# Analysis of Mechanical Parameters Using End-Diastolic Measurements

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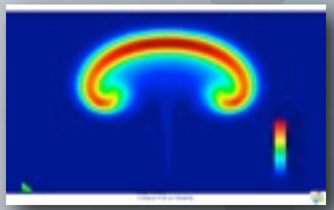
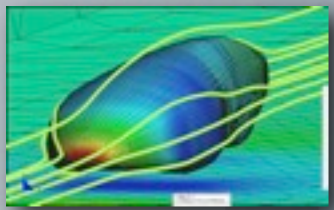
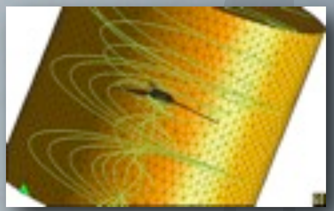
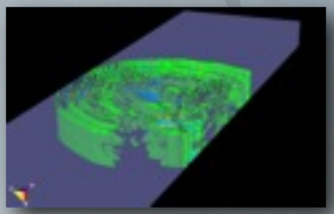
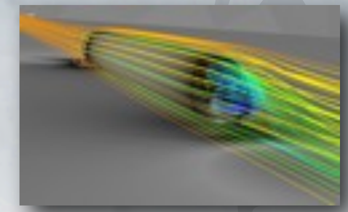
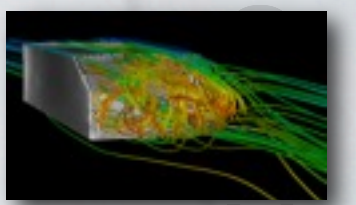
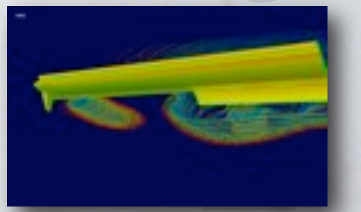
ALYA (2004)

Simulation Code for parallel computing

Designed from scratch to solve multiphysics problems with high parallel efficiency

* Numerical solution of PDE's
* Hybrid meshes, higher (up to Q3) and lower order
* Parallelization by MPI and OpenMP
* Automatic mesh partition using Metis
* Portability

# Alya System

Services

Kernel

Modules

Multiphysics computational tool with high parallel efficiency

HPC-based

Supercomputing facilities

FEM method

Modules and services can be turned on/off

Solvers are in-house, no external libraries

Incompressible flows

Compressible flows

Turbulence

Non-linear Solid Mechanics

Electromagnetism

Heat transport

Combustion and chemical reactions

Arbitrary Lagrangian-Eulerian Fluid-Structure Interaction

Adjoint-based optimization

# HPC Simulation Tools: Alya

**Alya is one of the two CFD codes of the PRACE benchmark suite**

respective user communities, as well the coverage of scientific a
a final list of 12 codes to form the initial version of UEABS, wh

| | |
|---|---|
| **Particle Physics:** | QCD |
| **Classical MD:** | NAMD, GROMACS |
| **Quantum MD:** | Quantum Espresso, CP2K, GPAW |
| **CFD:** | Code_Saturne, ALYA |
| **Earth Sciences:** | NEMO, SPECFEM3D |
| **Plasma Physics:** | GENE |
| **Astrophysics:** | GADGET |

Available online at www.prace-ri.eu

PRACE

**Partnership for Advanced Computing in Europe**

Selection of a Unified European Application Benchmark Suite

J. Mark Bull[a]*, Andrew Emerson[b]

[a]EPCC, University of Edinburgh, King's Buildings, Mayfield Road, Edinburgh EH9 3JZ, UK.
[b]CINECA, via Magnanelli 6/3, 40033 Casalecchio di Reno, Bologna, Italy.

**Lindgren** (Sweden), Cray XE system at PDC, incompressible flow **12288** CPU's (collaboration with Jing Gong from PDC)

**Huygens**, (The Netherlands), IBM power 6, incompressible flow, **2128** CPU's

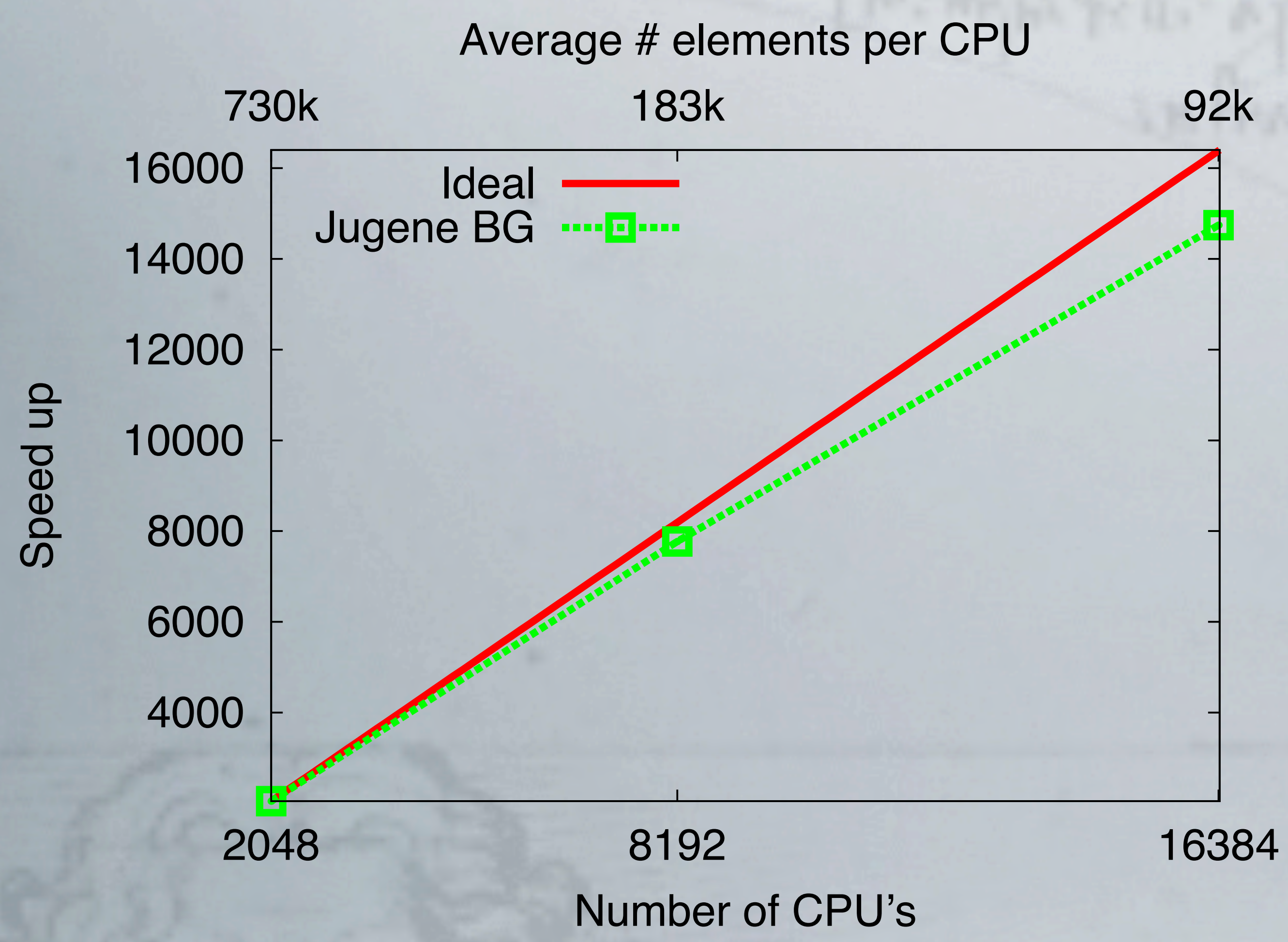
**Jugene** BG (Germany): **16384** CPU's, incompressible flow (Prace project for Mesh multiplication) and, running first tests of FSI in collaboration with Paolo Crosetto (Julich)

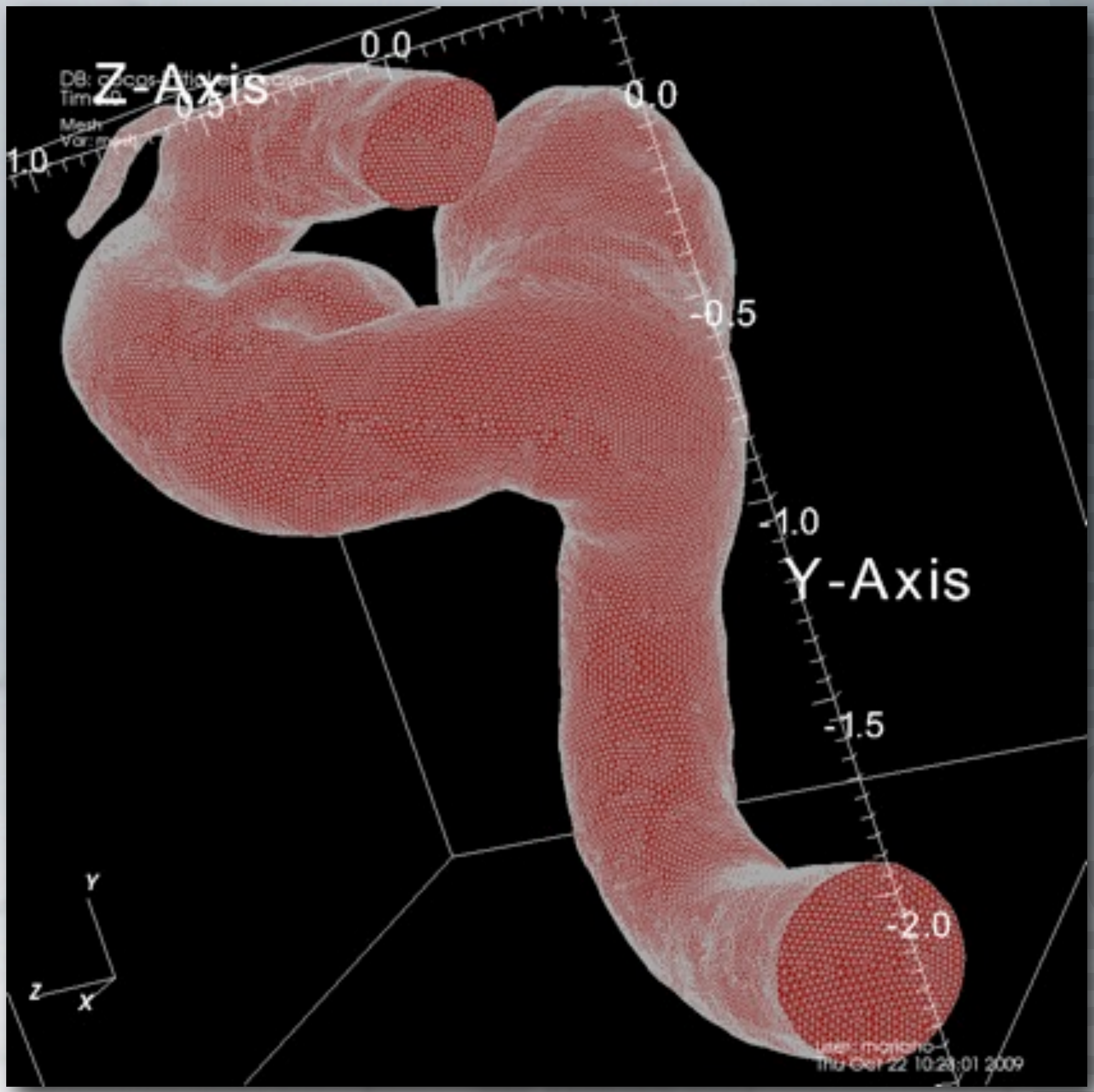
**Fermi** BG (Italy): **16384** CPU's, incompressible flow + species transport + Lagrangian particles (Prace project for nose)

**Curie** Bullx (France): **22528** CPU's, incompressible flow (collaboration with Jing Gong - PDC)

**Marenostrum**: **8000** CPU's compressible flow, incompressible flow, solid mechanics... (scalability test)

# HPC Simulation Tools: Alya




**Benchmark**

**Aneurism geometry provided by R. Cebral**

**Uniform refinement up to 1.6B tetrahedra**

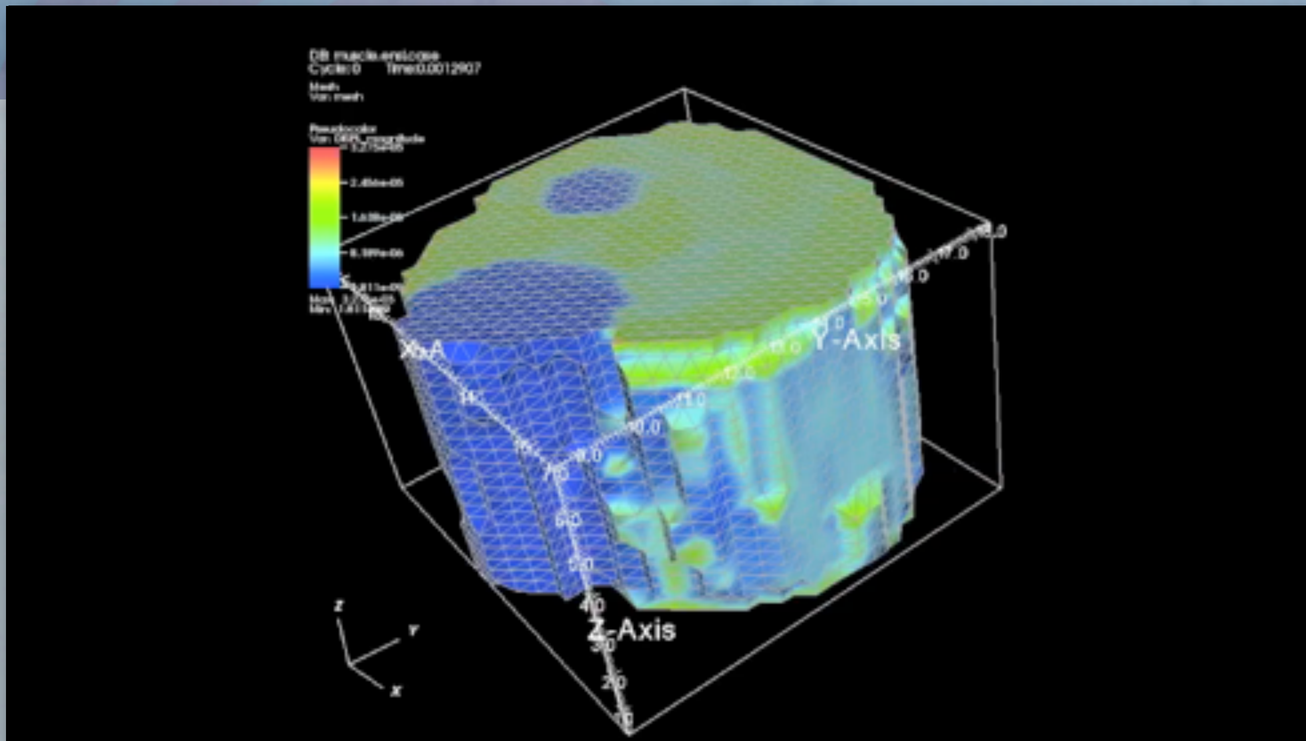
**Incompressible flow**

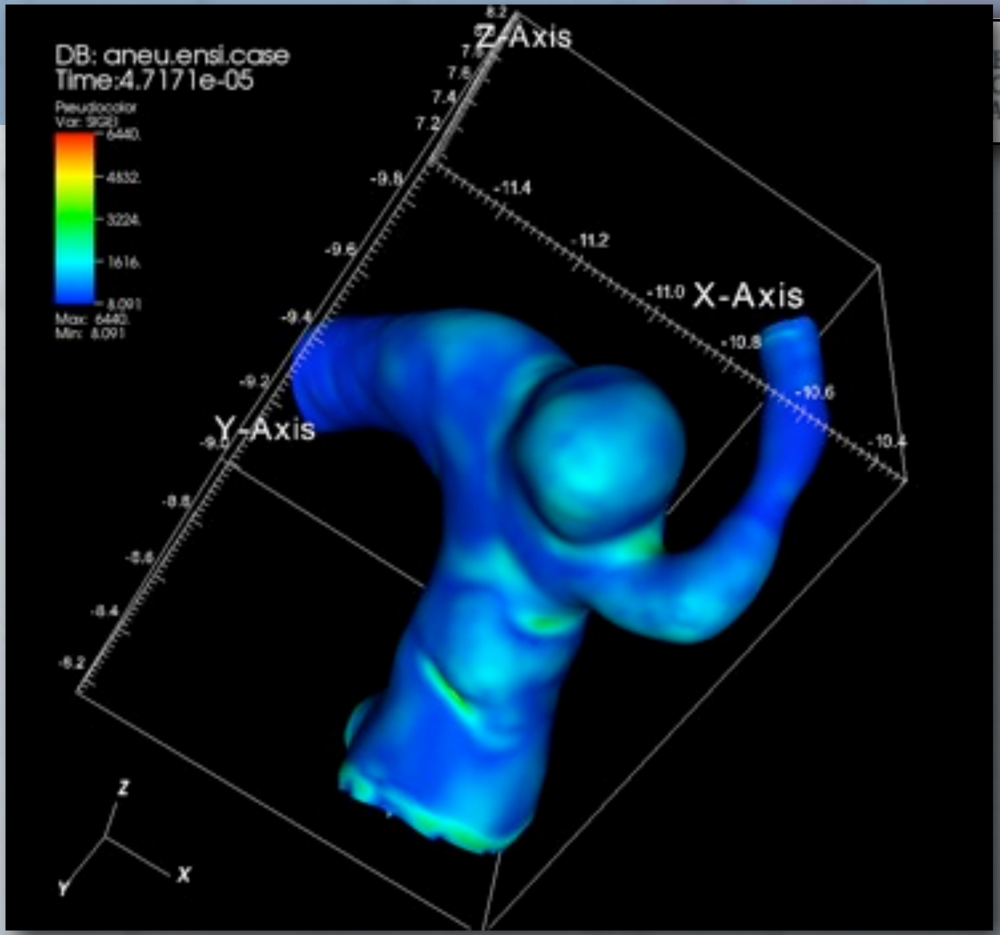
**Implicit formulation**

**Algebraic Fractional Step: BCGStab + Deflated CG**

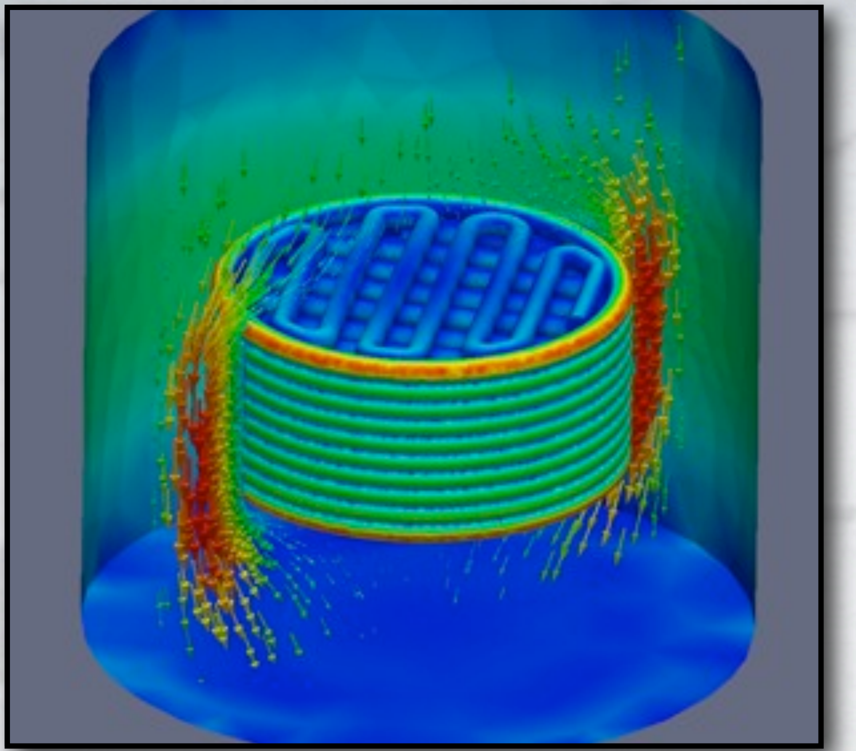
# Alya Red

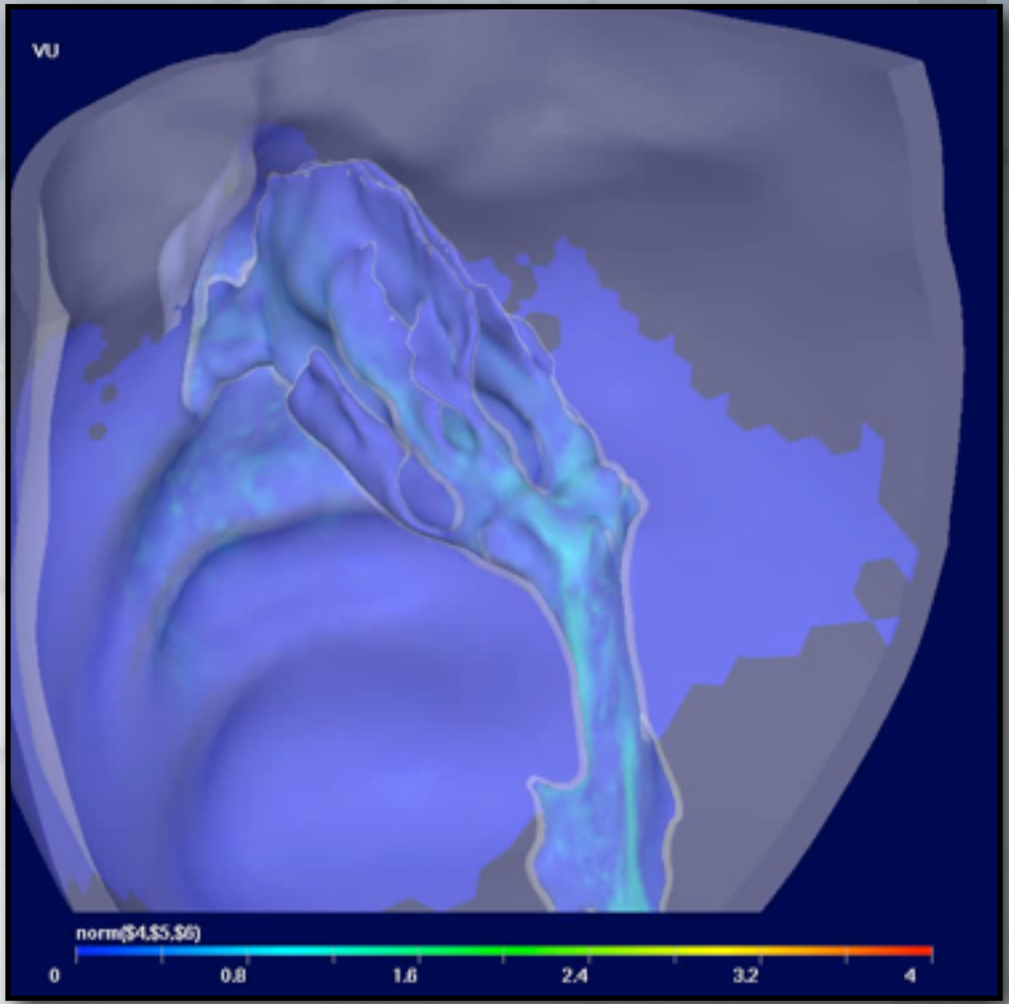
# HPC-based Biomechanical Simulations



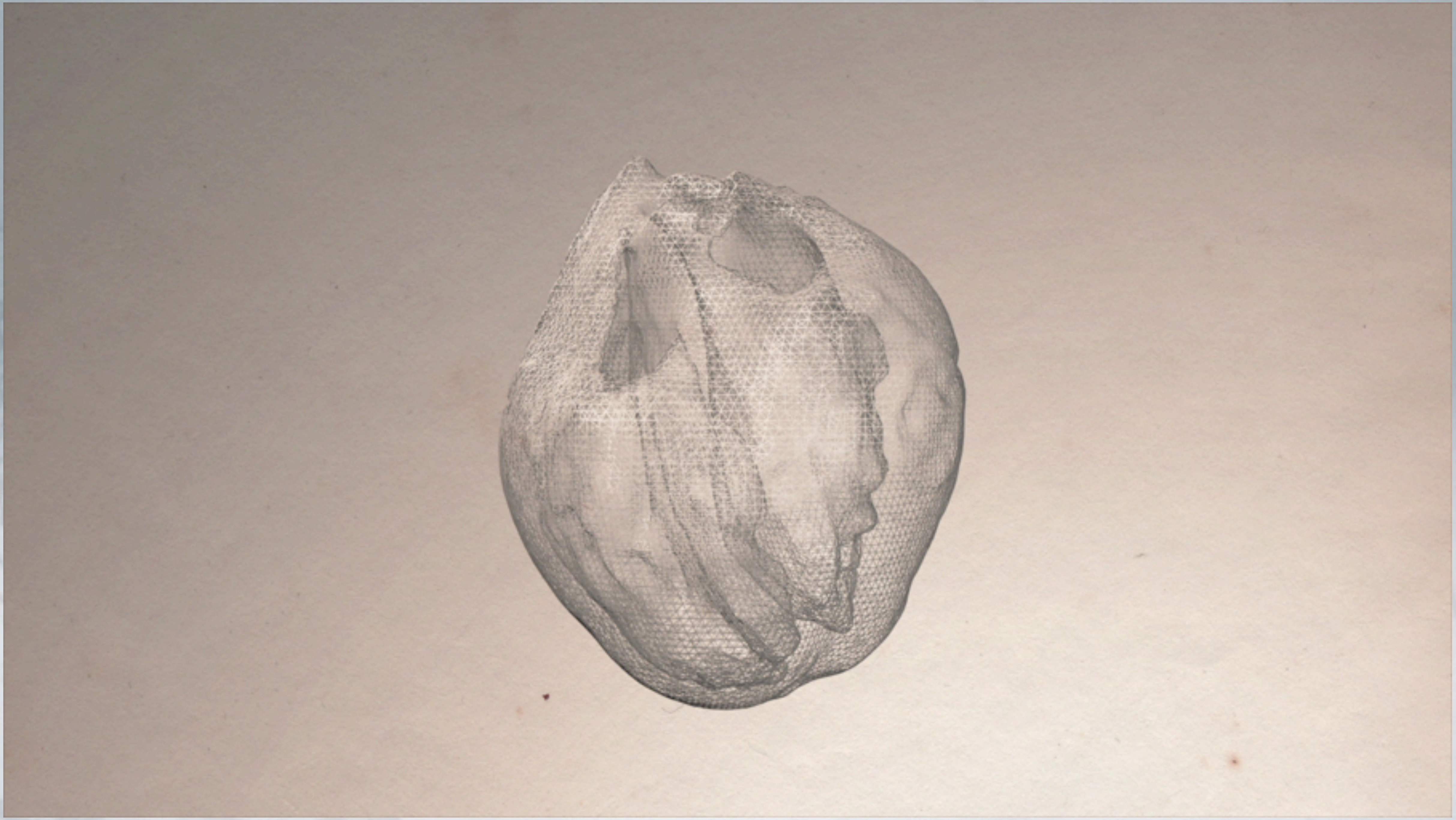




**Respiratory system**
**Cerebral aneurisms rupture risk**
**Long skeletal muscles**
**Biomaterials and tissue engineering**
**Cardiac computational model**





**The goal:**
**Use of HPC-based simulation codes and HPC resources in Biomedical research**



EXCELENCIA SEVERO OCHOA

## Alya Red: Cardiac Computational Model

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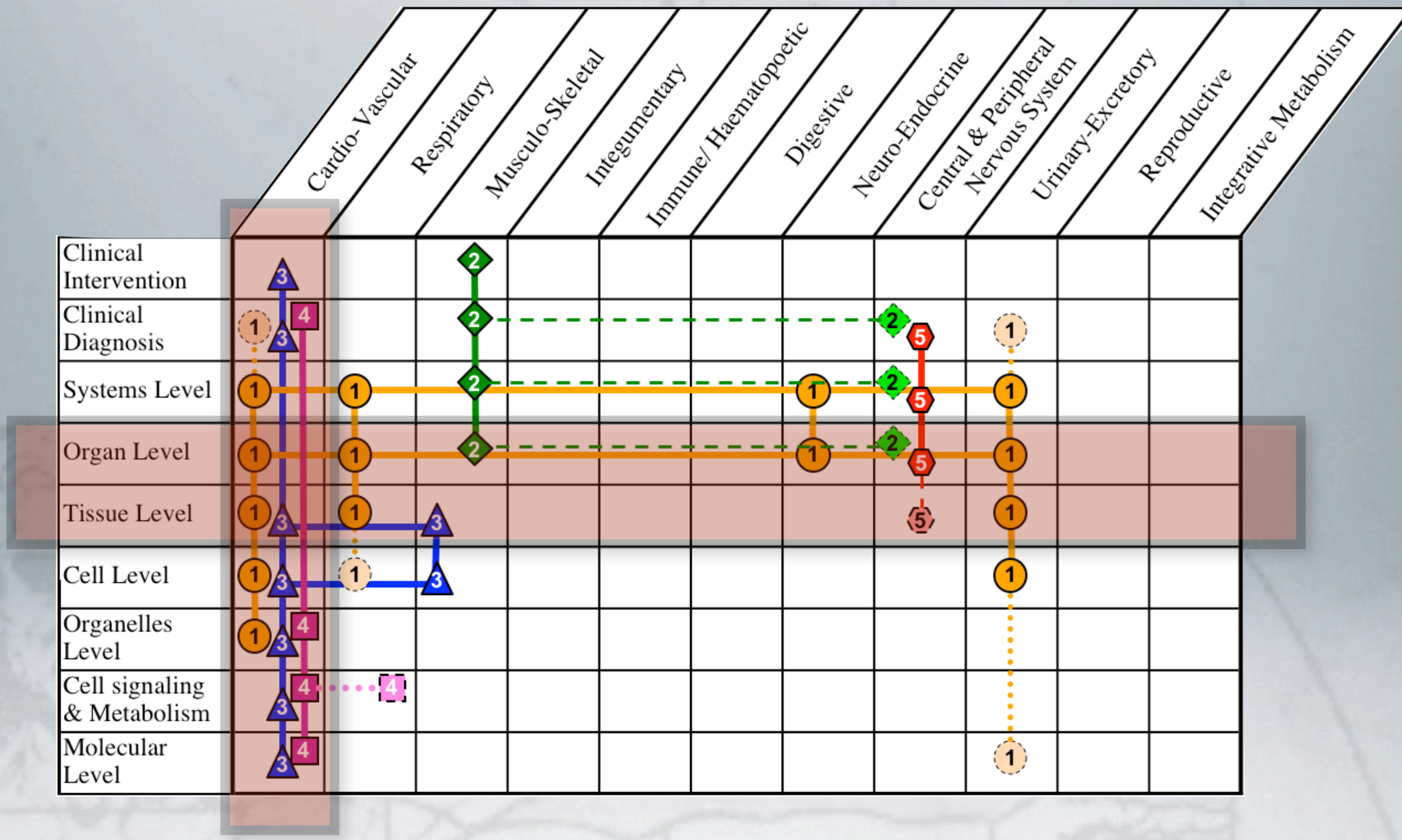
**Pablo Lamata, Liya Asner and David Nordsletten, King's College London (UK)**

# The heart as a Physical System



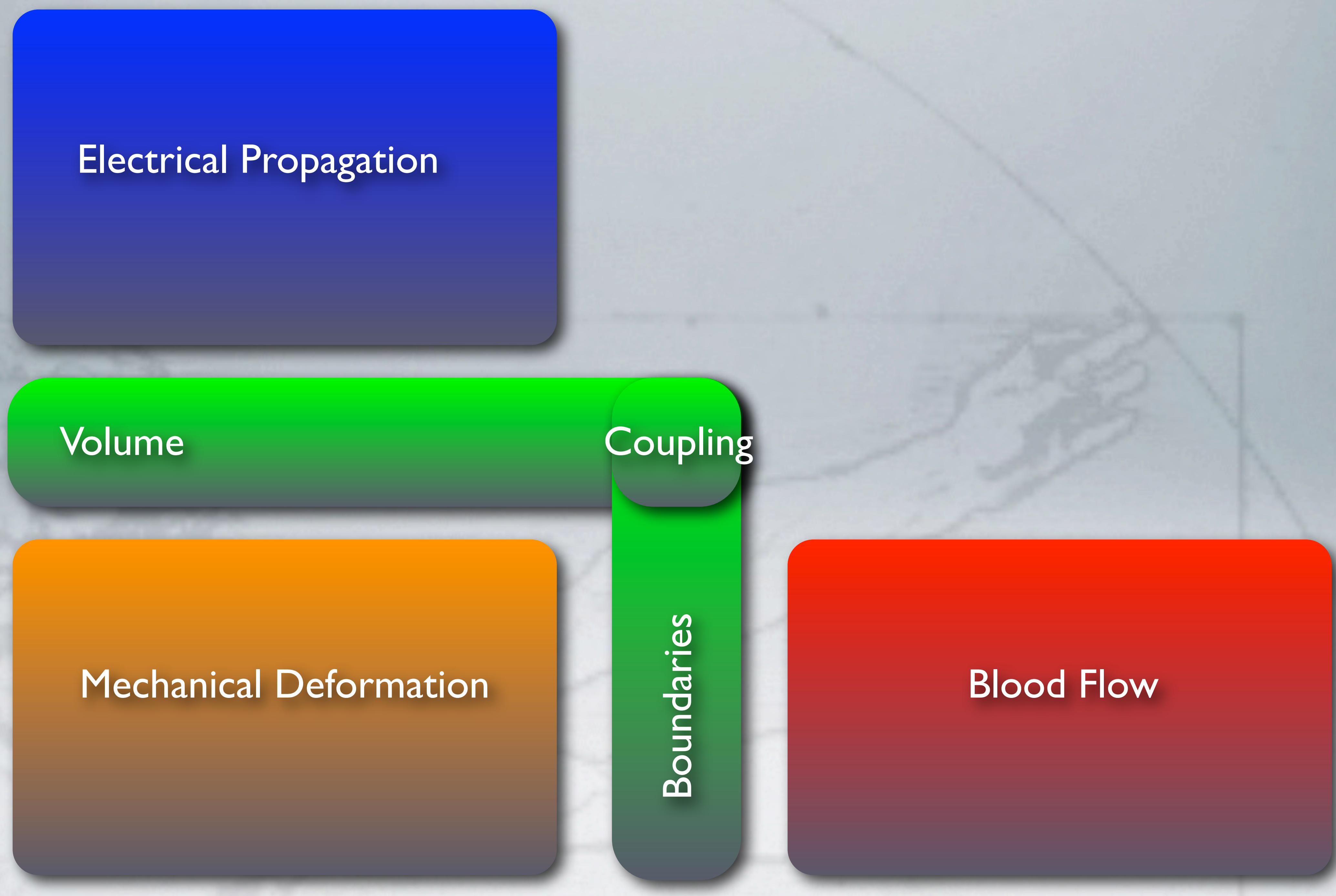

**Organ Systems vs. Levels of Organizations**
**Extracted from S.R. Thomas et al., VPH Exemplar Project Strategy Document. Deliverable 9, VPH NoE. 2008**

# The Heart as a Physical System



At organ level,

the heart can be seen as the following coupled problem:



# Cardiac Computational Model CCM

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Electrical Propagation

**Electrophysiology:**
**Linear anisotropic (fibers) diffusion + non-linear source terms**

Volume

**Electro-mechanical coupling, $Ca^{2+}$ is the key**

**ALE + Immersed Boundaries**

Mechanical Deformation

Boundaries

**Blood Flow**

**Mechanical deformation:**
**Large deformations + non-linear material models**

**Incompressible Flow**

* Four coupled problems:

Electrophysiology, Solid Mechanics, Blood flow and Mesh deformation

* One single mesh for EP and CSM, one single mesh for CFD and MD

* Non-structured mesh coming from medical image processing

* Anisotropic media

* One parallel code to simulate the full problem: Alya

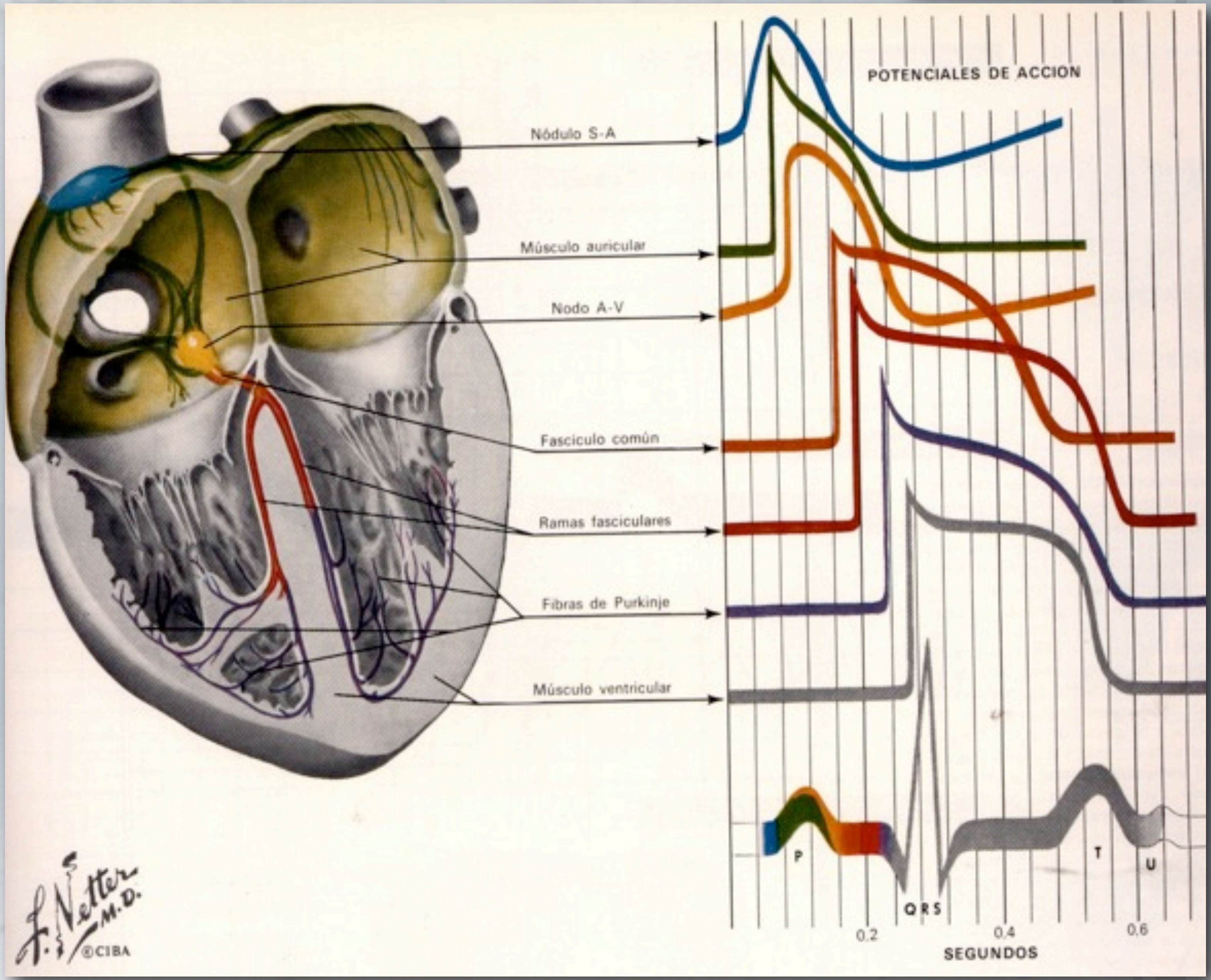
Staggered strategy: solving the problems sequentially for each time step

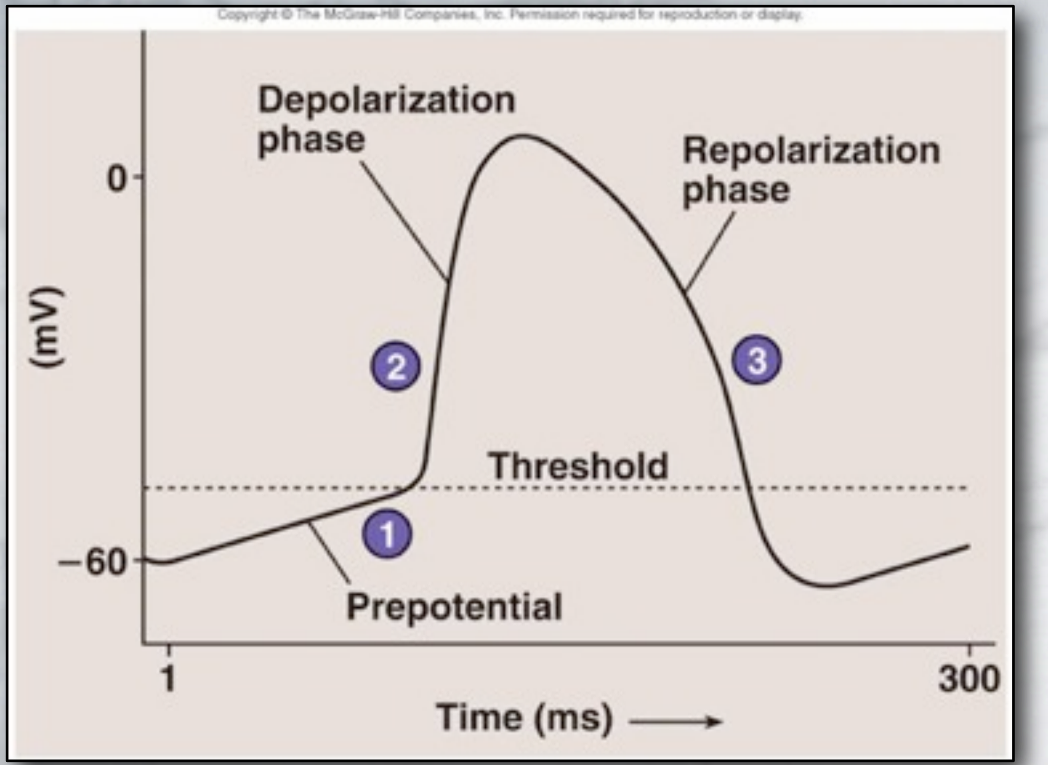
Eventually, allowing sub-iterations or sub-cycling, asynchronous strategies...

Fully transient (dynamic terms) problem

Diffusion equation + non-linear terms
Supplementary Poisson equation (mono and bidomain)

Non-linear terms: FitzHugh-Nagumo, Fenton-Karma, Ten-Tuscher, O'Hara...




$$\frac{\partial \phi_\alpha}{\partial t} - \frac{\partial}{\partial x_i}\left(D_{ij}\frac{\partial \phi_\alpha}{\partial x_j}\right) = L(\phi_\alpha)$$

## Electrophysiology

$$\frac{\partial \phi_\alpha}{\partial t} - \frac{\partial}{\partial x_i}\left( D_{ij} \frac{\partial \phi_\alpha}{\partial x_j} \right) = L(\phi_\alpha)$$

Phenomenological models based on Hodgkin-Huxley

FitzHugh-Nagumo model (1961)

$$L(\phi) = c_1 \phi (\phi - c_3)(\phi - 1) + c_2 W$$

$$\frac{\partial W}{\partial t} = \varepsilon\left(\phi - \gamma W\right)$$

Fenton-Karma model (2005)

$$L(\phi) = J_{\mathrm{fi}}(\phi, V) + J_{\mathrm{so}}(\phi) + J_{\mathrm{si}}(\phi, W)$$

$$\frac{\partial V}{\partial t} = \Theta(\phi_{\mathrm{c}} - \phi)(1 - V)/\tau_{\mathrm{V}}^{-} - \Theta(\phi - \phi_{\mathrm{c}}) V/\tau_{\mathrm{V}}^{+}$$

$$\frac{\partial W}{\partial t} = \Theta(\phi_{\mathrm{c}} - \phi)(1 - W)/\tau_{\mathrm{W}}^{-} - \Theta(\phi - \phi_{\mathrm{c}}) W/\tau_{\mathrm{W}}^{+}$$

$$J_{\mathrm{fi}}(\phi, V) = -\frac{V}{\tau_{\mathrm{d}}} \Theta(\phi - \phi_{\mathrm{c}})(1 - \phi)(\phi - \phi_{\mathrm{c}})$$

$$J_{\mathrm{so}}(\phi) = \frac{\phi}{\tau_0} \Theta(\phi_{\mathrm{c}} - \phi) + \frac{1}{\tau_{\mathrm{r}}} \Theta(\phi - \phi_{\mathrm{c}})$$

$$J_{\mathrm{si}}(\phi, W) = -\frac{W}{2\tau_{\mathrm{si}}}(1 + \tanh[k(\phi - \phi_c^{\mathrm{si}})])$$

Cell models on ionic currents

Ten Tusscher - Noble - Panfilov 2005

Electrophysiology

$$h_\infty = \frac{1}{[1 + e^{(V+71.55)/7.43}]^2} \quad (32)$$

$$\alpha_h = 0 \quad \text{if} \quad V \geq -40 \quad (33)$$

...erwise

...$\geq -40$ (34)

...rwise

$$\tau_h = \frac{1}{\alpha_h + \beta_h} \quad (35)$$

$$j_\infty = \frac{1}{[1 + e^{(V+71.55)/7.43}]^2} \quad (36)$$

$$\alpha_j = 0 \quad \text{if} \quad V \geq -40 \quad (37)$$

$$\alpha_j = \frac{\left(\begin{matrix}-2.5428 \times 10^4 e^{0.2444V} - 6.948 \\ \times 10^{-6} e^{-0.04391V}\end{matrix}\right)(V + 37.78)}{1 + e^{0.311(V+79.23)}} \quad \text{otherwise}$$

$$\beta_j = \frac{0.6e^{0.057V}}{1 + e^{-0.1(V+32)}} \quad \text{if} \quad V \geq -40 \quad (38)$$

$$\beta_j = \frac{0.02424e^{-0.01052V}}{1 + e^{-0.1378(V+40.14)}} \quad \text{otherwise}$$

$$\tau_j = \frac{1}{\alpha_j + \beta_j} \quad (39)$$

*L-type $Ca^{2+}$ Current*

$$I_{CaL} = G_{CaL} d f f_{Ca} 4 \frac{VF^2}{RT} \frac{Ca_i e^{2VF/RT} - 0.341 Ca_o}{e^{2VF/RT} - 1} \quad (40)$$

$$d_\infty = \frac{1}{1 + e^{(-5-V)/7.5}} \quad (41)$$

$$\alpha_d = \frac{1.4}{1 + e^{(-35-V)/13}} + 0.25 \quad (42)$$

$$\beta_d = \frac{1.4}{1 + e^{(V+5)/5}} \quad (43)$$

$$\gamma_d = \frac{1}{1 + e^{(50-V)/20}} \quad (44)$$

$$\tau_d = \alpha_d \beta_d + \gamma_d \quad (45)$$

$$f_\infty = \frac{1}{1 + e^{(V+20)/7}} \quad (46)$$

$$\tau_f = 1125e^{-(V+27)^2/240} + \frac{165}{\ldots} + 80 \quad (47)$$

$$\tau_{fca} = 2 \text{ ms}$$

$$\frac{df_{ca}}{dt} = k \frac{f_{ca\infty} - f_{ca}}{\tau_{fca}}$$

$$k = 0 \quad \text{if} \quad f_{ca\infty} > f_{ca} \quad \text{and} \quad V > -60 \text{ mV}$$

$$k = 1 \quad \text{otherwise}$$

*Transient Outward Current*

$$I_{to} = G_{to} r s (V - E_K)$$

For all cell types

$$r_\infty = \frac{1}{1 + e^{(20-V)/6}}$$

$$\tau_r = 9.5e^{-(V+40)^2/1800} + 0.8$$

For epicardial and M cells

$$s_\infty = \frac{1}{1 + e^{(V+20)/5}}$$

$$\tau_s = 85e^{-(V+45)^2/320} + \frac{5}{1 + e^{(V-20)/5}} + 3$$

For endocardial cells

$$s_\infty = \frac{1}{1 + e^{(V+28)/5}}$$

$$\tau_s = 1{,}000e^{-(V+67)^2/1{,}000} + 8$$

*Slow Delayed Rectifier Current*

$$I_{Ks} = G_{Ks} x_s^2 (V - E_{Ks})$$

$$x_{s\infty} = \frac{1}{1 + e^{(-5-V)/14}}$$

$$\alpha_{xs} = \frac{1{,}100}{\sqrt{1 + e^{(-10-V)/6}}}$$

$$\beta_{xs} = \frac{1}{1 + e^{(V-60)/20}}$$

$$\tau_{xs} = \alpha_{xs} \beta_{xs}$$

*Rapid Delayed Rectifier Current*

$$I_{Kr} = G_{Kr} \sqrt{\frac{K_o}{5.4}} x_{r1} x_{r2} (V - E_K)$$

$$x_{r1\infty} = \frac{1}{1 + e^{(-26-V)/7}}$$

$$\alpha_{xr1} = \frac{450}{1 + e^{(-45-V)/10}}$$

$$\tau_{xr2} = \alpha_{xr2} \beta_{xr2}$$

*Inward Rectifier $K^+$ Current*

$$I_{K1} = G_{K1} \sqrt{\frac{K_o}{5.4}} x_{K1\infty} (V - E_K)$$

$$\alpha_{K1} = \frac{0.1}{1 + e^{0.06(V-E_K-200)}}$$

$$\beta_{K1} = \frac{3e^{0.0002(V-E_K+100)} + e^{0.1(V-E_K-10)}}{1 + e^{-0.5(V-E_K)}}$$

$$x_{K1\infty} = \frac{\alpha_{K1}}{\alpha_{K1} + \beta_{K1}}$$

*$Na^+/Ca^{2+}$ Exchanger Current*

$$I_{NaCa} = k_{NaCa} \frac{e^{\gamma VF/RT} Na_i^3 Ca_o - e^{(\gamma-1)VF/RT} Na_o^3 Ca_i \alpha}{(K_{mNai}^3 + Na_o^3)(K_{mCa} + Ca_o)(1 + k_{sat} e^{(\gamma-1)VF/RT})}$$

*$Na^+/K^+$ Pump Current*

$$I_{NaK} = P_{NaK} \frac{K_o Na_i}{(K_o + K_{mK})(Na_i + K_{mNa})(1 + 0.1245e^{-0.1VF/RT} + 0.0353e^{\ldots}}$$

*$I_{pCa}$*

$$I_{pCa} = G_{pCa} \frac{Ca_i}{K_{pCa} + Ca_i}$$

*$I_{pK}$*

$$I_{pK} = G_{pK} \frac{V - E_K}{1 + e^{(25-V)/5.98}}$$

*Background Currents*

$$I_{bNa} = G_{bNa}(V - E_{Na})$$

$$I_{bCa} = G_{bCa}(V - E_{Ca})$$

*Calcium Dynamics*

$$I_{leak} = V_{leak}(Ca_{sr} - Ca_i)$$

$$I_{up} = \frac{V_{maxup}}{1 + K_{up}^2/Ca_i^2}$$

$$I_{rel} = \left(a_{rel} \frac{Ca_{sr}^2}{b_{rel}^2 + Ca_{sr}^2} + c_{rel}\right) d g$$

$$g_\infty = \frac{1}{1 + Ca_i^6/0.00035^6} \quad \text{if} \quad Ca_i \leq 0.00035$$

$$g_\infty = \frac{1}{1 + Ca_i^{16}/0.00035^{16}} \quad \text{otherwise}$$

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## Mechanical deformation: Material model

**Mechanical properties of the cardiac tissue are defined through the Cauchy stress**

$$\boldsymbol{\sigma} = J^{-1} \boldsymbol{P} \boldsymbol{F}^T$$

**Stress is composed by passive and active parts**

$$\boldsymbol{\sigma} = \boldsymbol{\sigma}_{pas} + \sigma_{act}(\lambda, [Ca^{2+}]) \boldsymbol{f} \otimes \boldsymbol{f}$$

Passive stress + Active stress
Material Models based on biaxial testing of excised myocardium (Lin & Yin, 1998)

**Passive stress is (based on Holtzapfel 2009, but compressible and transversally isotropic)**

$$J\boldsymbol{\sigma}_{pas} = (a\ e^{b(I_1-3)} - a)\boldsymbol{b} + 2a_f(I_4 - 1)e^{b_f(I_4-1)^2} \bar{\boldsymbol{f}} \otimes \bar{\boldsymbol{f}}$$

$$+K(J-1)\boldsymbol{I}$$

P. Lafortune, R. Arís, M. Vázquez, G. Houzeaux. Coupled electromechanical model of the heart: Parallel finite element formulation, 2012

## Mechanical deformation: Coupling

Active stress is (Hunter and co-workers)

$$\sigma_{act} = \alpha \, \frac{[Ca^{2+}]^n}{[Ca^{2+}]^n + C_{50}^n} \sigma_{max}(1 + \beta(\lambda_f - 1))$$

where free calcium concentration comes from the chosen EP model.

$\alpha$ controls the strength of the coupling.

## Synthetic Purkinje System

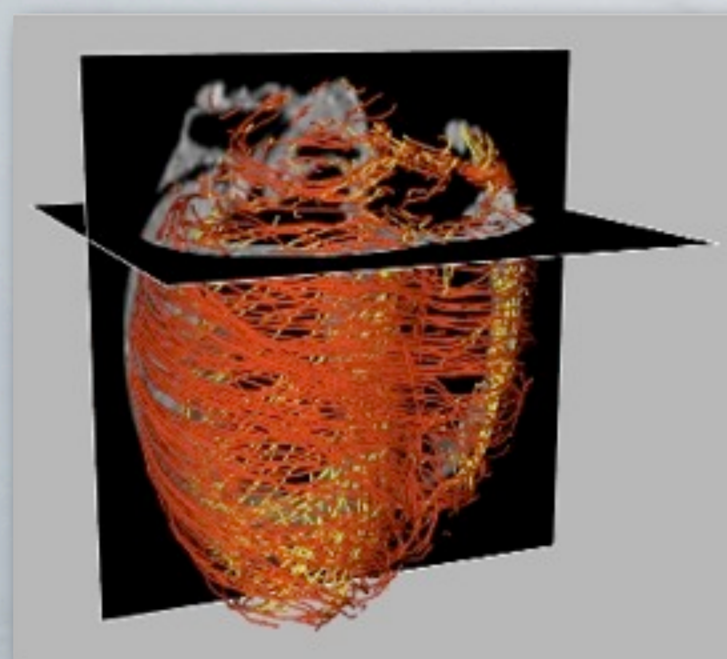
Electrical propagation through the Purkinje system.

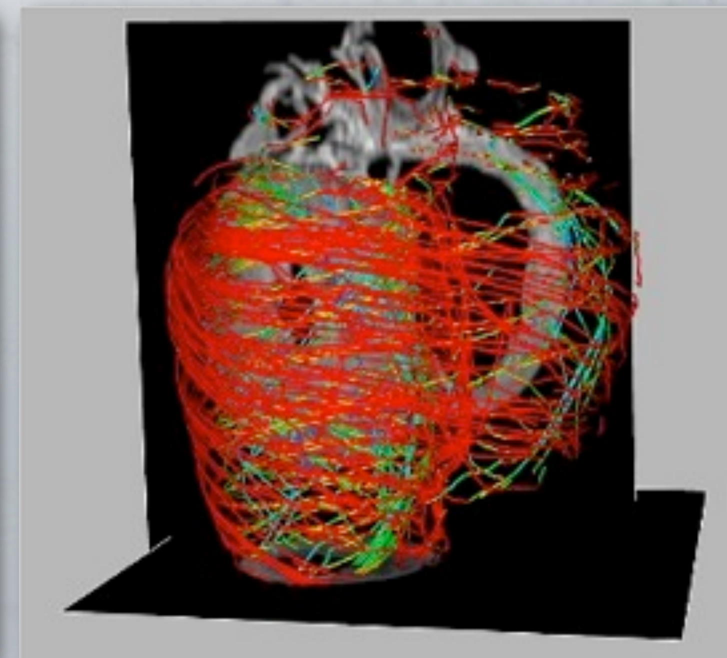
It delivers the initial impulse.

Sebastian R. et al.
Characterization and Modeling of the Peripheral Cardiac Conduction System, 2012.

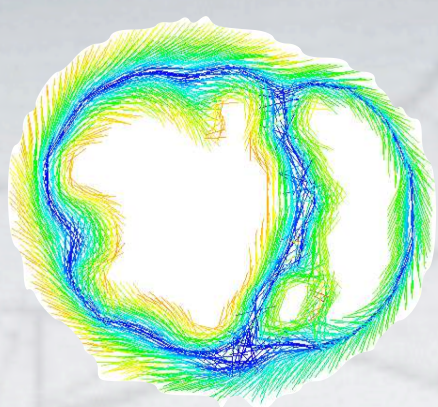
# Inputs of the simulation

## DTI (Ex-vivo and In-vivo)

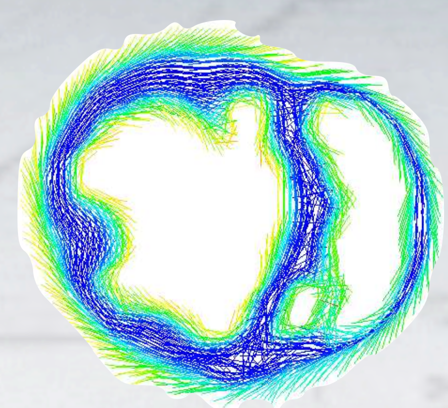




## Anisotropic fiber model: Rule-based (Streeter)



Linear Model

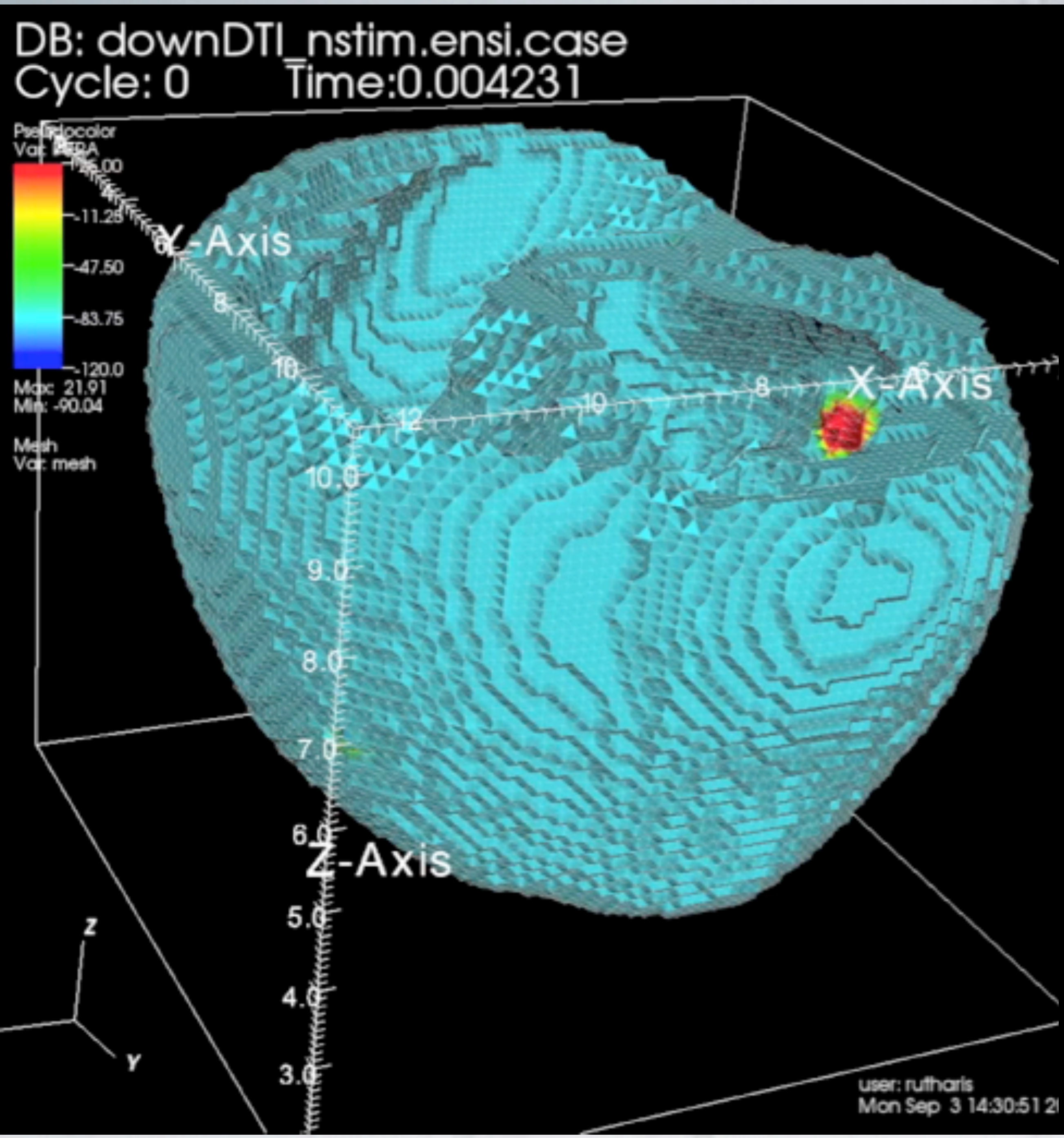


Cubic Model

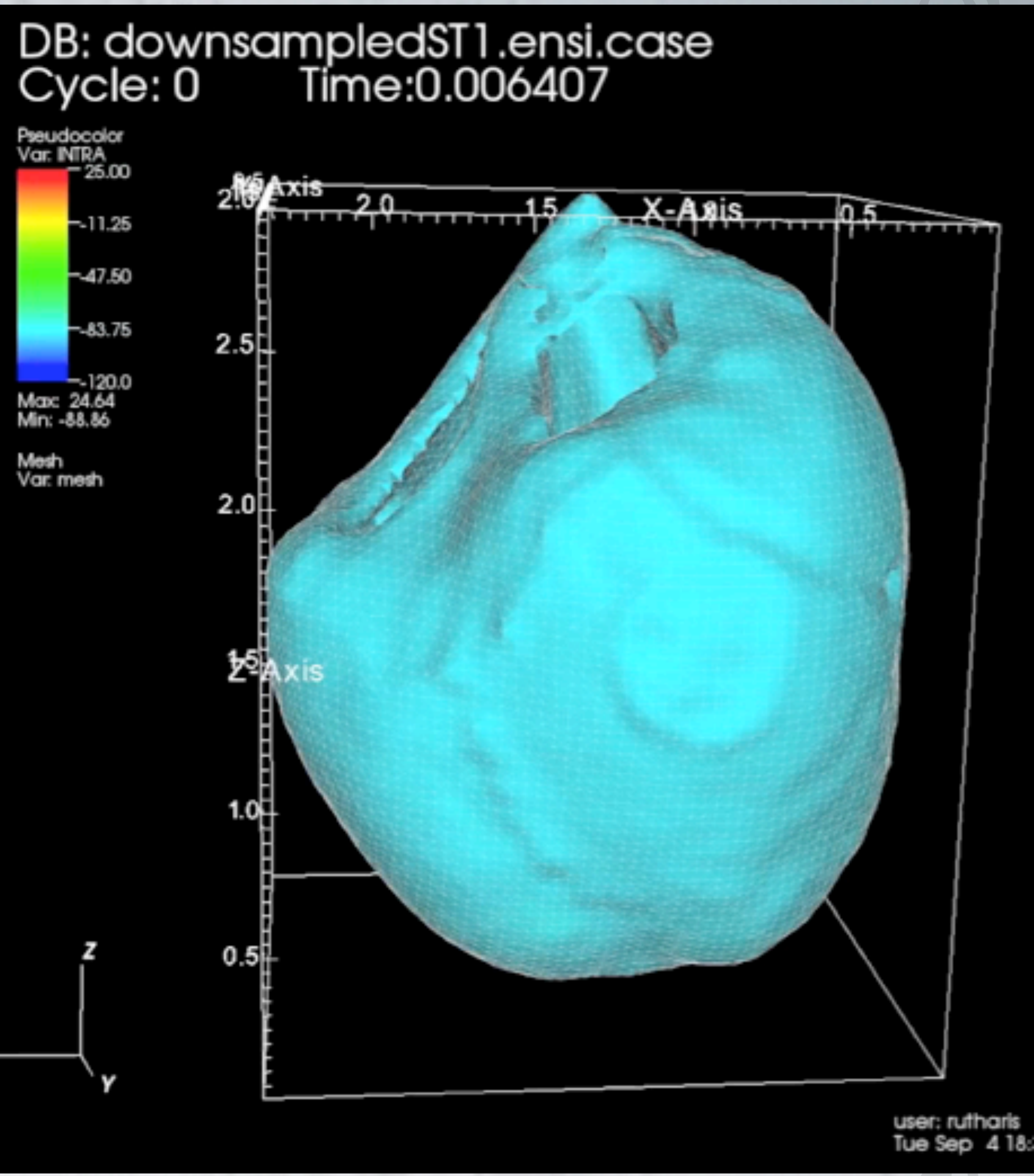
Fiber orientation: Rule-Based approach (Potse et al., 2006)

# Geometries

Dog (Johns Hopkins University)

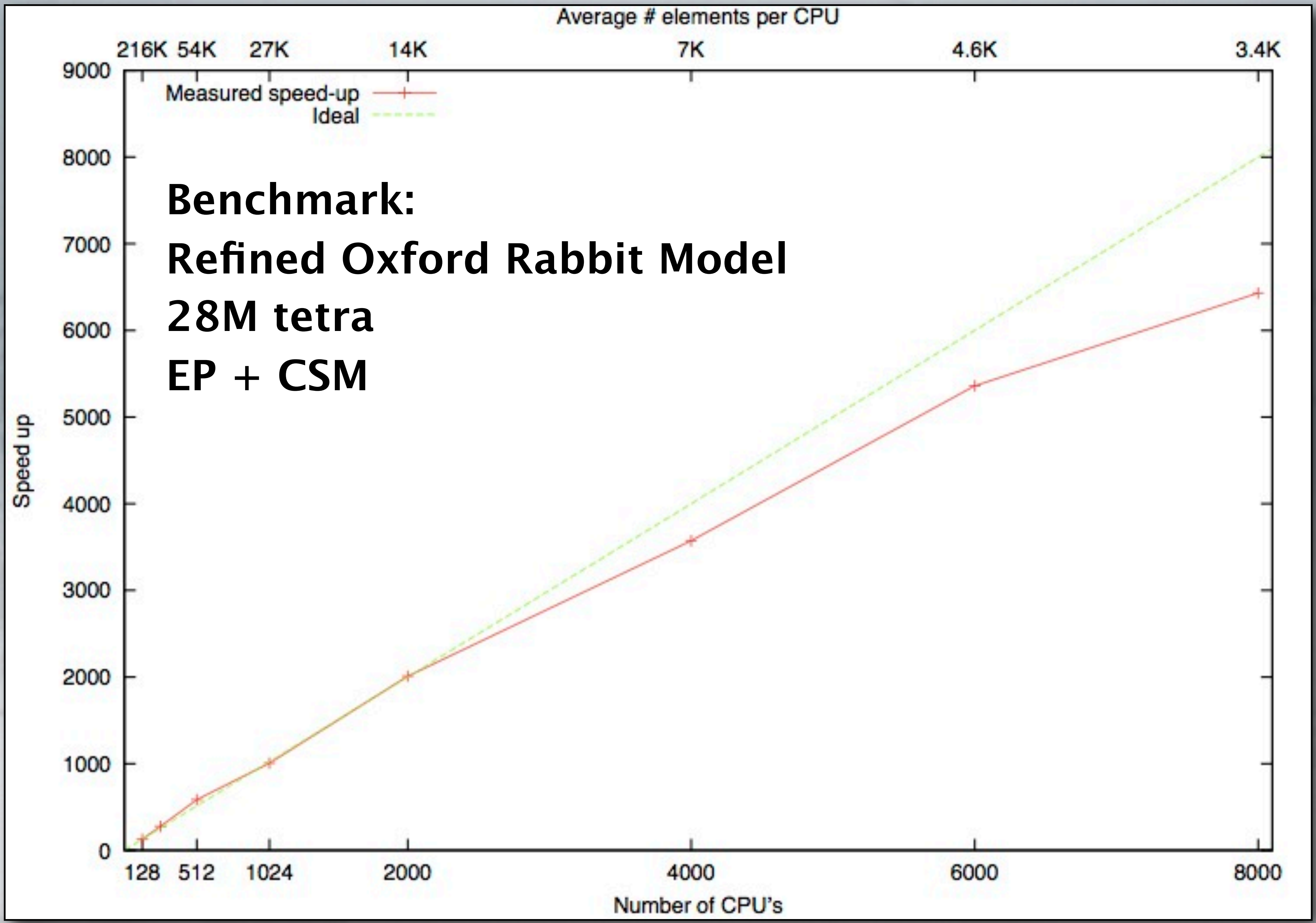



Rabbit (University of Oxford)




Electromechanical Coupling:
Electrical Activation + Mechanical Deformation

## Scalability: Electro - Mechanical problem
## Marenostrum III - BSC



# BSC - KCL

**Cardiologists:**

Understanding biological systems
Physiological models

They provide the main motivation and insight to the problem

BSC

**Computational scientists:**

Developing computational tools to run simulations

Provide the required simulation capacity

High Performance Computational Mechanics

**Bio-mechanics researchers:**

Develop the Physiological models
Deal with medical image processing
Design data acquisition tools

KCL

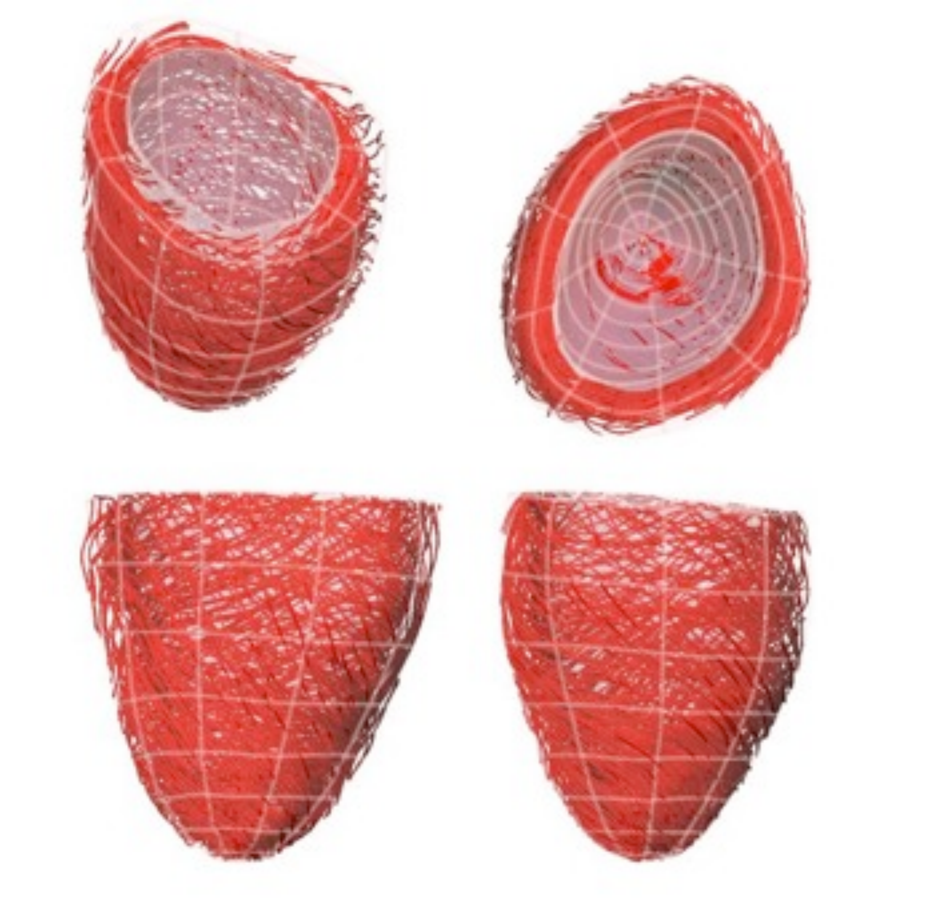
**St Thoma's Hospital**

**Pablo Lamata, Liya Asner and David Nordsletten**

# Sensitivity Analysis: diastolic inverse problem



**Cardiac Image (LV)**
**+**
**Fibers (DTI)**



**Human LV**
**Code: CHeart**

$$W = C_1 e^{AC_2 + BC_3 + DC_4}$$

$$\alpha = C_1 + C_2 + C_3$$

$$r_3 = \frac{C_3}{\alpha}$$

$$r_4 = \frac{C_4}{\alpha}$$

# Sensitivity Analysis: diastolic inverse problem

**Functional to characterize the minimum:**
**Averaged distance between equivalent Gauss point of the reference and simulated**

$$J_i(x_i, y_i) = \sqrt{\frac{1}{G}\sum_g \|x_{ig} - y_{ig}\|^2}$$

Forward Model:

* $C_1 - \alpha$ space
* $r_3 - r_4$ space

$$W = C_1 e^{AC_2 + BC_3 + DC_4}$$

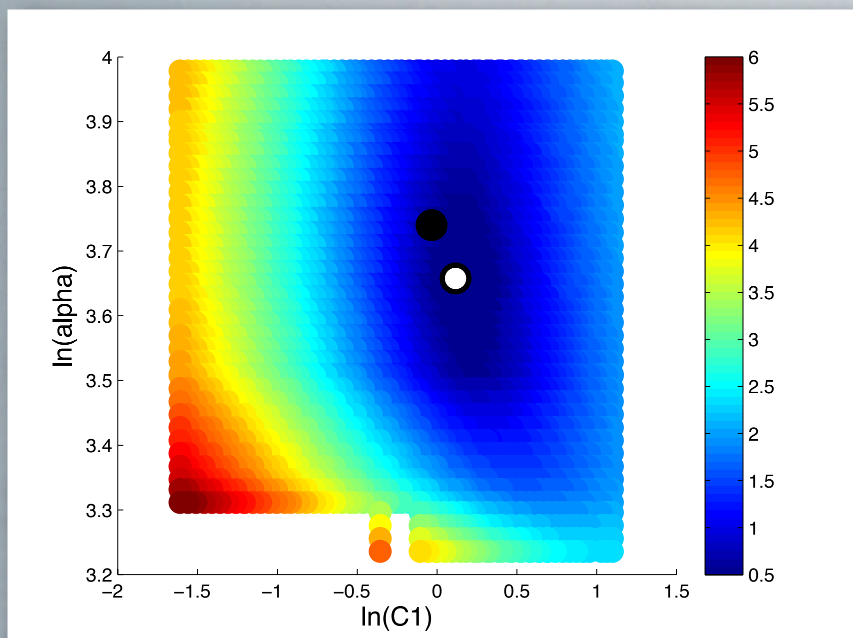
$$\alpha = C_1 + C_2 + C_3$$

$$r_3 = \frac{C_3}{\alpha}$$

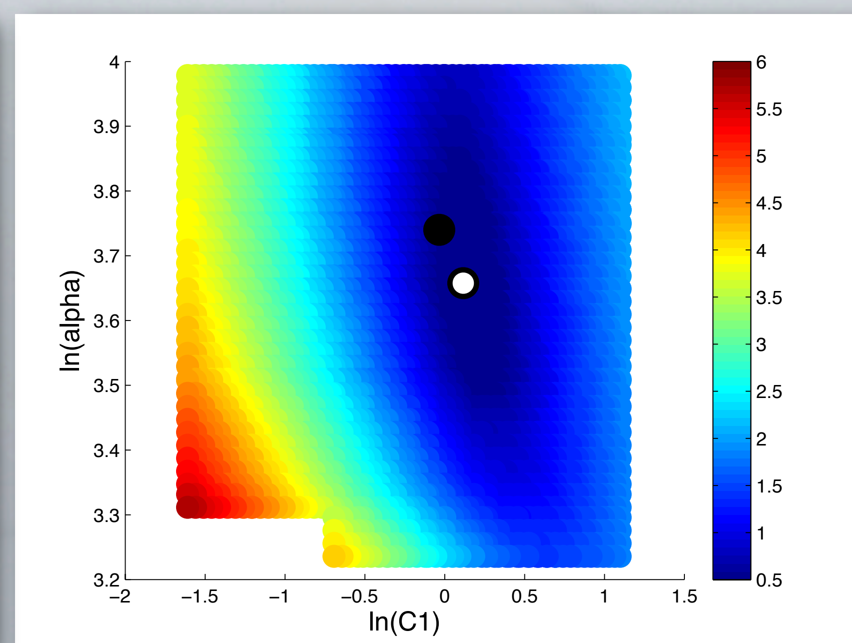
$$r_4 = \frac{C_4}{\alpha}$$

# Characterization of the Functional

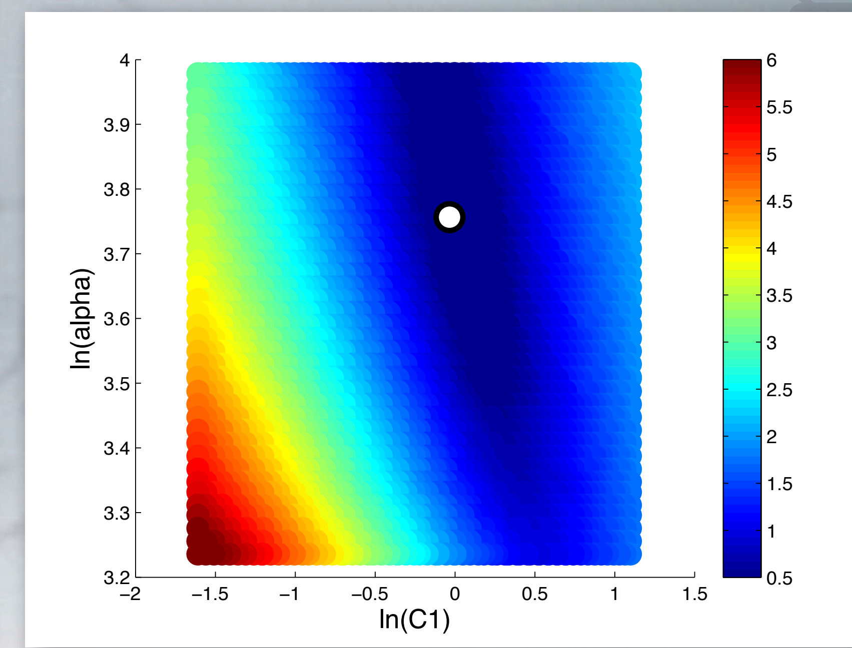
$$C_1 - \alpha$$



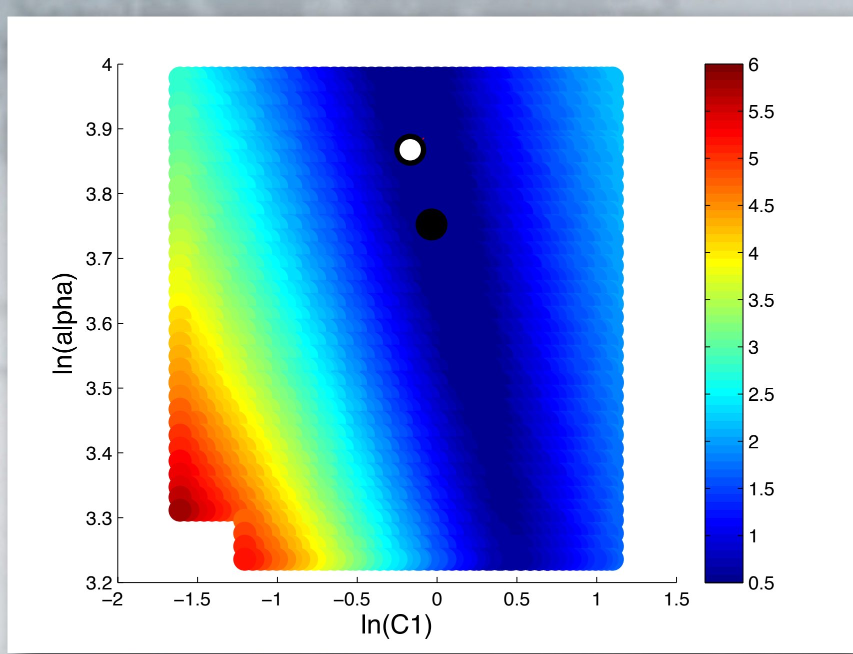

**Angle 0**



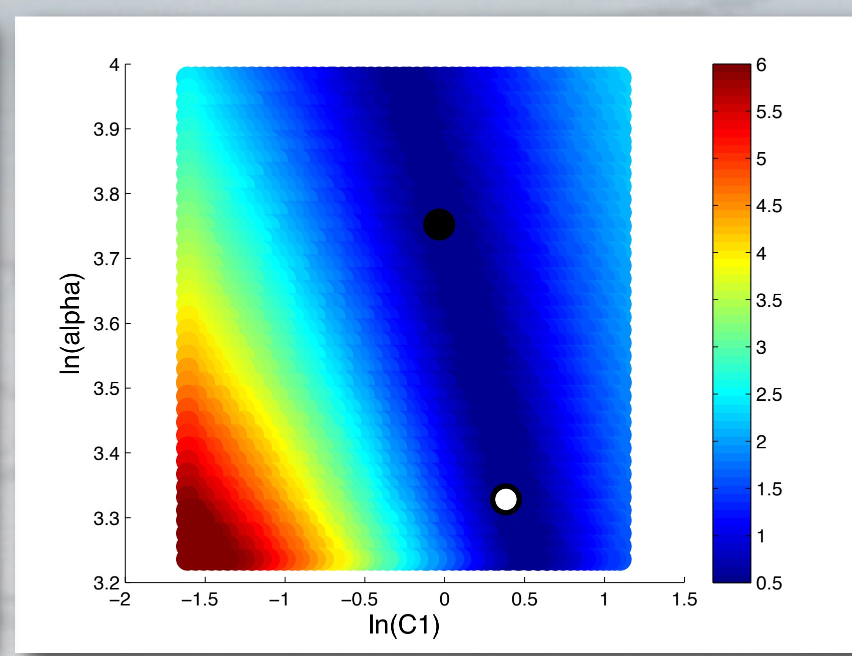

**Angle 30**




**DTI**



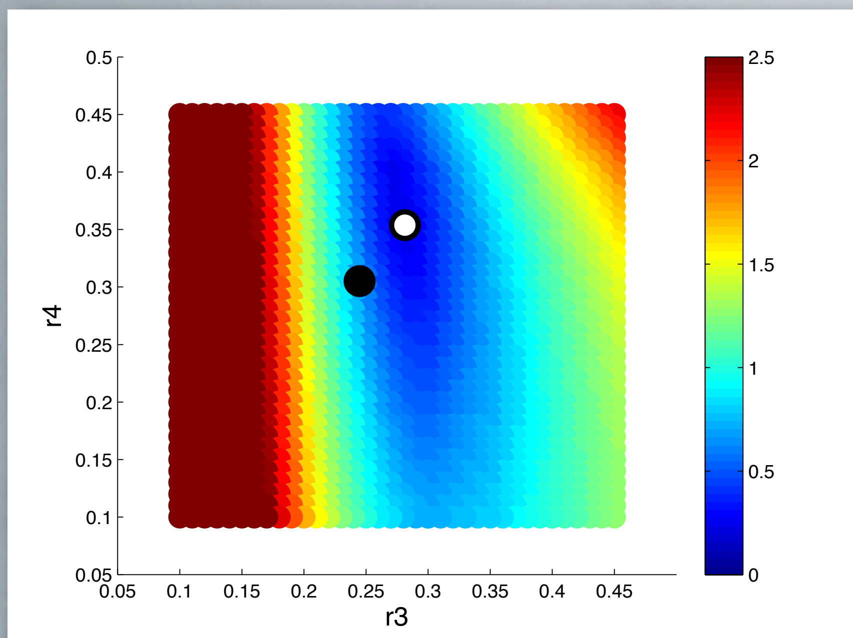

**Angle 60**



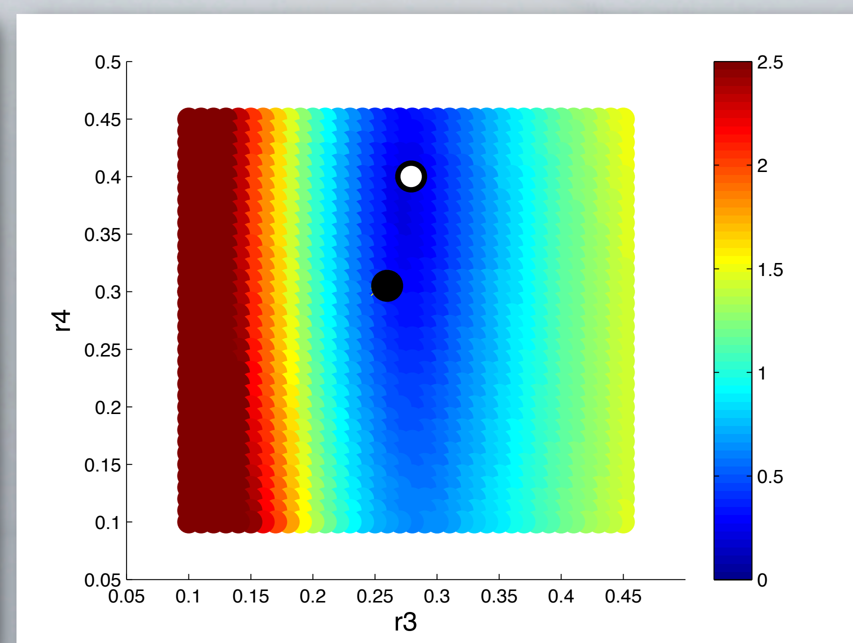

**Angle 90**

# Sensitivity Analysis Guccione Parameters- Human LV

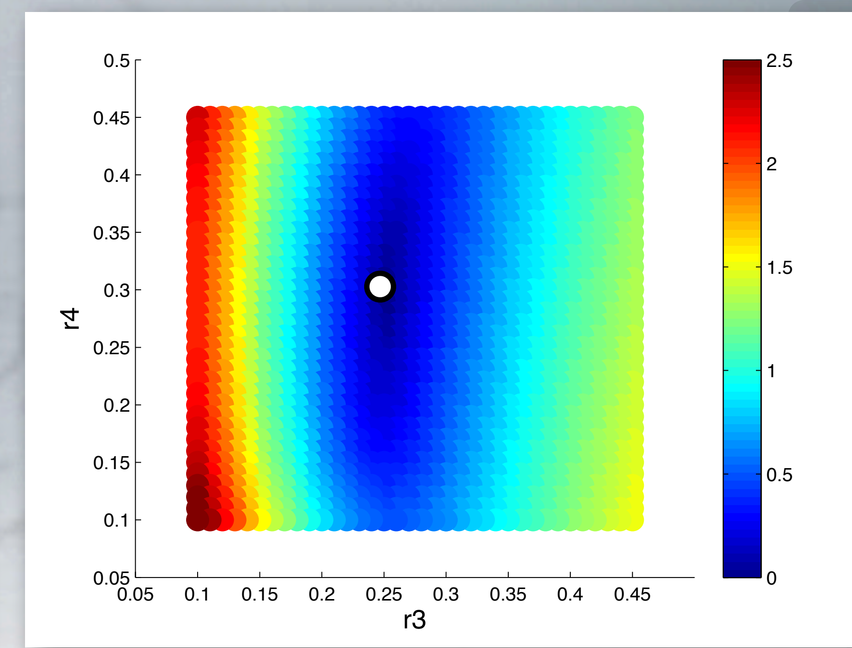
$$r_3 - r_4$$



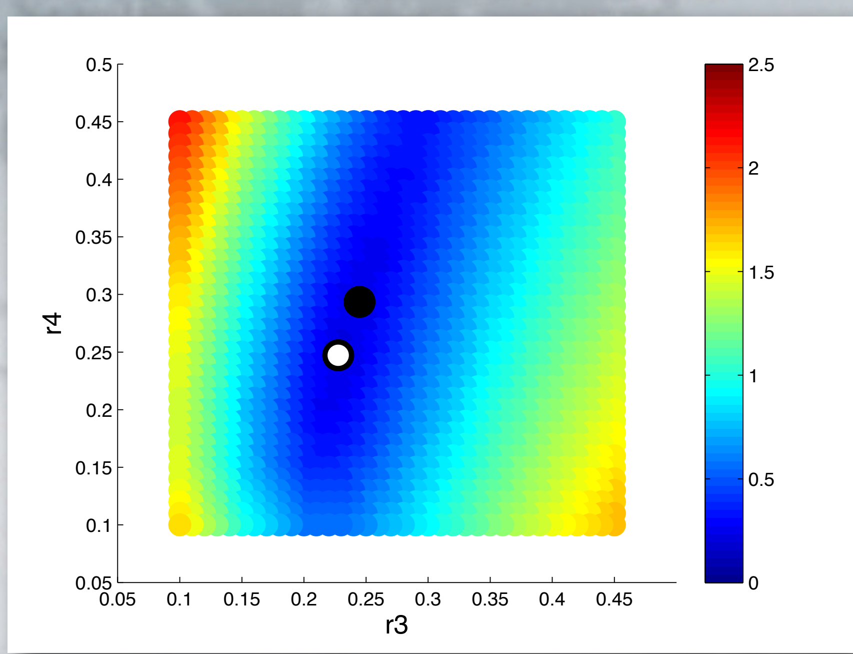

Angle 0



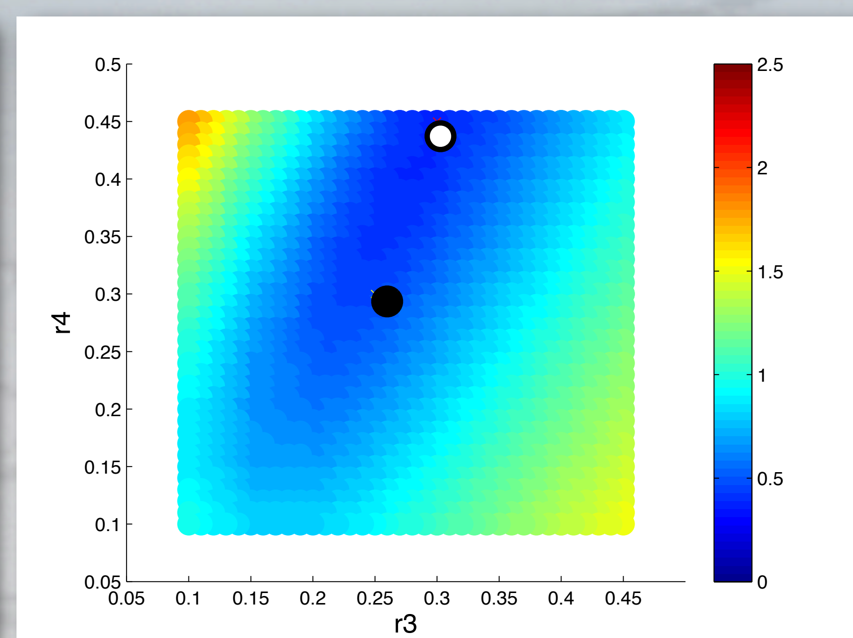

Angle 30




DTI




Angle 60




Angle 90

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