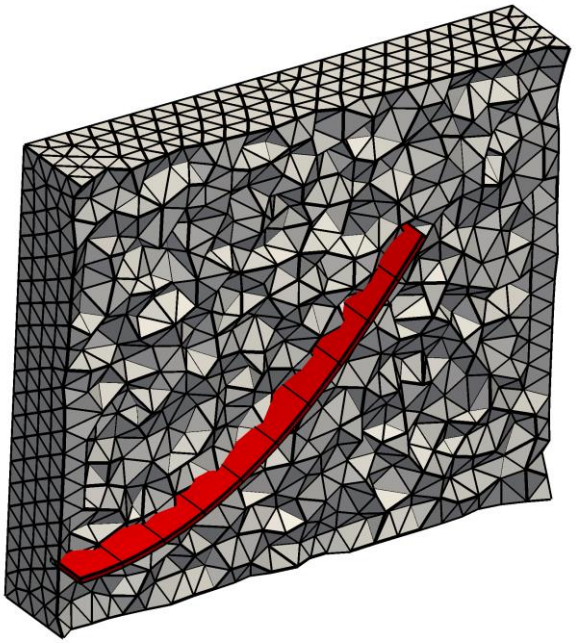
Navier-Stokes eqs
+
Membrane forces

REGULARIZATION

Membrane forces

Finite volumes

STATIC EULERIAN FLUID MESH



DEFORMABLE LAGRANGIAN STRUCTURAL MESH

Finite elements

Fluid velocity

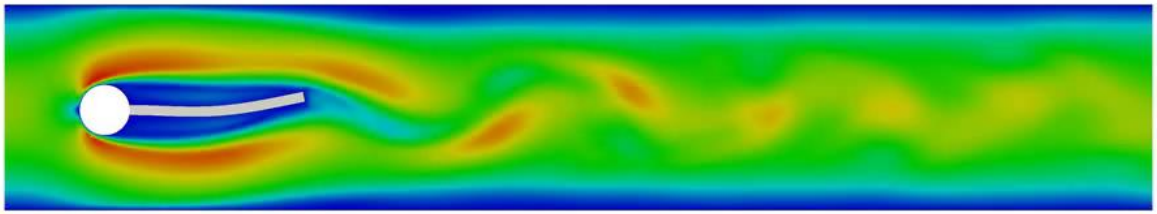
INTERPOLATION

Mechanical laws
+
Membrane displacements

Peskin (2002); Pinelli et al. (2011); Sigüenza et al., J. Comp. Physics, 2016

Fluid-structure Interaction

FLUID MECHANICS **STRUCTURAL MECHANICS**



Flow induced vibration of an elastic beam behind a cylinder

Results in agreement with Turek et al., 2010

LMGC90 : collaboration with D. Ambard, F. Dubois, F. Jourdan et R. Mozul (LMGC, Montpellier)

YALES2BIO: blood flows dedicated solver developed at IMAG, University of Montpellier

Sigüenza *et al., J. Comp. Physics, 2016*

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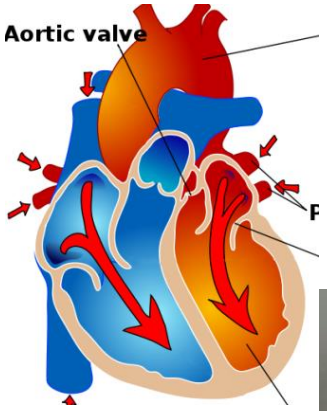
AN "AORTIC" VALVE EXPERIMENT

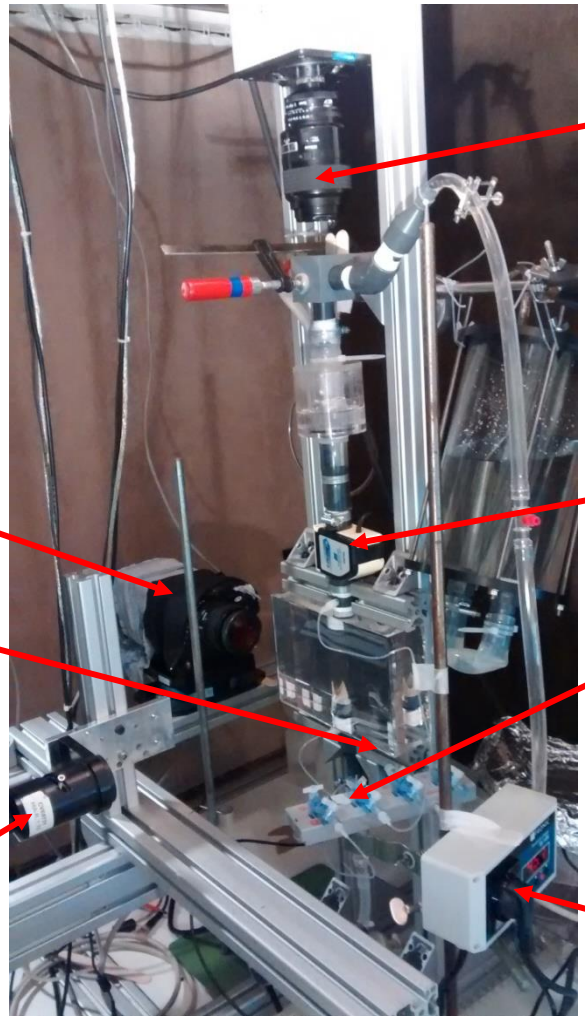


RIGID FRAME

VALVE

PIV camera

Laser



Camera

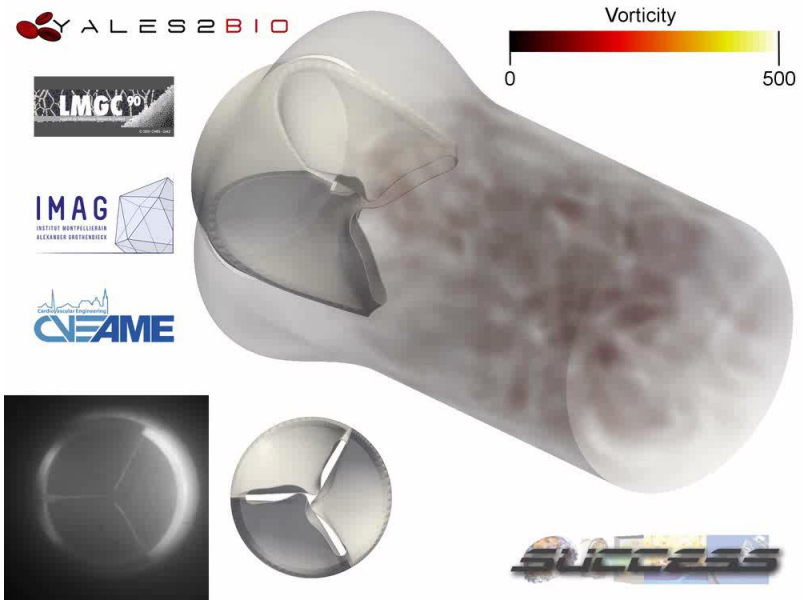
Flowmeter

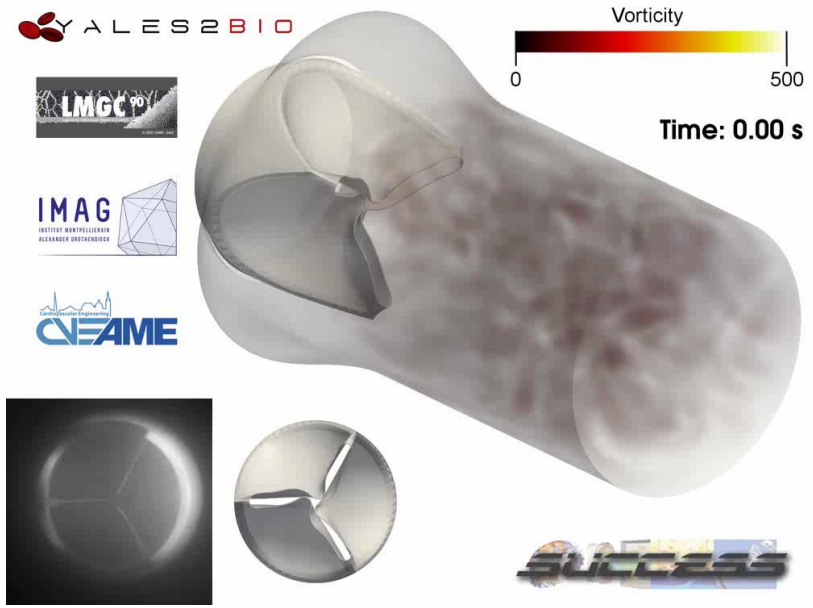
Pressure probes

Thermometer

Pott et al., ESAO, 2015

FSI SIMULATION OF THE AORTIC VALVE



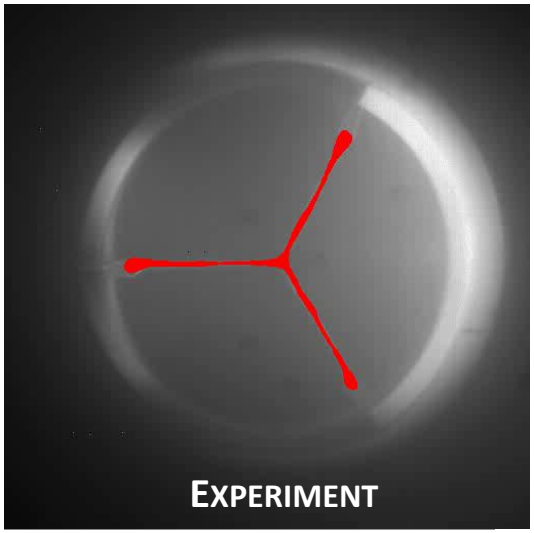


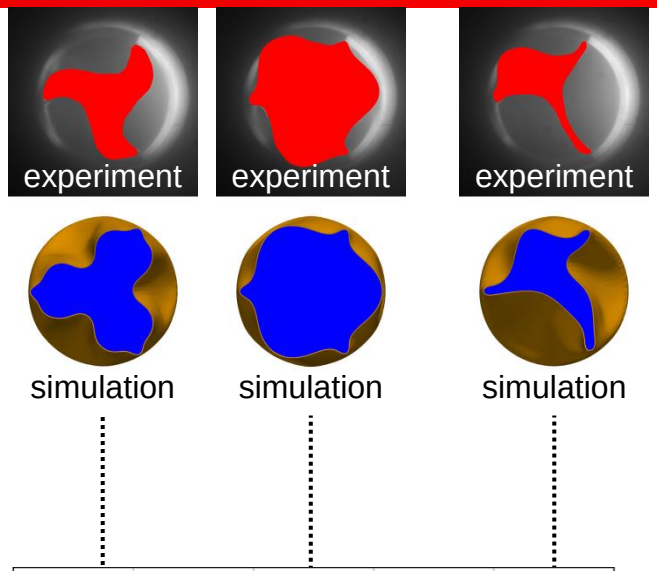
REAL SPEED

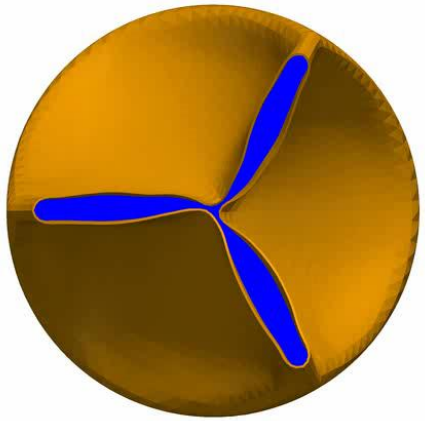
SLOW MOTION

J. Siguenza (IMAG - Montpellier)

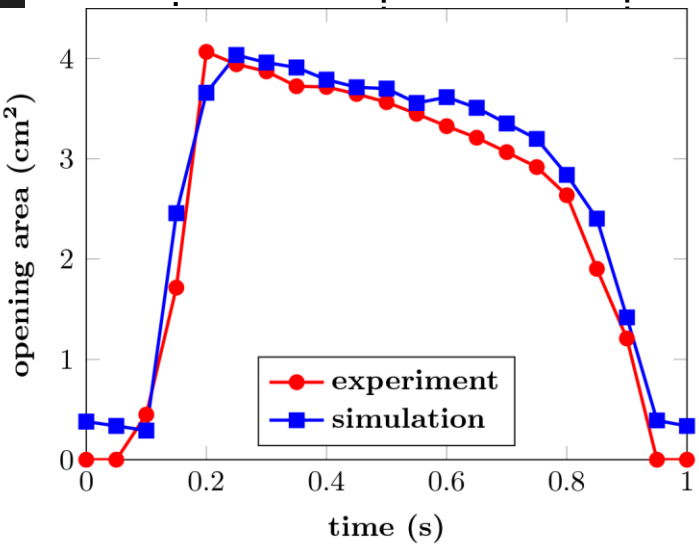
AORTIC VALVE DYNAMICS







FSI SIMULATION



≠ detailed dynamics:

- buckling
- swirling

≈ global dynamics:

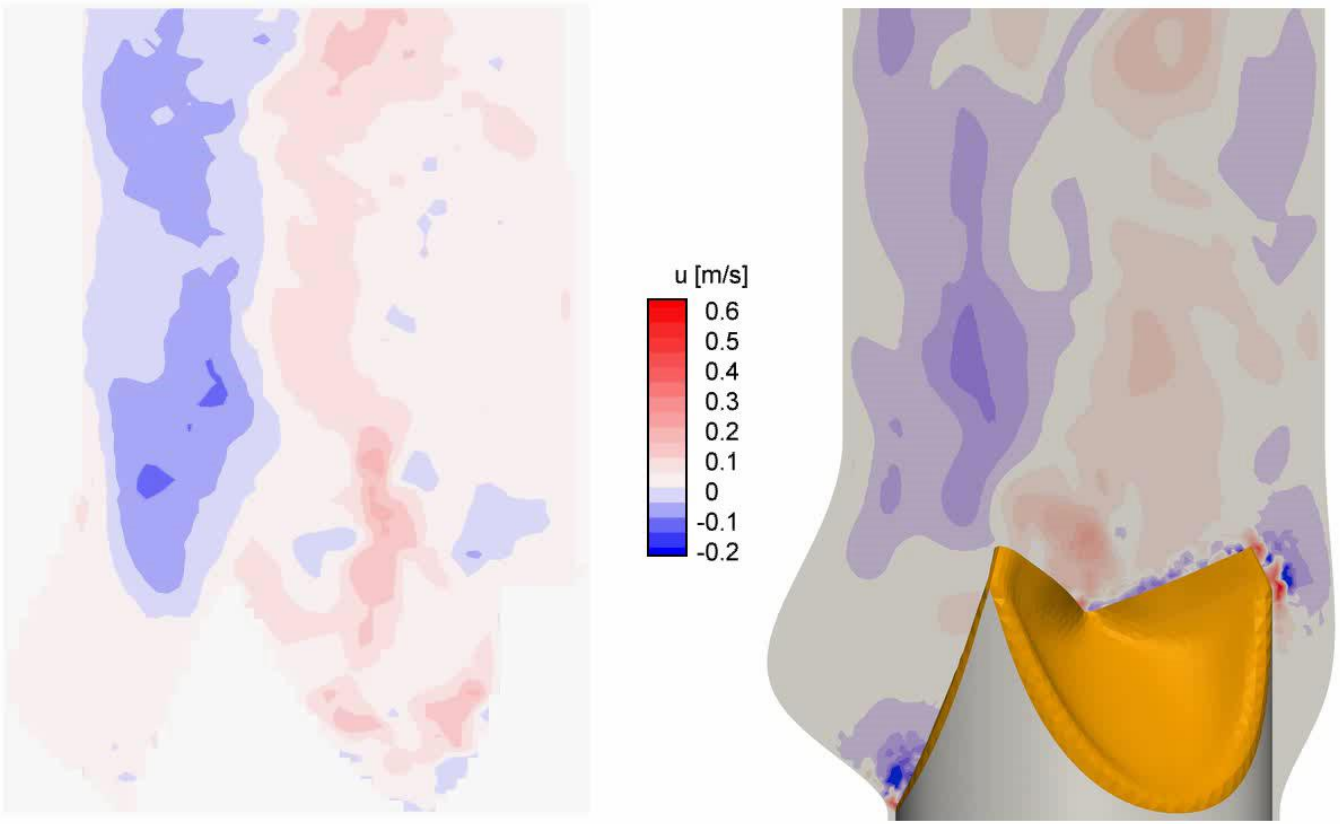
- opening time
- closure time
- opening area evolution

Pott et al., ESAO, 2015
Sigüenza, PhD thesis, 2016

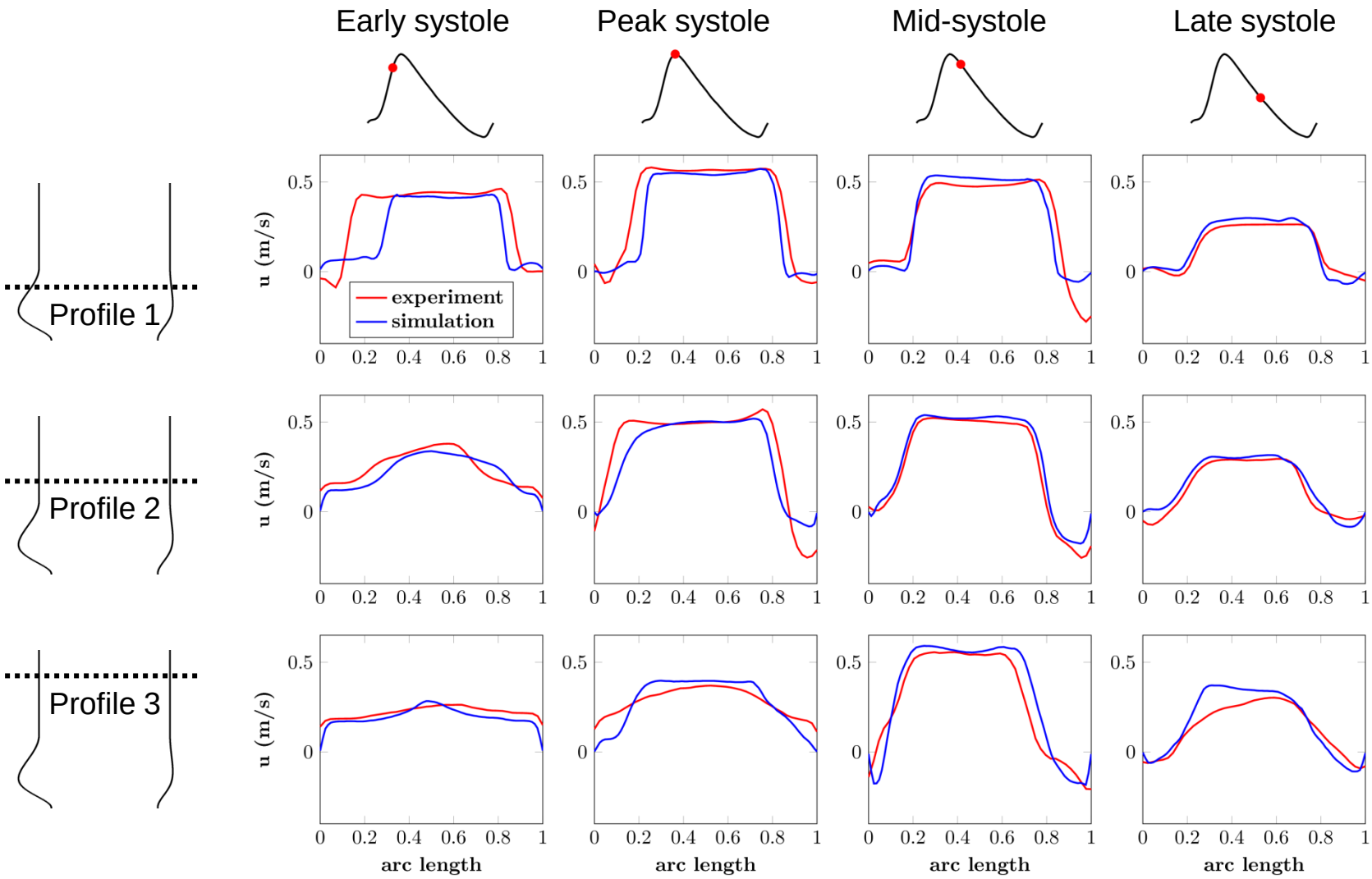
STREAMWISE VELOCITY

EXPERIMENT (PIV)
CVEAME lab – D. Pott

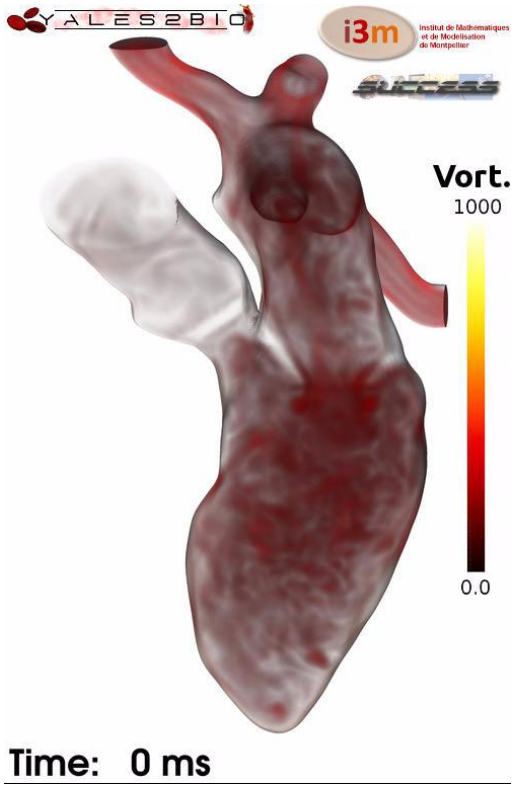
FSI SIMULATION
IMAG lab – J. Sigüenza



PHASE-AVERAGED STREAMWISE VELOCITY

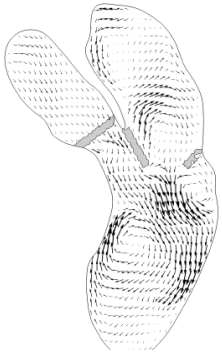


INTRA-CARDIAC TRANSITIONAL FLOWS

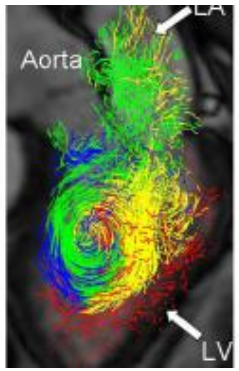


- Used together with ALE, LES was successfully applied to a **human left heart**
- **Cycle-to-cycle fluctuations** and **turbulence** were also found at some phases of the cardiac cycle, especially at **late diastole**
- **Phase averaged** solutions in agreement with advanced medical imaging data

Phase-averaged LES



Phase-averaged MRI

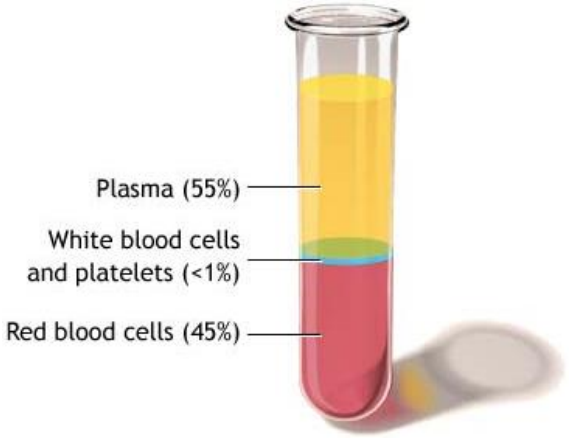


Eriksson et al., 2012

Chnafa et al., Comp & Fluids, 2014; Chnafa et al., ABME, 2016

MIND THE STEP: BLOOD IS A COMPLEX FLUID !

- COMPOSITION
  - Plasma (55%)
  - Red blood cells (≈45%)
  - White blood cells, Platlets



- 4-5 MILLIONS OF CELLS / mm^3…
- ITS EFFECTIVE VISCOSITY DEPENDS ON THE RED BLOOD CELLS **CONCENTRATION**
- THE HEMATOCRIT FIELD AND EFFECTIVE BLOOD **RHEOLOGY** DEPENDS ON THE RED BLOOD CELLS **DEFORMABILITY**

Lanotte et al., PNAS, 2016

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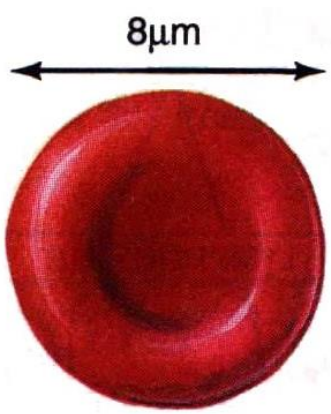
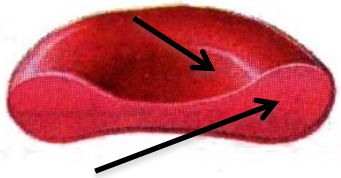
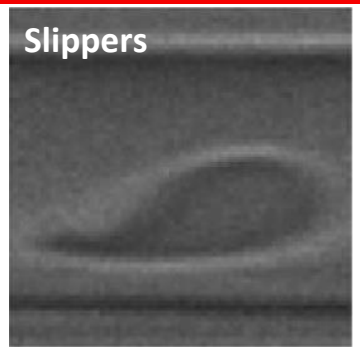
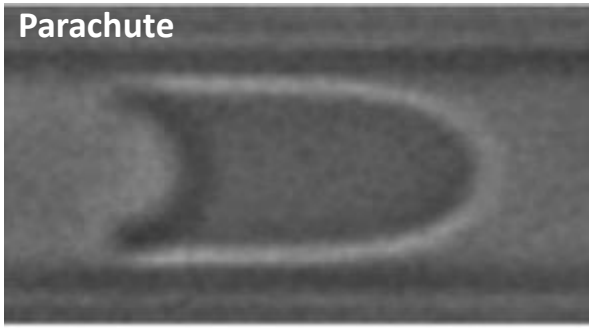
RED BLOOD CELLS



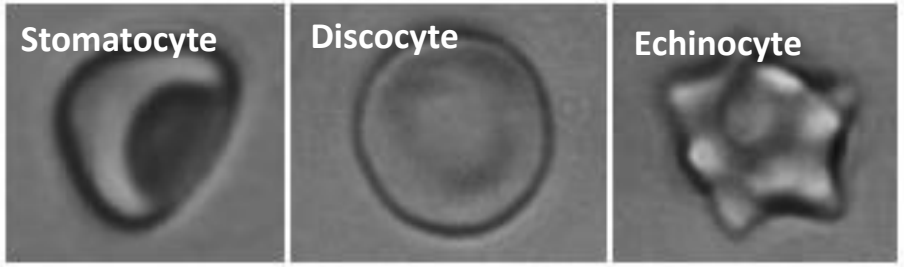


Mohandas, 2008.





Tomaiuolo et al. 2009



Abkarian et Viallat, 2015

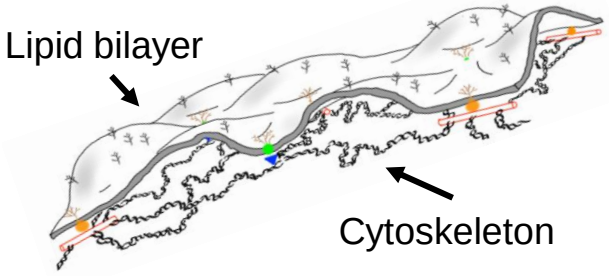
- RED BLOOD CELLS MAY BE SEEN AS **DEFLATED BALLOONS** SURROUNDED BY PLASMA
- THEIR **COMPLEX** DYNAMICS STRONGLY IMPACT THE **EFFECTIVE RHEOLOGY** OF BLOOD

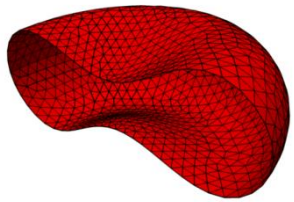
Lanotte et al., PNAS, 2016

RED BLOOD CELLS MEMBRANE MODELING

- THE LIPID BILAYER
  - is **quasi-incompressible** (4% area before rupture) - Mohandas 2008
  - resists to **bending** - Seifert 1997
- THE CYTOSKELETON MAINLY RESISTS TO **SHEAR** - Lenormand et al. 2001
- THE MEMBRANE IS MODELLED AS AN **INTERFACE** WITH APPROPRIATE **ENERGY FORMS**

Abkarian & Viallat (2016)



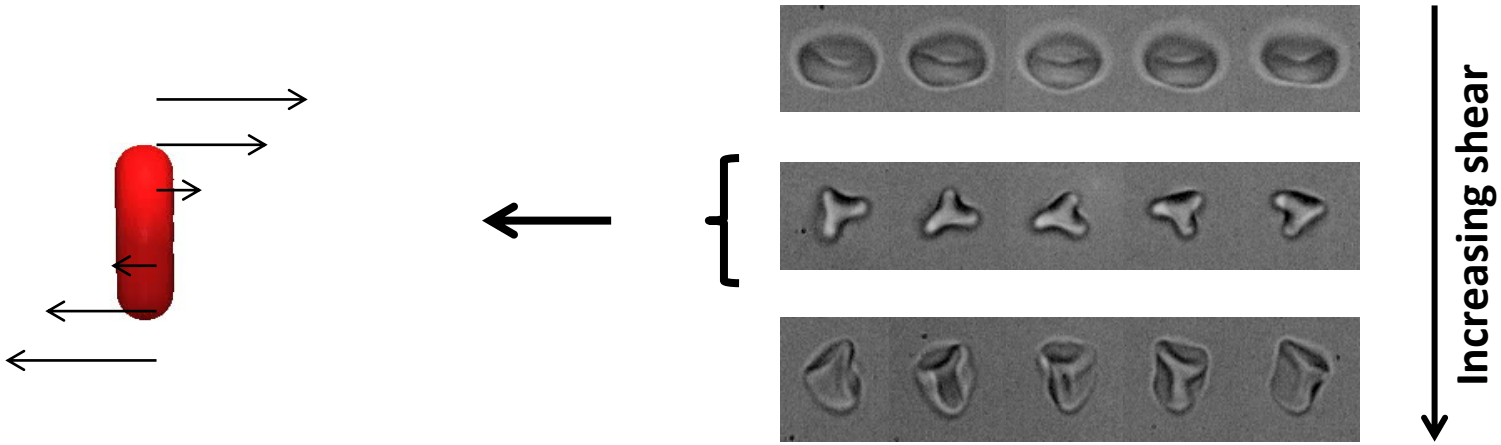


Membrane component	Mechanical resistance	Energy modeling
Lipid bilayer	Bending	$\varepsilon_b = \frac{\kappa_b}{2}\int_S (2H - c_0)^2\, dS$ *(H: mean curvature - Helfrich 1973)*
	Area-dilatation	$W_{SKALAK} = \frac{E_s}{4}\left[\left({\lambda_1}^2 + {\lambda_2}^2 - 2\right)^2 + 2\left({\lambda_1}^2 + {\lambda_2}^2 - {\lambda_1}^2{\lambda_2}^2 - 1\right) + C\left({\lambda_1}^2{\lambda_2}^2 - 1\right)^2\right]$ *(λ_1 and λ_2 principal stretches - Skalak et al. 1973)*
Cytoskeleton	Shear	

RBC DYNAMICS IN A SHEAR FLOW

FSI SIMULATION

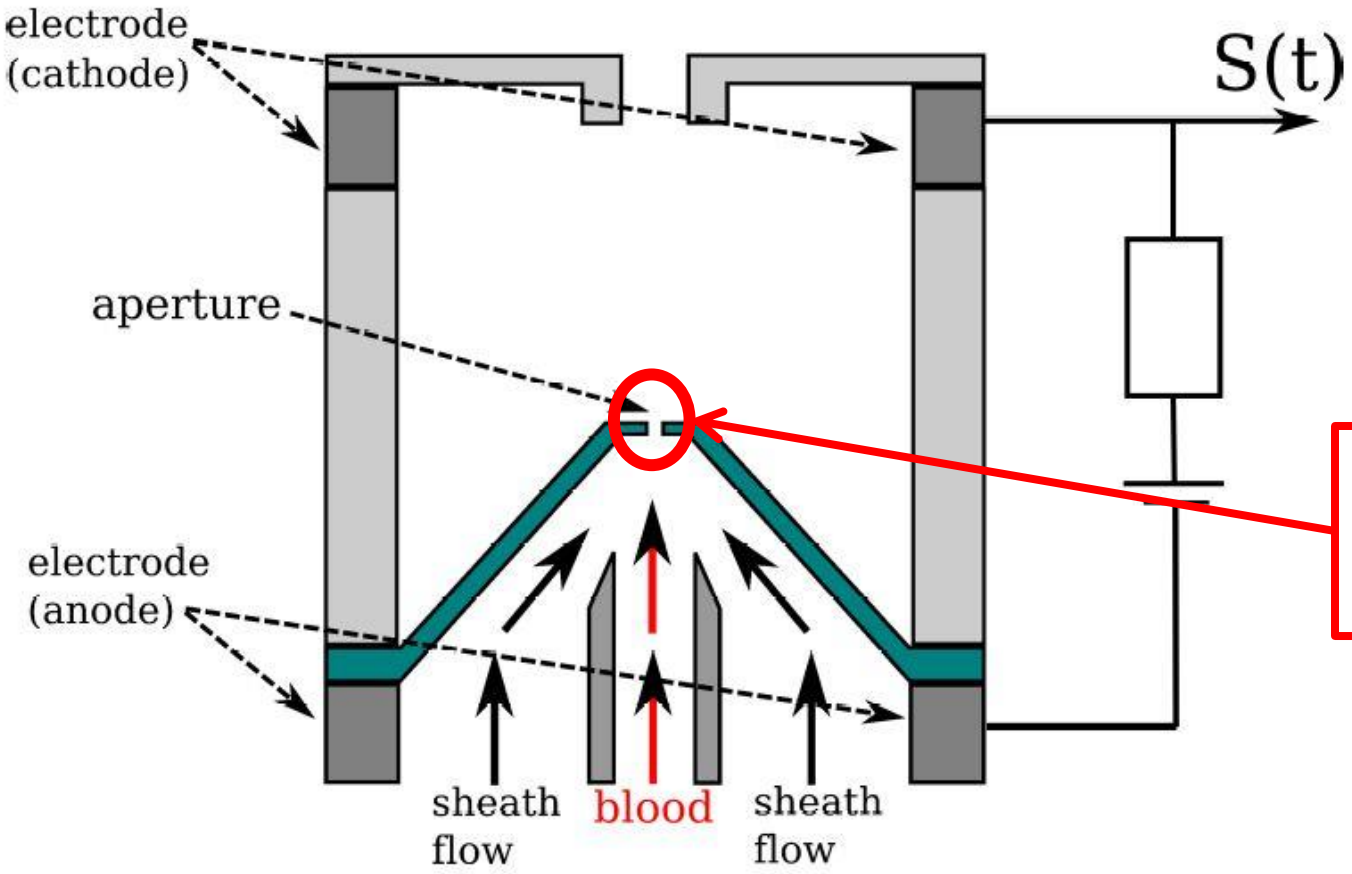
EXPERIMENTAL OBSERVATIONS



Lanotte et al., PNAS, 2016

MORE VALIDATION TEST CASES IN : Mendez et al., JCP, 2014; Martins Afonso et al., JFM, 2014, Sigüenza et al., JCP, 2016

INDUSTRIAL APPLICATION: COUNTING AND SIZING



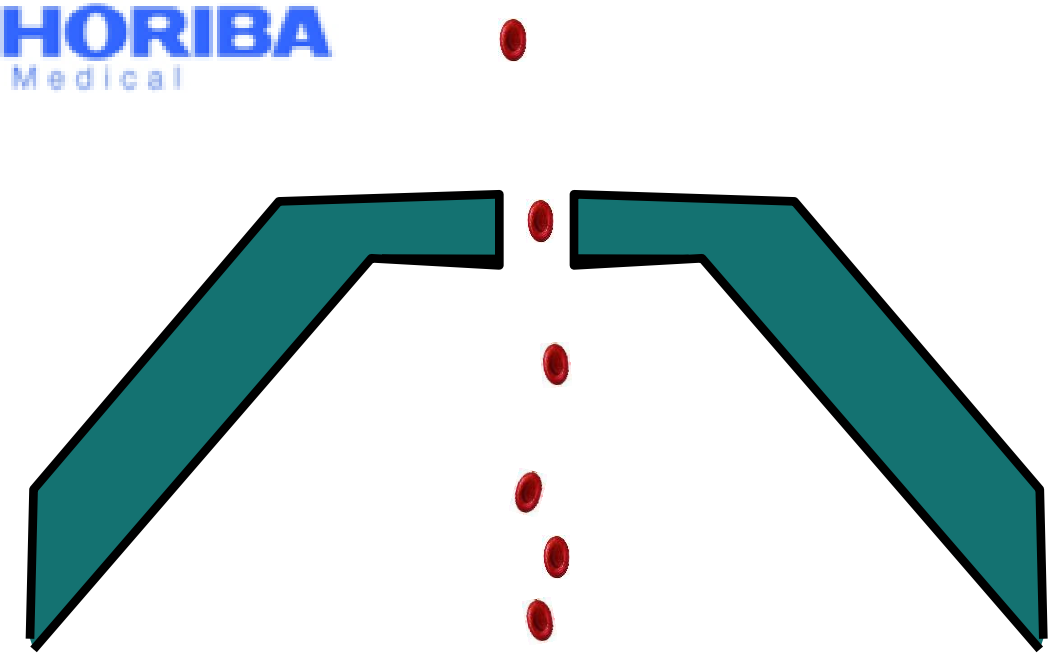
Region of interest

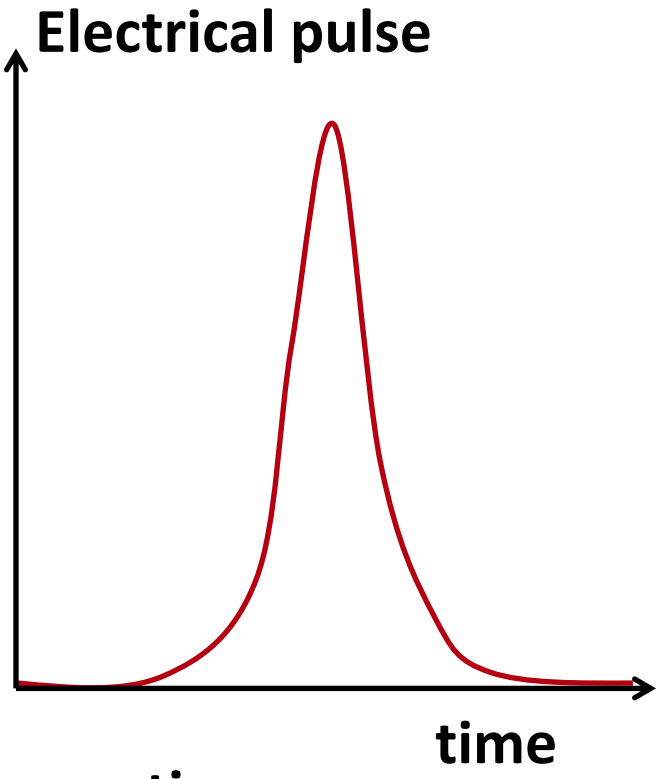
Re ~ 300

in a 50µm aperture

INDUSTRIAL APPLICATION: CYTOMETER

HORIBA Medical



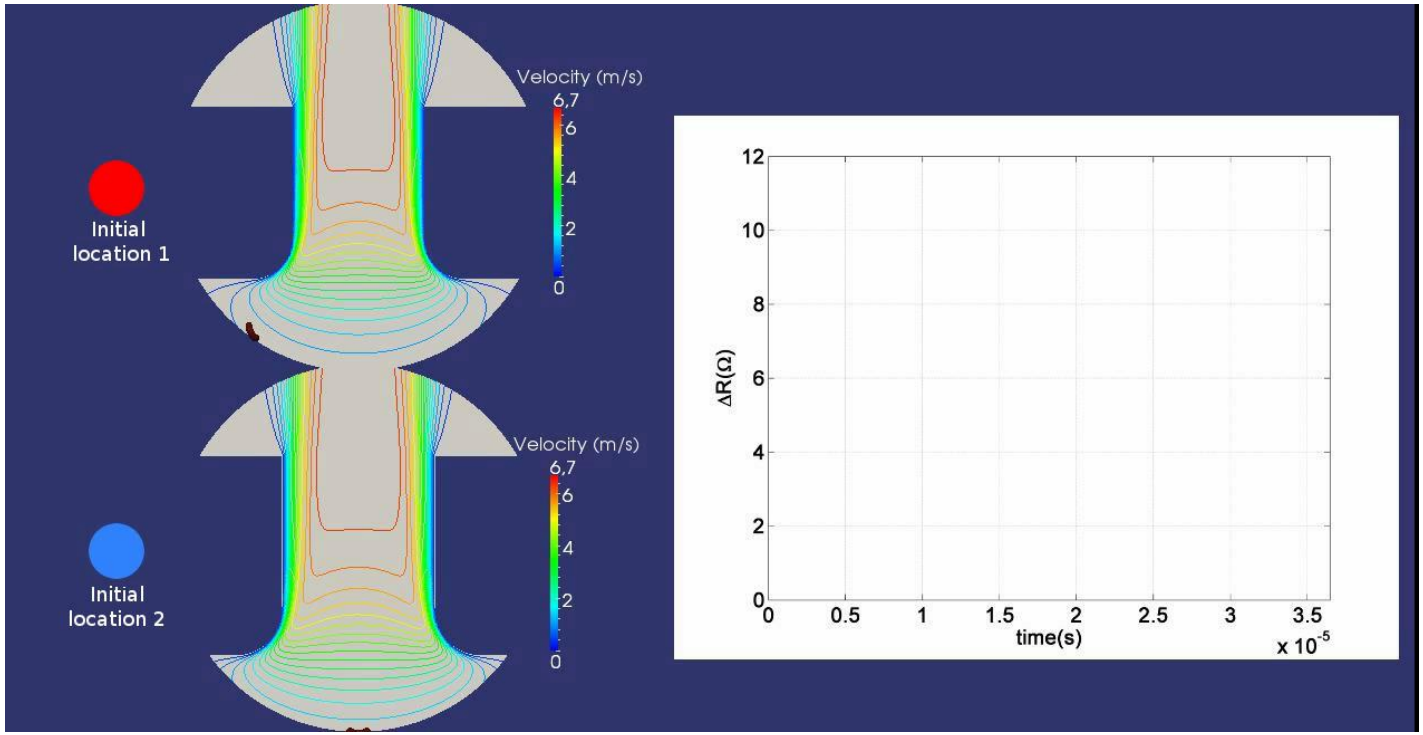


The measurement relies on two major assumptions:

- **Counting:** 1 pulse = 1 red blood cell
- **Sizing:** Pulse amplitude **proportional** to cell volume

INDUSTRIAL APPLICATION: CYTOMETER

2 identical cells at 2 different initial locations



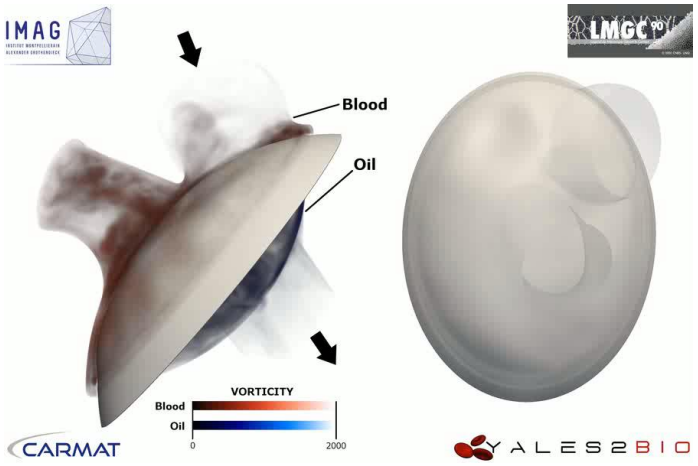
GIBAUD, PHD THESIS, 2015

Pulse characteristics are **not** related only to cell volume

COLLABORATORS

- IMAG LAB @ UNIVERSITY OF MONTPELLIER – **CARDIOVASCULAR BIOMECHANICS**
  - S. Mendez, J. Siguenza, V. Zmijanovic, E. Gibaud, A. Larroque, T. Puiseux, P. Taraconat
  - C. Chnafa (now at University of Toronto)
- LMGC LAB @ UNIVERSITY OF MONTPELLIER – **BIOMECHANICS AND SOFT TISSUES**
  - F. Jourdan, D. Ambard, R. Mozul, F. Dubois
- UNIVERSITY HOSPITALS @ TOULOUSE AND MONTPELLIER – **RADIOLOGY / CARDIOLOGY / IMAGE REGISTRATION**
  - H. Rousseau, I. Schuster, R. Moreno
- CBS LAB @ UNIVERSITY OF MONTPELLIER – **BIOPHYSICS AND BLOOD RHEOLOGY**
  - M. Abkarian, L. Lanotte
- IFPEN IN PARIS – **EXPERIMENTAL DATA**
  - H. Bata Toda
- HELMHOLTZ INSTITUTE IN AACHEN – **EXPERIMENTAL DATA**
  - D. Pott, S. Sonntag
- INDUSTRIAL COLLABORATORS – **FUNDING AND VERY CHALLENGING QUESTIONS**
  - Horiba Medical, Carmat SA, ALARA Expertise, Sim&Cure

Thank you for your attention



Preliminary application to the Carmat TAH

www.math.univ-montp2.fr/~yales2bio

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cnrs
ANR
Numev
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