Parallel computational framework for electrophysiology problems

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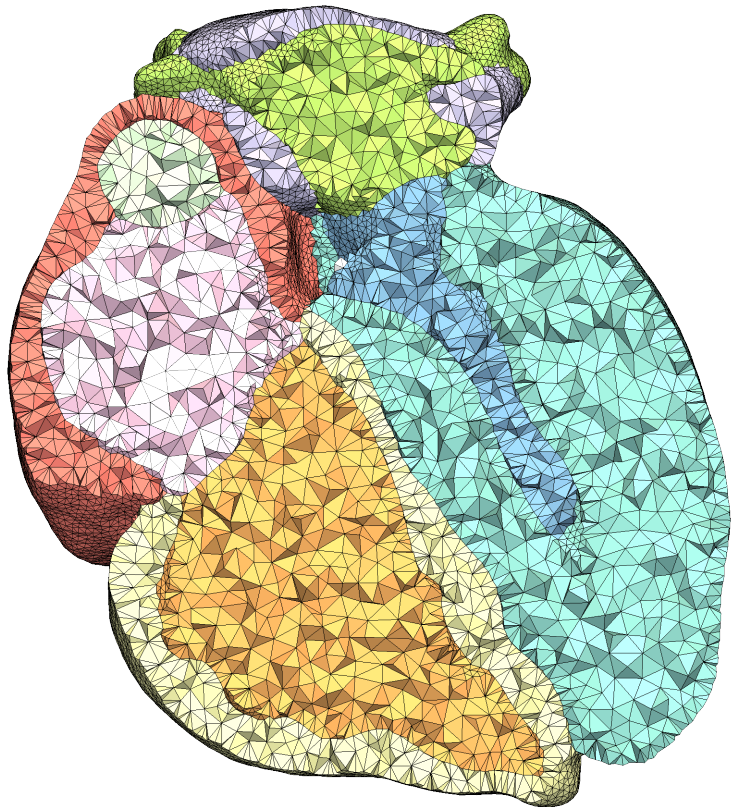
Motivation

- Mathematical modeling of cardiac electrophysiology is one of important and widely developing problems in personalized medicine
- Clinical applications: prediction of the arrhythmias, defibrillation therapy optimization, study of the effects of drugs, determination of the most effective location for a pacemakers' electrodes and others.
- Computational framework must be fast
- World Projects: Chaste (Oxford), Alya Red CC (Barcelona), CardioSolv, CARPentry Modeling Environment, CMISS/openCMISS ...

Modelling components for cardiac electrophysiology

1. Geometrical models + mesh generation
2. Tissue anisotropy
3. Ionic currents cell model
4. Equations and numerical schemes



VHP heart/MRI/ceCT data + segmentation

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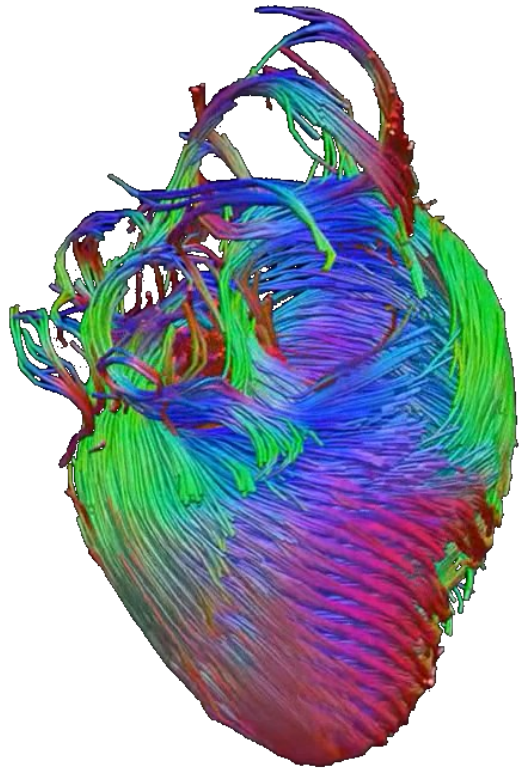

Bayer JD, Blake RC, Plank G, Trayanova N. *A novel rule-based algorithm for assigning myocardial fiber orientation to computational heart models.*// Ann Biomed Eng. (2012); **40**

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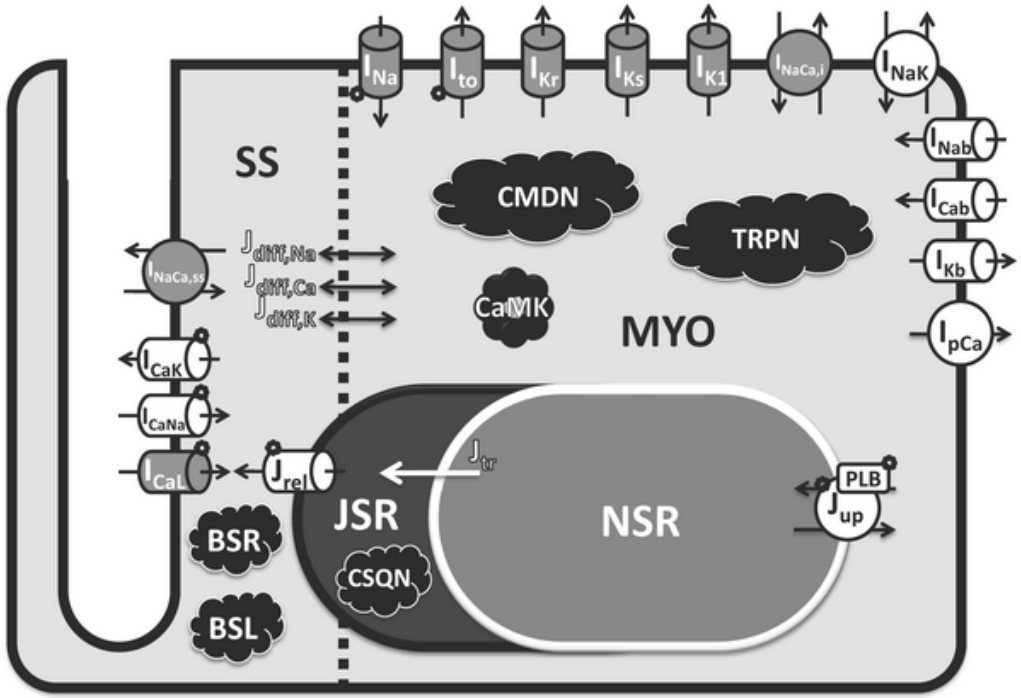

O'Hara T, Virág L, Varró A, Rudy Y *Simulation of the Undiseased Human Cardiac Ventricular Action Potential: Model Formulation and Experimental Validation*// PLoS Comput Biol. 2011, 7(5).
Any model from cellml.org

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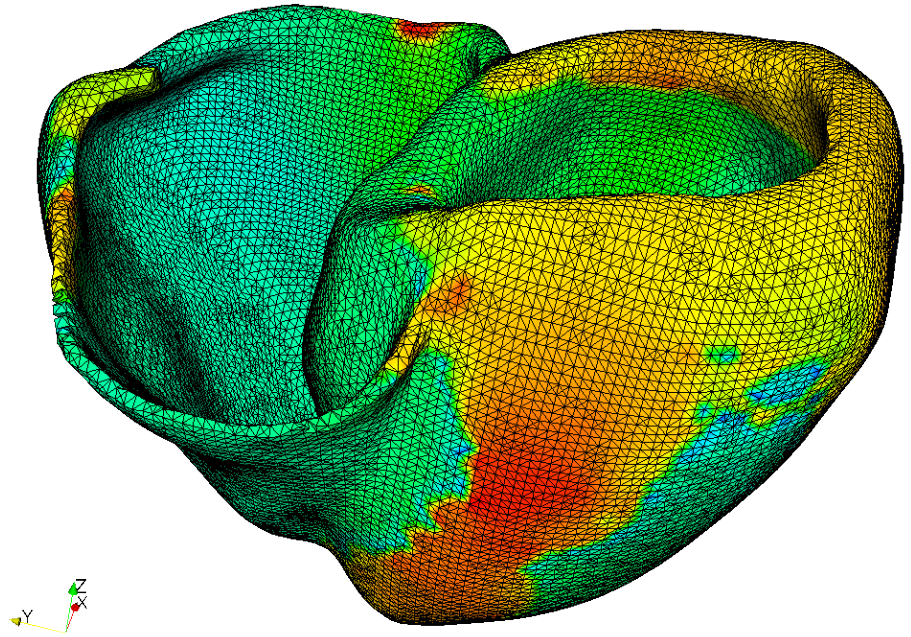

Bidomain/monodomain solution

Bidomain/monodomain model

Bidomain/monodomain model - most appropriate description of the electrical activity in cardiac tissues
Clinical applications for a bidomain problem:

- prediction of the arrhythmias
- defibrillation therapy optimization
- study of the effects of drugs
- others

Bidomain problem

Domain Ω with boundary $\partial\Omega$

ϕ_e extracellular electrical potential

v transmembrane voltage

$$\begin{aligned} \chi\left(C_m\frac{\partial v}{\partial t} + I_{ion}(\mathbf{u}, v)\right) - \nabla\cdot(\sigma_\mathbf{i}\nabla(v+\phi_e)) &= I_i, \\ \nabla\cdot((\sigma_\mathbf{i}+\sigma_\mathbf{e})\nabla\phi_e + \sigma_\mathbf{i}\nabla v) &= -I_{total}, \\ \frac{\partial \mathbf{u}}{\partial t} &= \mathbf{f}(\mathbf{u}, v), \end{aligned}$$

C_m cell membrane capacitance

χ cell membrane surface-to-volume ratio

σ_i & σ_e intra- & extracellular conductivity tensors

I_i, I_e intra- and extra-cellular stimulus currents

$I_{\text{total}} = I_i + I_e$ total stimulus current

I_{ion} - current in ionic channels, $\mathbf{f}$ cellular model

$\mathbf{u}$ state variables

Bidomain problem and ECG model

Boundary conditions for bidomain problem

$$\begin{aligned} \mathbf{n} \cdot (\sigma_i \nabla (v + \phi_e)) &= 0 \quad \text{on } \partial\Omega \\ \mathbf{n} \cdot (\sigma_e \nabla \phi_e) &= 0 \quad \text{on } \partial\Omega \end{aligned}$$

ECG model:

$\mathcal{T}$ human body around heart

$\partial\mathcal{T}$ external body surface

σ_0 conductivity tensor in body

ϕ_e - potential in body

$$\begin{aligned} -\nabla \cdot ((\sigma_\mathbf{i} + \sigma_\mathbf{e}) \nabla \phi_e) &= \nabla \cdot (\sigma_\mathbf{i} \nabla v) \quad \text{in } \Omega \\ \nabla \cdot (\sigma_0 \nabla \phi_e) &= 0 \quad \text{in } \mathcal{T} \setminus \Omega \\ \mathbf{n} \cdot \sigma_0 \nabla \phi_e &= 0 \quad \text{on } \partial\mathcal{T} \end{aligned}$$

Numerical methods

- FEM discretization on tetrahedral meshes
- implicit first time order time scheme

FEM system for bidomain problem

$$\begin{bmatrix} \kappa\mathbf{M}+\mathbf{K_i} & \mathbf{K_i} \\ \mathbf{K_i} & \mathbf{K_{i+e}} \end{bmatrix} \begin{bmatrix} \mathbf{v^{n+1}} \\ \phi_\mathbf{e}^{\mathbf{n+1}} \end{bmatrix} = \begin{bmatrix} \mathbf{M}(\kappa\mathbf{v^n} - \chi\mathbf{i_{ion}} + \mathbf{i_i}) \\ \mathbf{M i_{total}} \end{bmatrix},$$

FEM system for monodomain problem

$$[\kappa\mathbf{M}+\mathbf{K}]\,\mathbf{v^{n+1}} = \mathbf{M}(\kappa\mathbf{v^n} - \chi\mathbf{i}_{\mathbf{ion}}^{\mathbf{n}} + \mathbf{i_{stim}})$$

$\mathbf{M}$ - mass matrix, $\mathbf{K_i}$, $\mathbf{K_{i+e}}$ stiffness matrices
$\mathbf{i_{ion}}, \mathbf{i_i}, \mathbf{i_{total}}$ - vectors of currents and stimulus.
$\kappa = \chi C_m/\tau$, τ - timestep

Computational framework for monodomain/bidomain problem

- User-guided ITK-SNAP based segmentation for ceCT/MRI data
- Unstructured tetrahedral meshes: CGAL (Delaunay mesh generation) + Ani3D MBA (mesh cosmetics)
- Finite Element Method: Ani3D framework (https://sourceforge.net/p/ani3d)
- BCGStab linear solver + ILU(0) preconditioner
- CVODE solver for ODEs
- Ionic cell models provided by CellML model repository
- INMOST platform for MPI parallelization, ParMETIS for partitioning

Verification on a series of benchmarks

A. Chernyshenko, A. Danilov, and Y.Vassilevski. Numerical Simulations for Cardiac Electrophysiology Problems. *to appear in BIOMAT 2018 book.*

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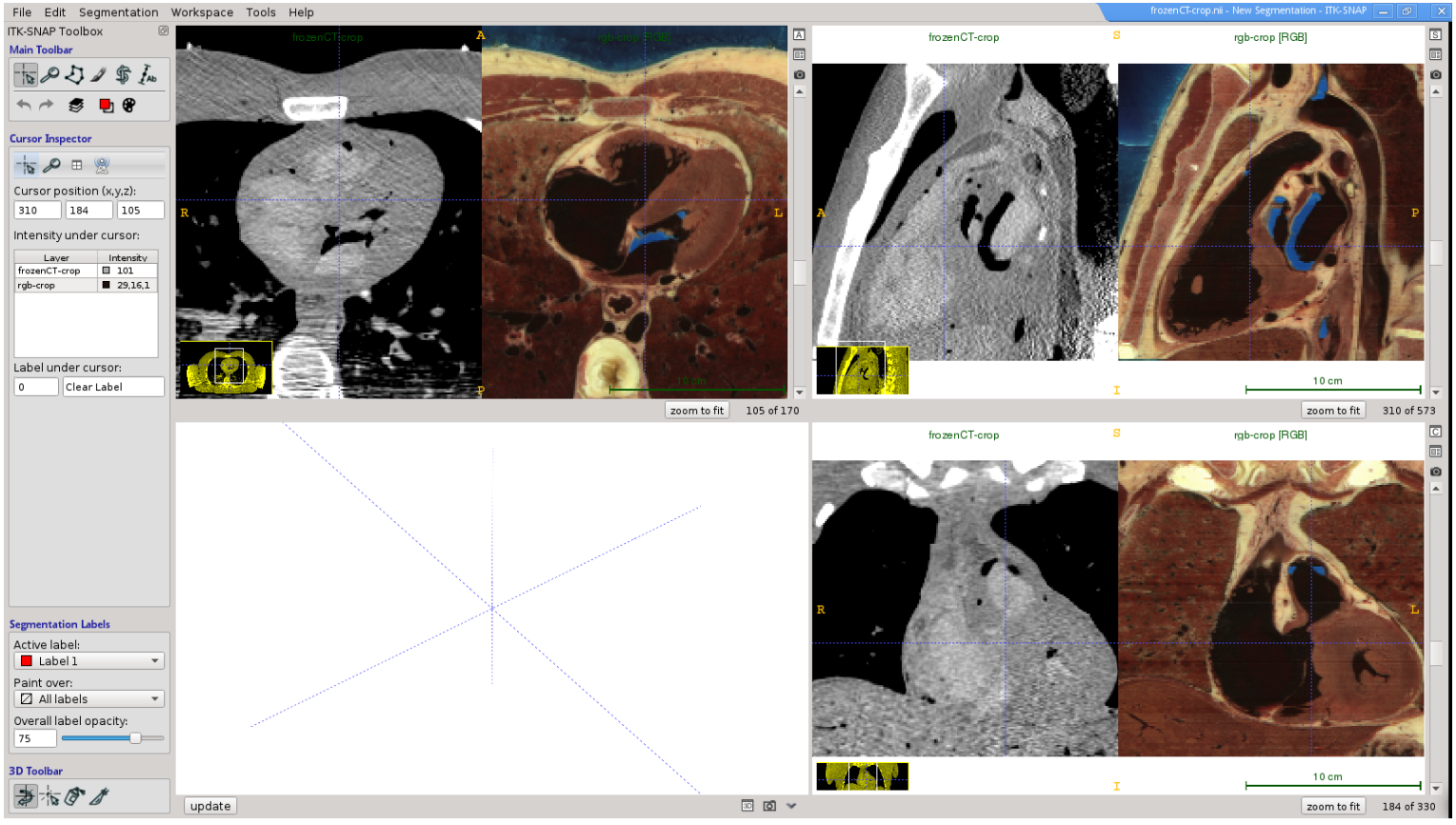
User-guided segmentation of VHP heart

ITK-SNAP: levelset segmentation with random forest classifier

A.Yurova, A.Danilov



We start with CT and cryosection images. Blood is quite distinctive

User-guided segmentation of VHP heart

ITK-SNAP: levelset segmentation with random forest classifier

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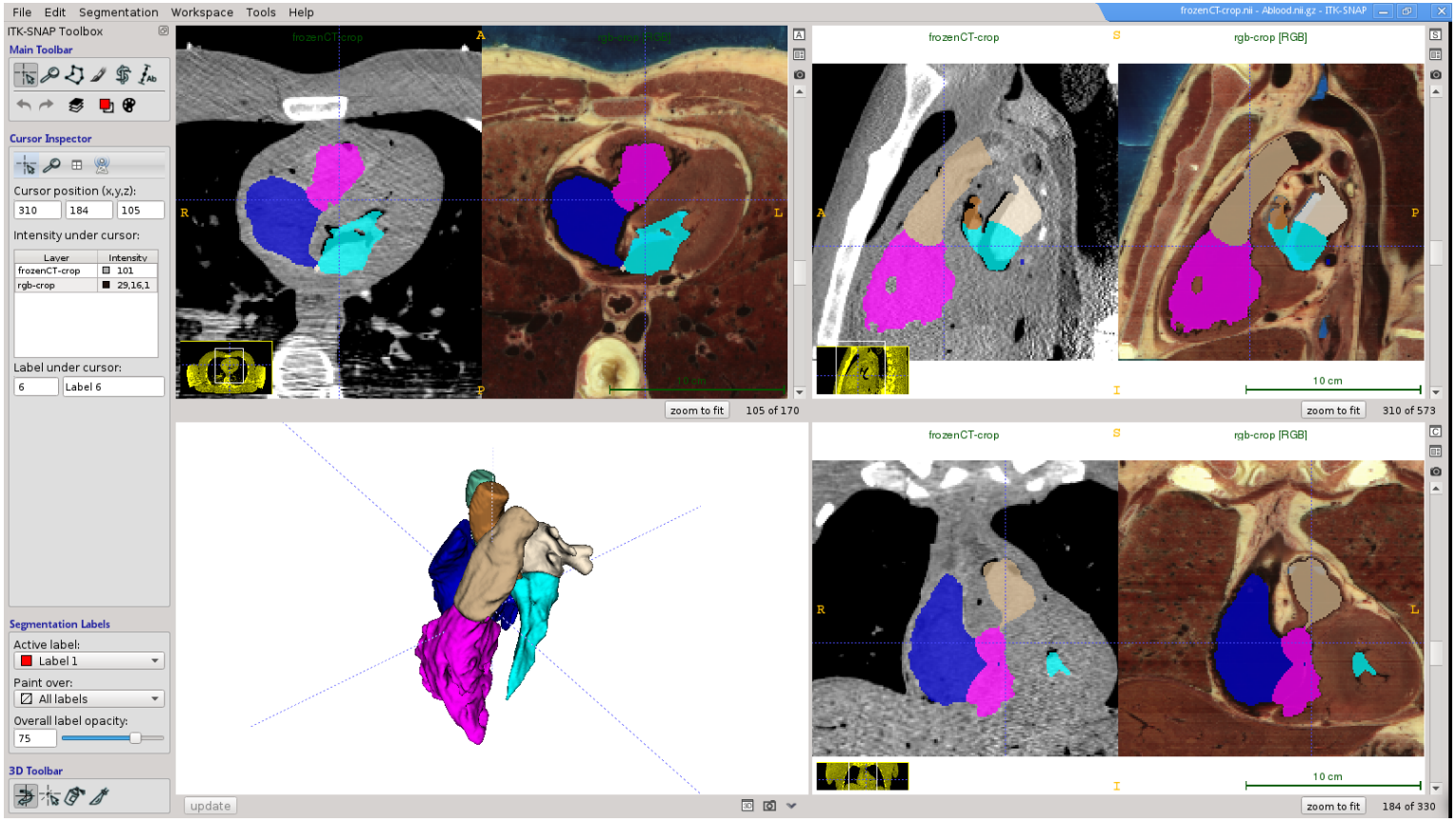

Heart ventricles and atria segmented interactively with threshold and levelset methods

User-guided segmentation of VHP heart

ITK-SNAP: levelset segmentation with random forest classifier

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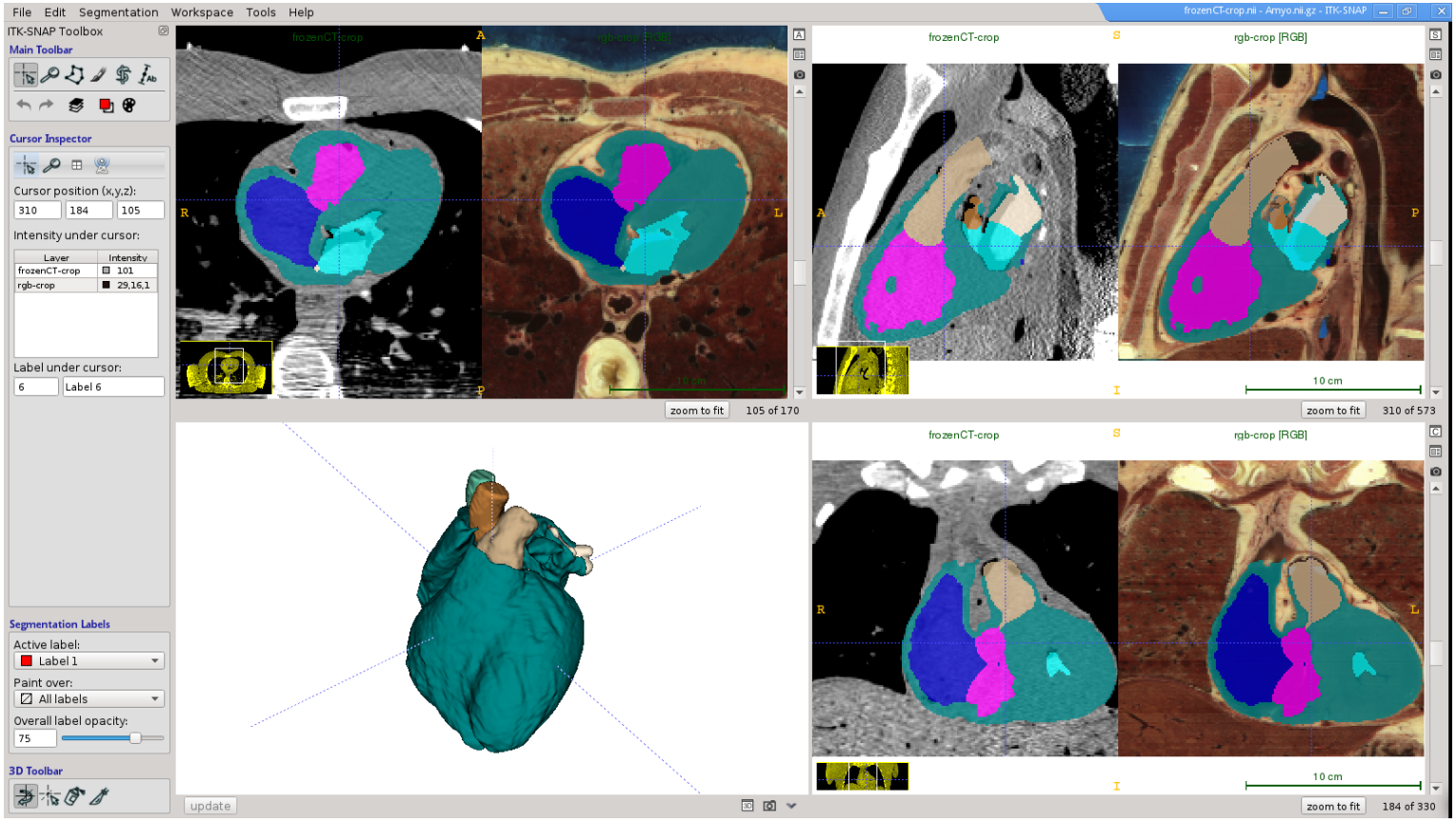

Segmentation of myocardium: RFC with the training samples on both CT and cryosection images

User-guided segmentation of VHP heart

ITK-SNAP: levelset segmentation with random forest classifier

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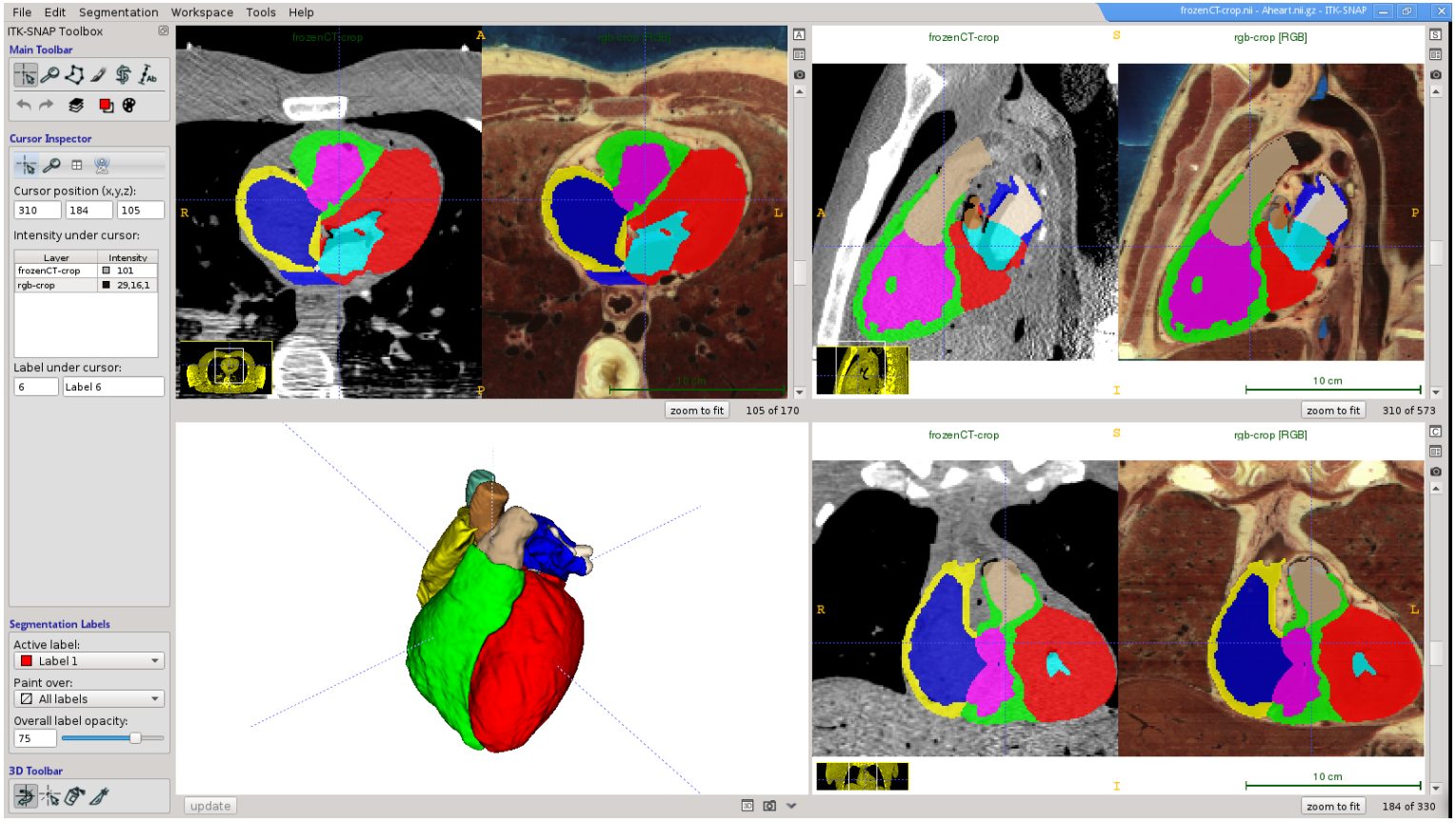
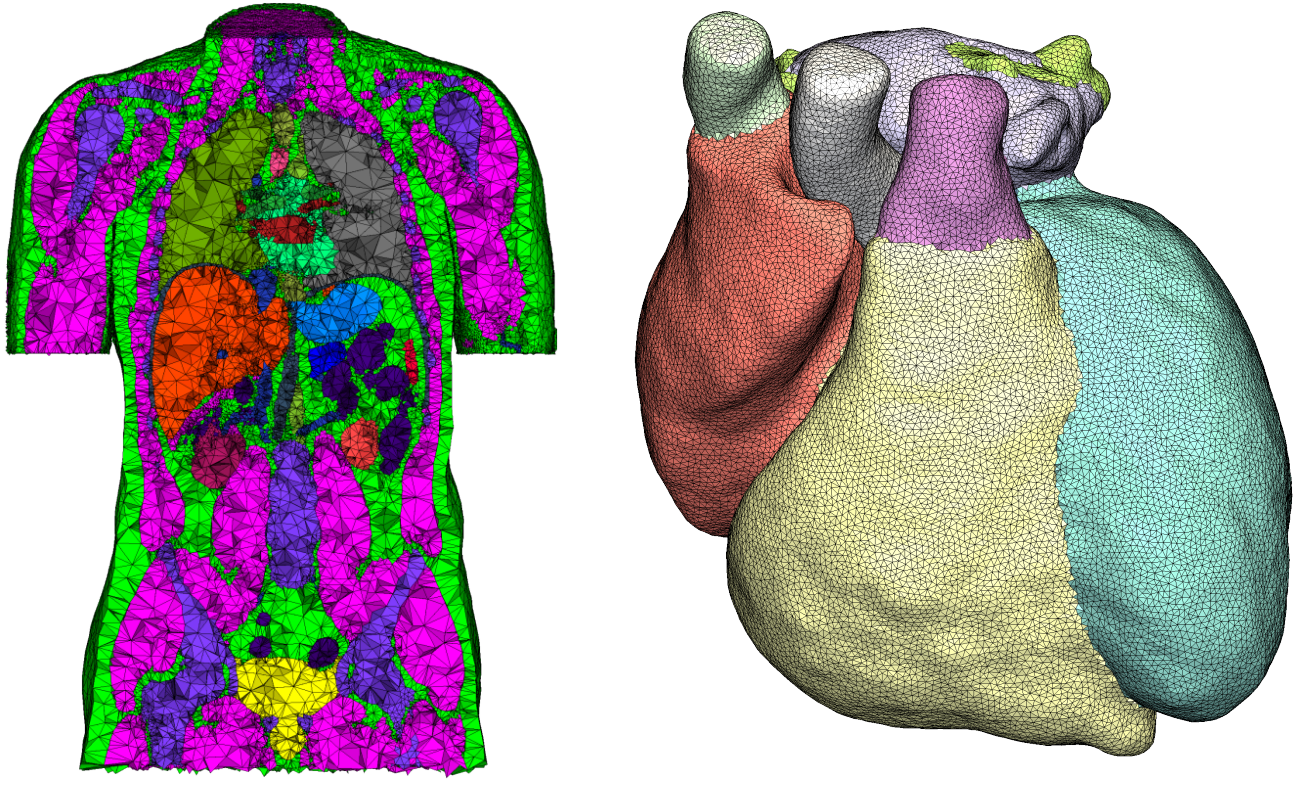


Split the myocardium into regions of left and right ventricles and left and right atria

Unstructured tetrahedral meshes

A.Danilov

CGAL Mesh (`www.cgal.org`) – Delaunay mesh generation
AniMBA (`sf.net/p/ani3d`) – mesh cosmetics



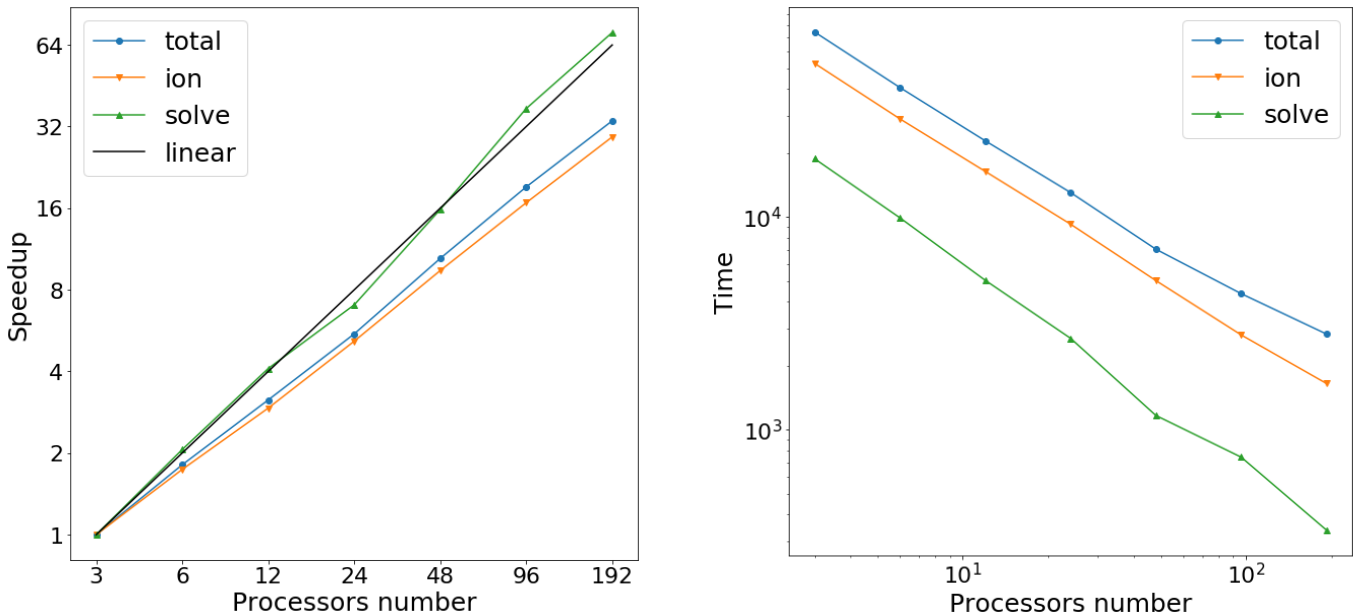
Meshes for full body and heart

Parallel Algorithm (monodomain model)

1. Preparing data
   - 1.1 Loading and partitioning a mesh
   - 1.2 Loading initial data
   - 1.3 Assembly matrices $\mathbf{M}$ and $[\varkappa\mathbf{M} + \mathbf{K}]$.
   - 1.4 Preparing initial conditions and work arrays.
2. For n-th time step:
   - 2.1 Calculation of ionic currents (may be used OpenMP)
   - 2.2 Calculation of vectors $(\varkappa\mathbf{v^n} - \chi\mathbf{i^n_{ion}} + \mathbf{i_{stim}})$ and $\mathbf{M}(\varkappa\mathbf{v^n} - \chi\mathbf{i^n_{ion}} + \mathbf{i_{stim}})$ using parallel built-in matrix-vector product.
   - 2.3 Solving system
   - 2.4 Exchanging solution between processors and preparing local arrays for the next time step.
3. Saving resulting potentials

Numerical experiment

Numerical experiment: INM cluster (8x24 proc.), mesh: $N_V = 0.4m$, $N_T = 2.4m$.



Speedup and computational time

Numerical experiment

Numerical experiment: INM cluster (8x24 proc.),
mesh: $N_V = 0.4m$, $N_T = 2.4m$.

p	T_{ion}	$S_{3,\text{ion}}$	T_{rhs}	T_{solve}	$S_{3,\text{solve}}$	T_{exch}	T_{total}	S_3
3	56774	1.00	1039	14850	1.00	659	73322	1.00
6	31736	1.78	589	7330	2.02	356	40011	1.83
12	19240	3.11	337	4299	3.45	210	24086	3.04
24	10289	5.51	229	1993	7.45	143	12654	5.79
48	6146	9.23	143	1136	13.07	95	7520	9.75
96	3523	16.11	60	711	20.88	54	4348	16.86
192	1999	28.40	33	449	33.07	32	2513	29.17

Table: Computation times and speedup for the first experiments set (mesh with 440857 vertices). Simulation time 150 ms.

Numerical experiment

INM cluster (8x24 proc.),
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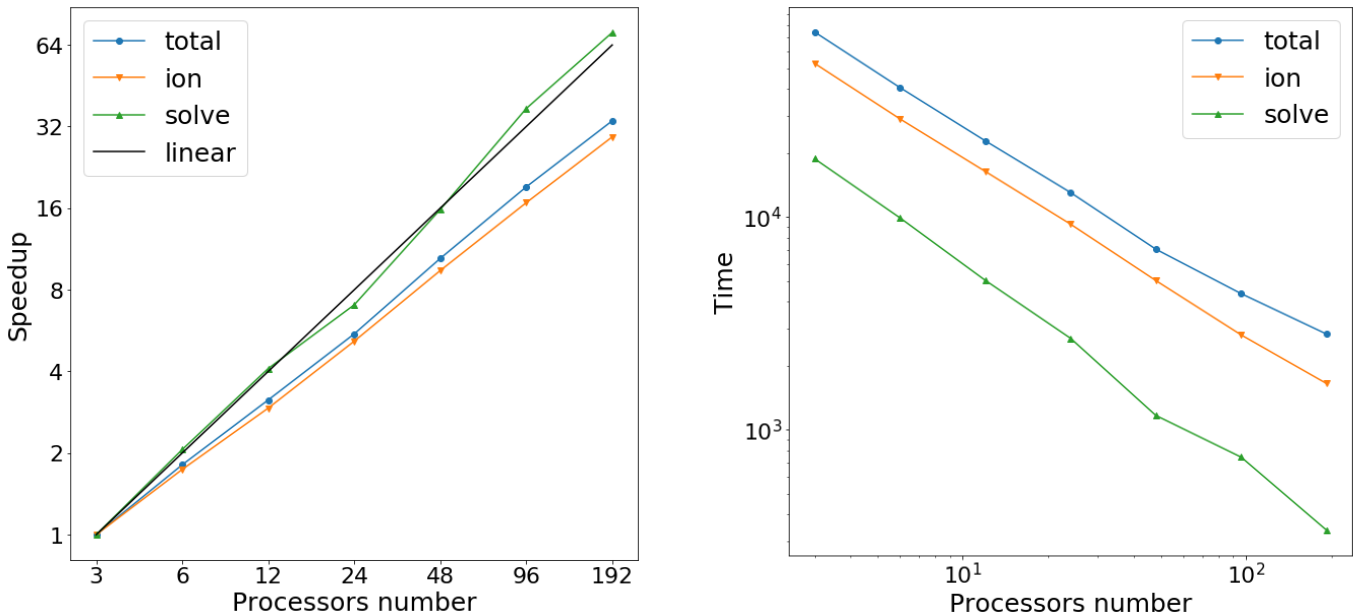

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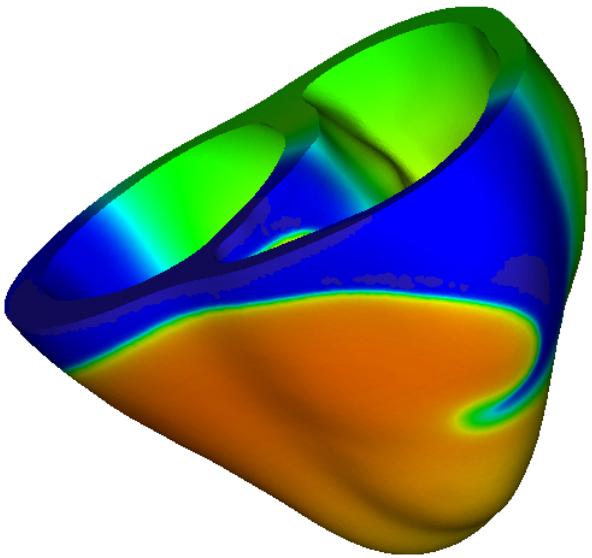
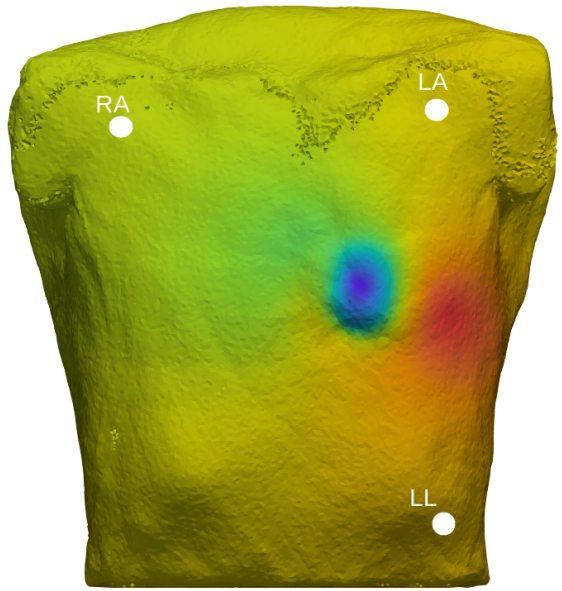
p	T_{ion}	$S_{3,\text{ion}}$	T_{rhs}	T_{solve}	$S_{3,\text{solve}}$	T_{exch}	T_{total}	S_3
3	245742	1.00	7885	68094	1.00	4698	326419	1.00
6	140456	1.74	3947	32946	2.06	2400	179749	1.81
12	83770	2.93	2148	16596	4.10	1261	103775	3.14
24	47497	5.17	1306	9659	7.04	813	59 275	5.5
48	26071	9.42	538	4304	15.82	338	31 251	10.44
96	14656	16.76	324	1826	37.29	219	17025	19.17
192	8382	29.31	215	957	71.15	159	9713	33.60

Table: Computation times and speedup for the second experiments set (mesh with 1945426 vertices). Simulation time 150 ms.

Postprocessing. Filaments trajectory

- Monodomain problem
- Reentry is induced by the S1–S2 protocol





Scroll wave on human ventricles (left) and distribution of potentials on the body surface and electrode positions used for computation of the leads (right)

Postprocessing. Filaments trajectory

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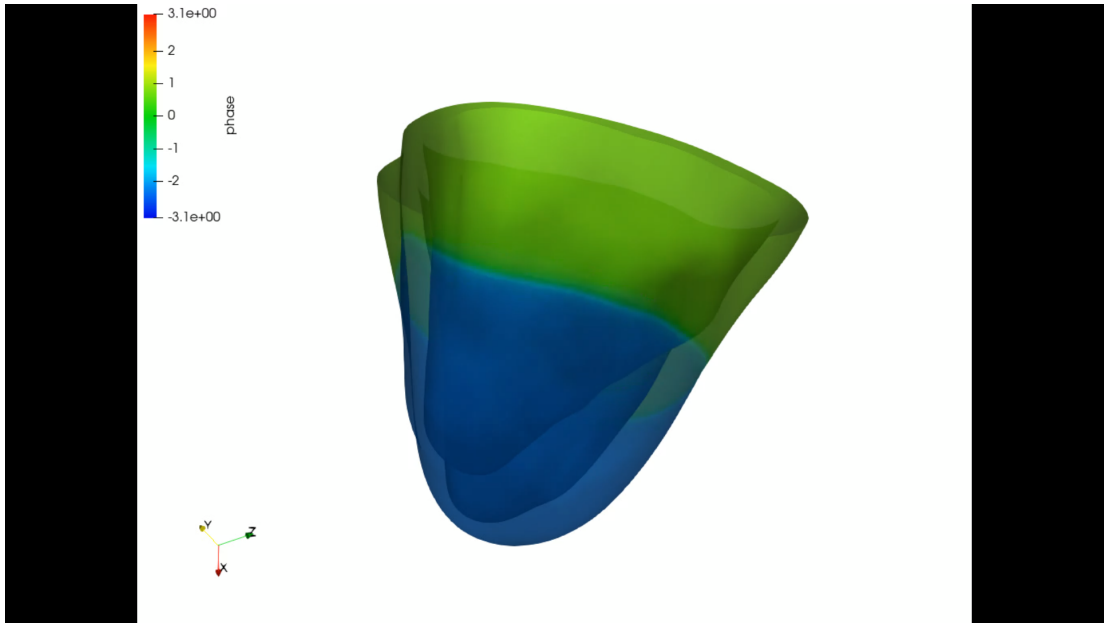


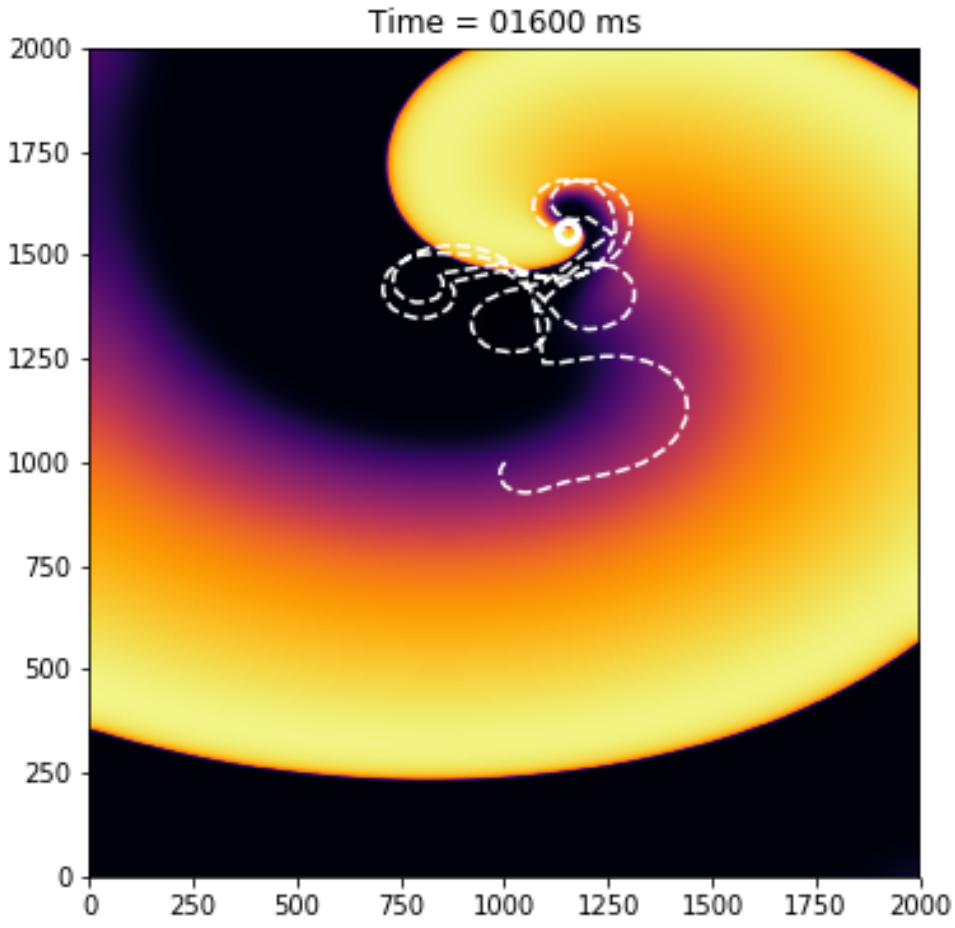
Rotor filaments trajectory

AP and IKatp

- Variation of AP duration may affect on arrhythmogenesis
- Shape and duration of AP change significantly with ischemia
- Main reason - activation of IK_{ATP}
- Study the influence of IK_{ATP} activation on arrhythmia mechanisms

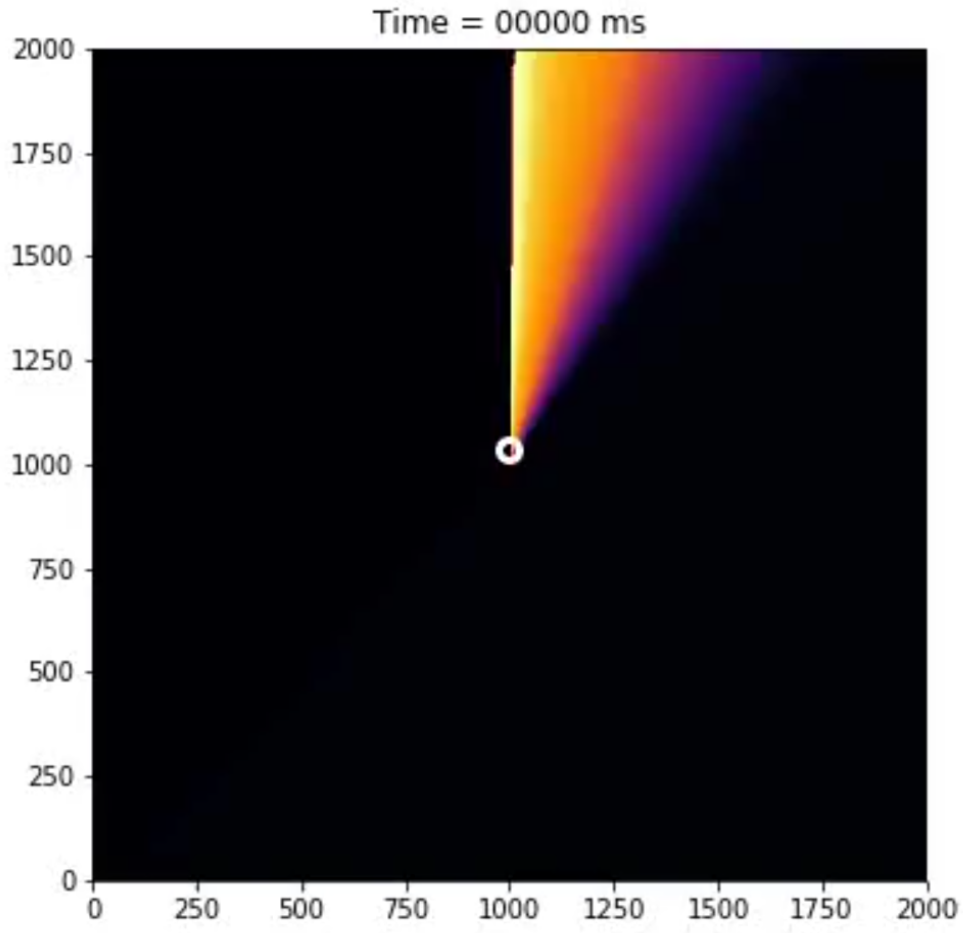
A. Pikunov and R. Syunyaev (MIPT) made a model for IK_{ATP} based on O'Hara-Rudy model

Filament trajectory: control



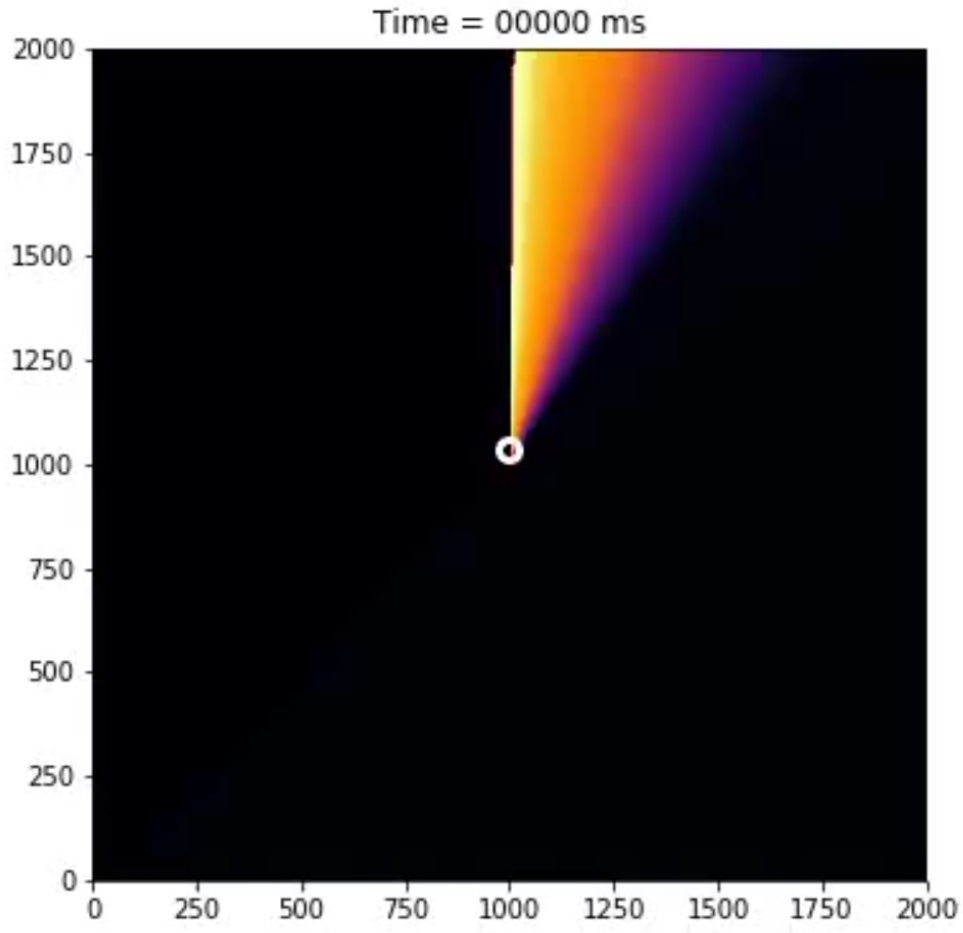
Rotor filament trajectory: control

Filament trajectory: pinacidil



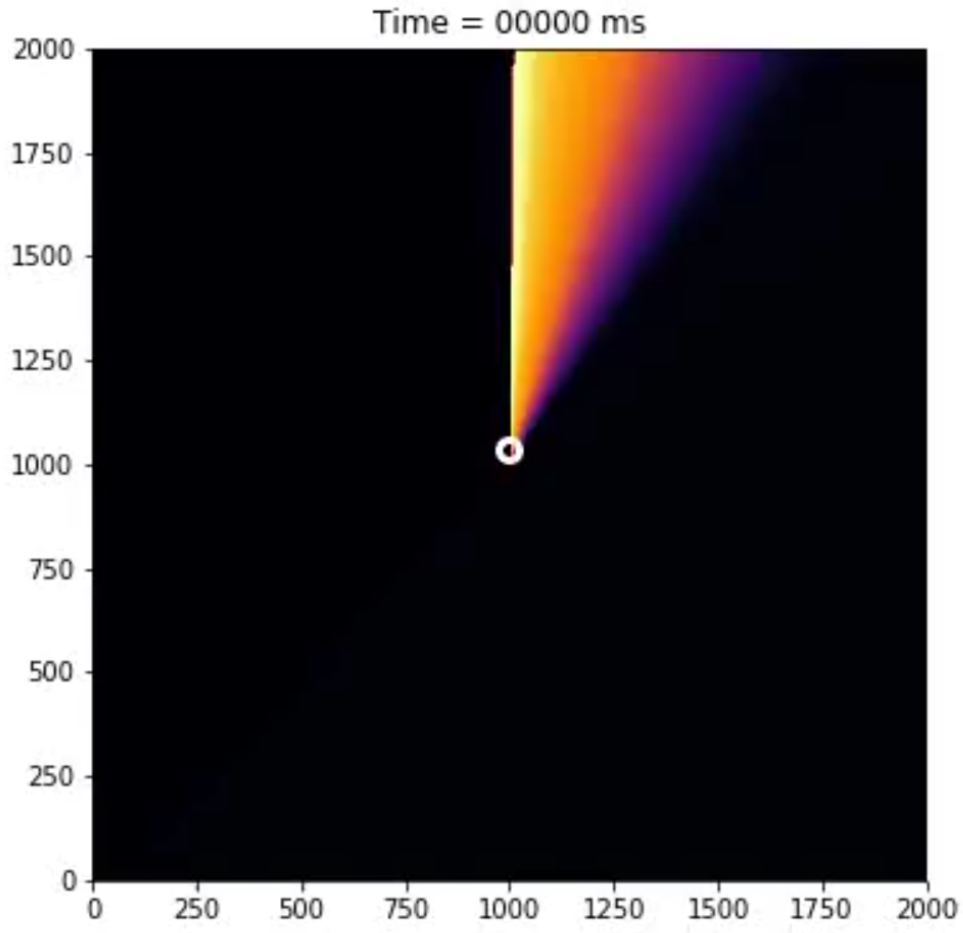
Rotor filament trajectory: pinacidil CL = 120

Filament trajectory: pinacidil



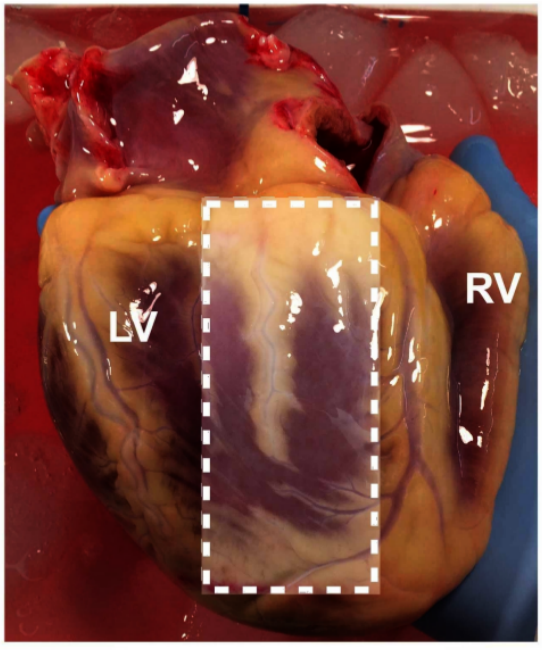
Rotor filament trajectory: pinacidil CL = 200

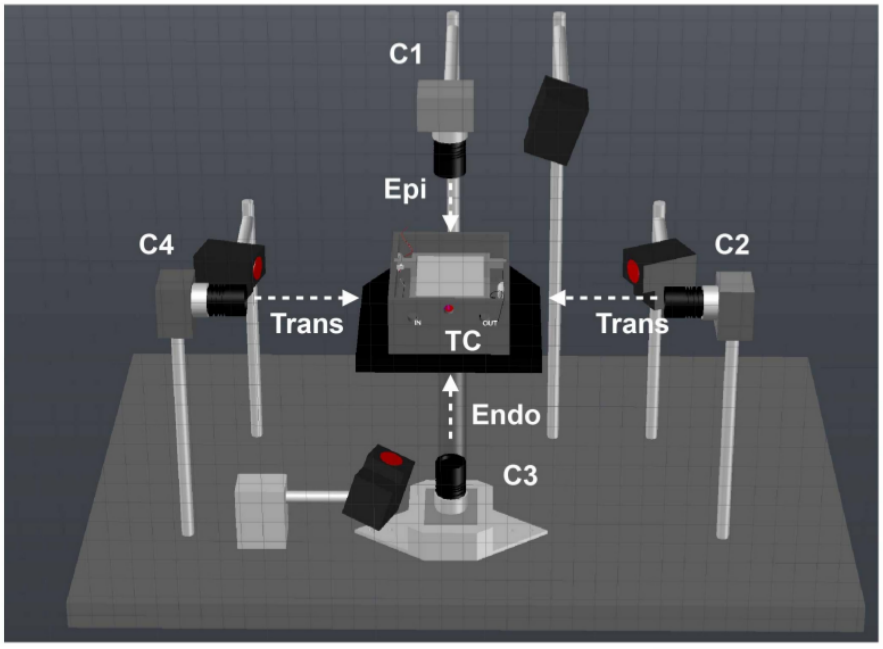
Filament trajectory: pinacidil



Rotor filament trajectory: pinacidil CL = 1000

Experiment: optical mapping



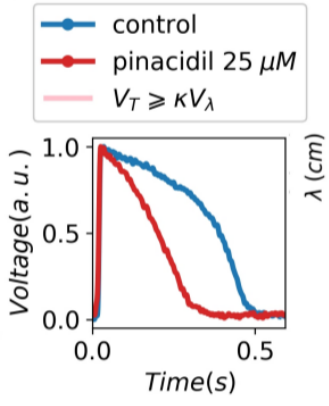


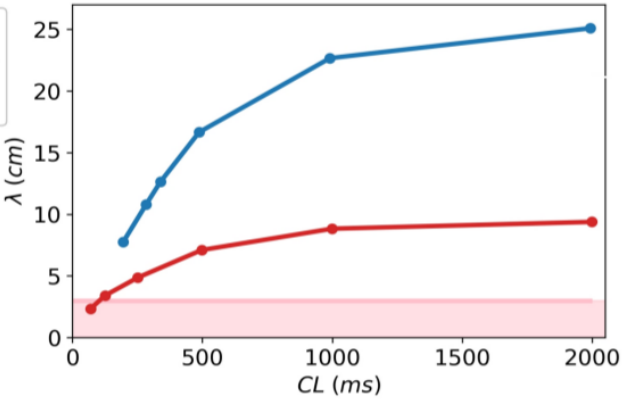
$V_T \geq \kappa V_\lambda$

V_T = Tissue Volume

V_λ = Wavelength Volume

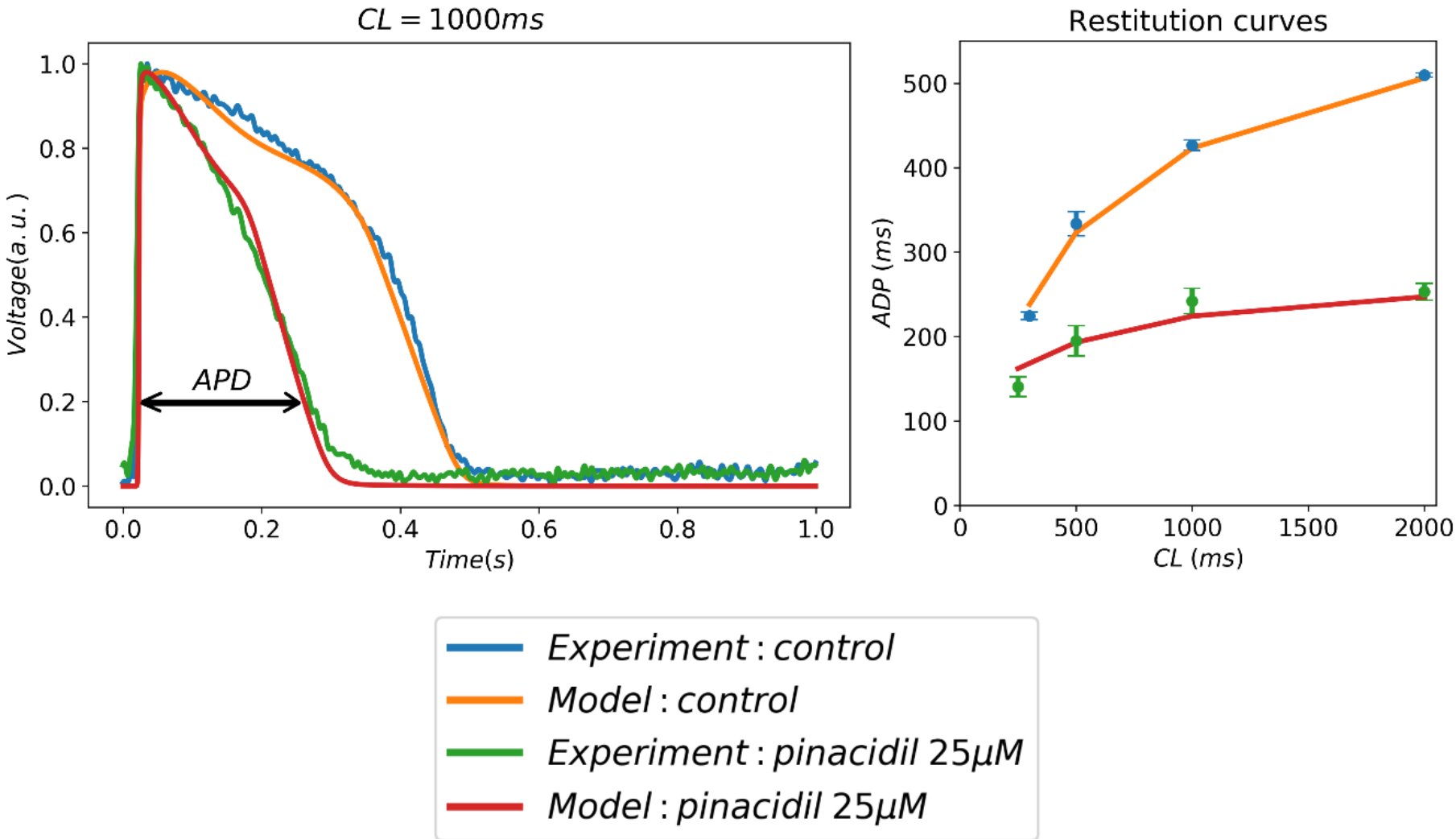
κ = Arrhythmia Vulnerability Coefficient





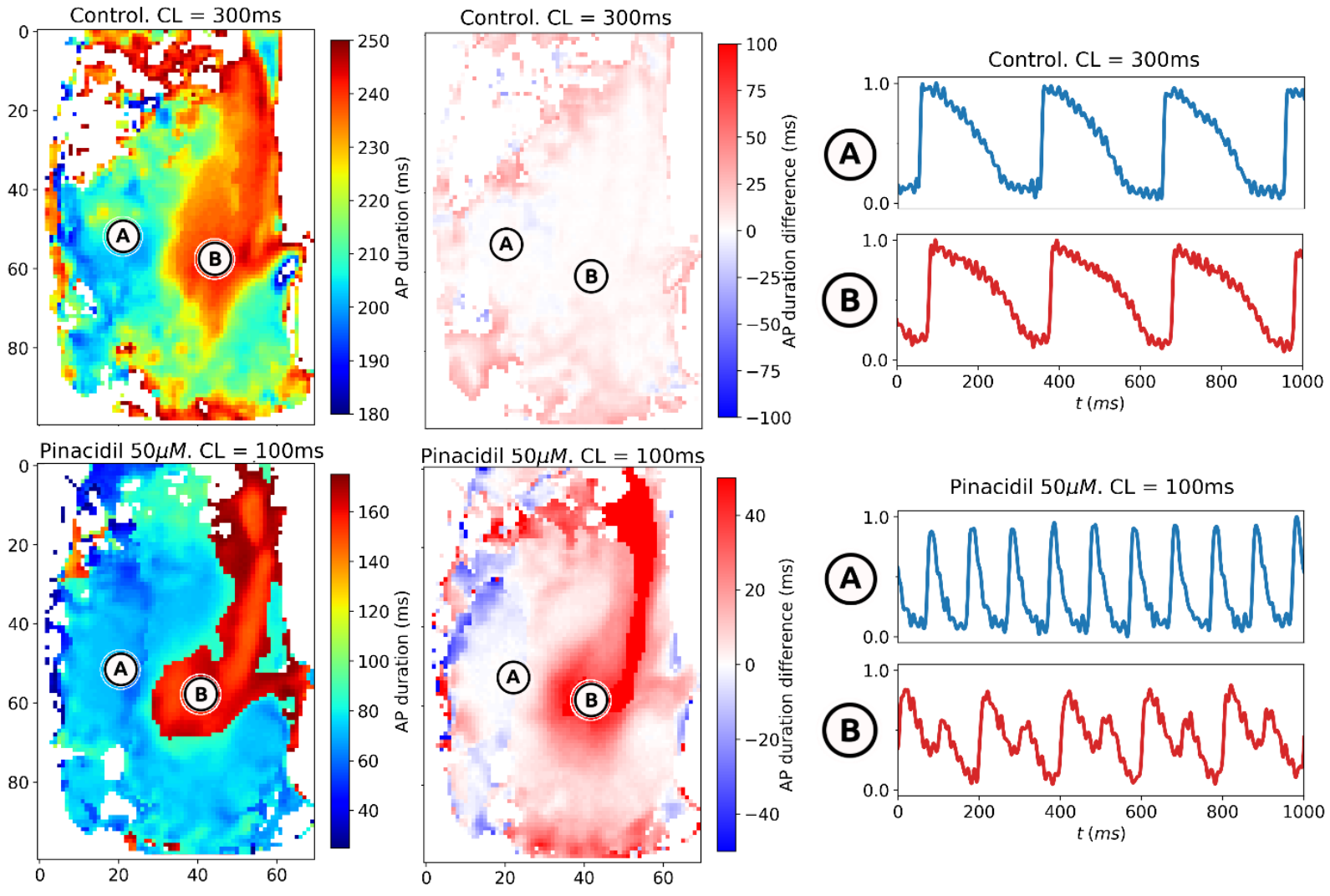
K. Aras, et. al, Critical Volume of Human Myocardium Necessary to Maintain Ventricular Fibrillation, 2018

Model vs Experiment



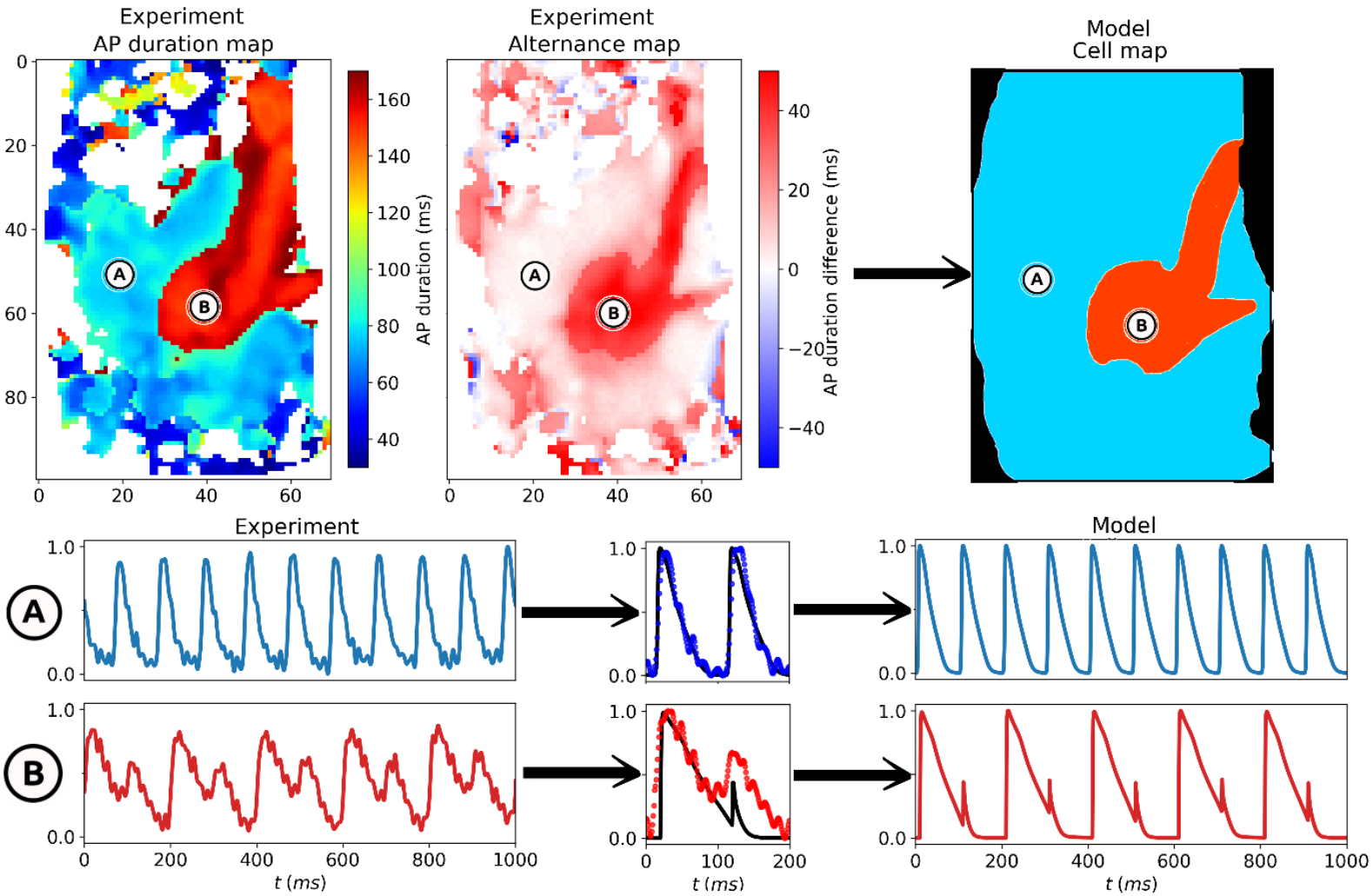
AP and restitution curves

Experiment: AP duration



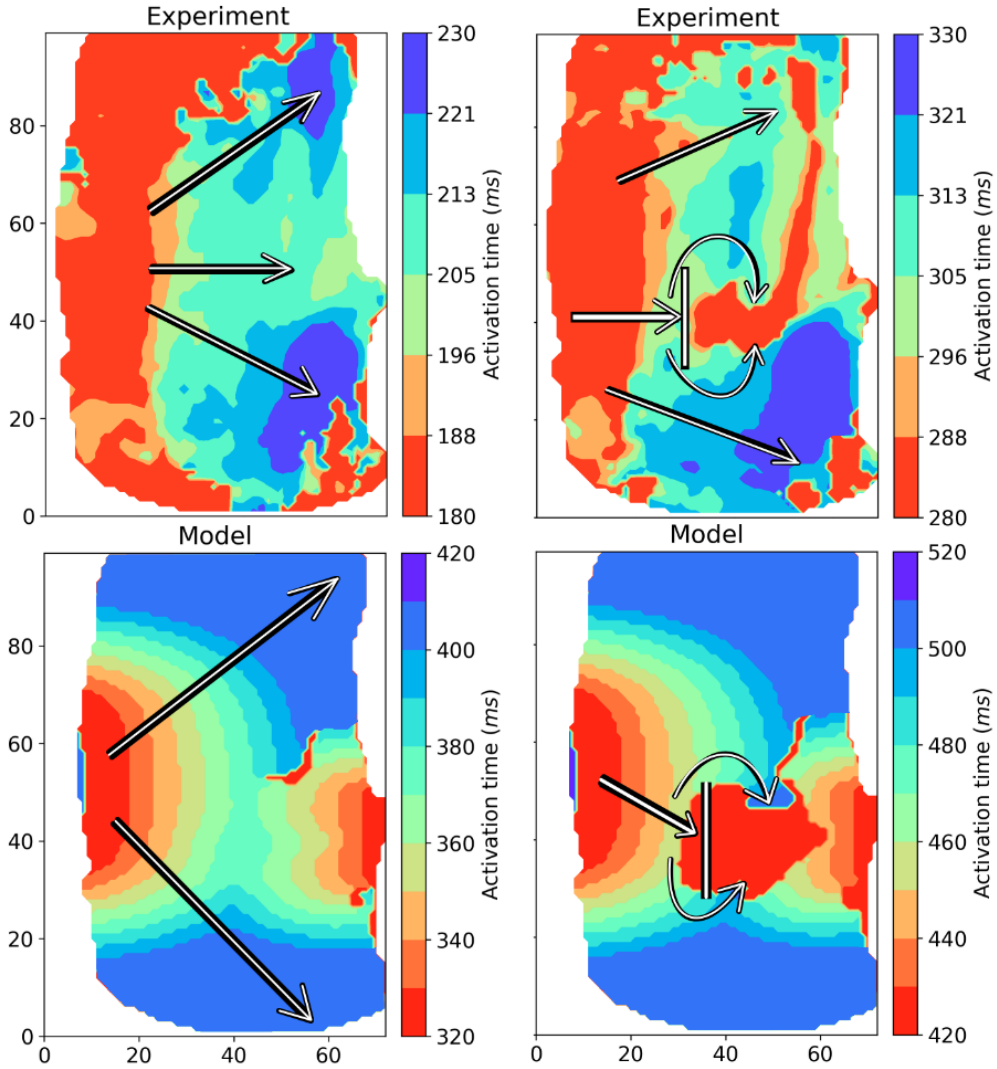
AP duration and alternans. Endocardium

Model: AP duration



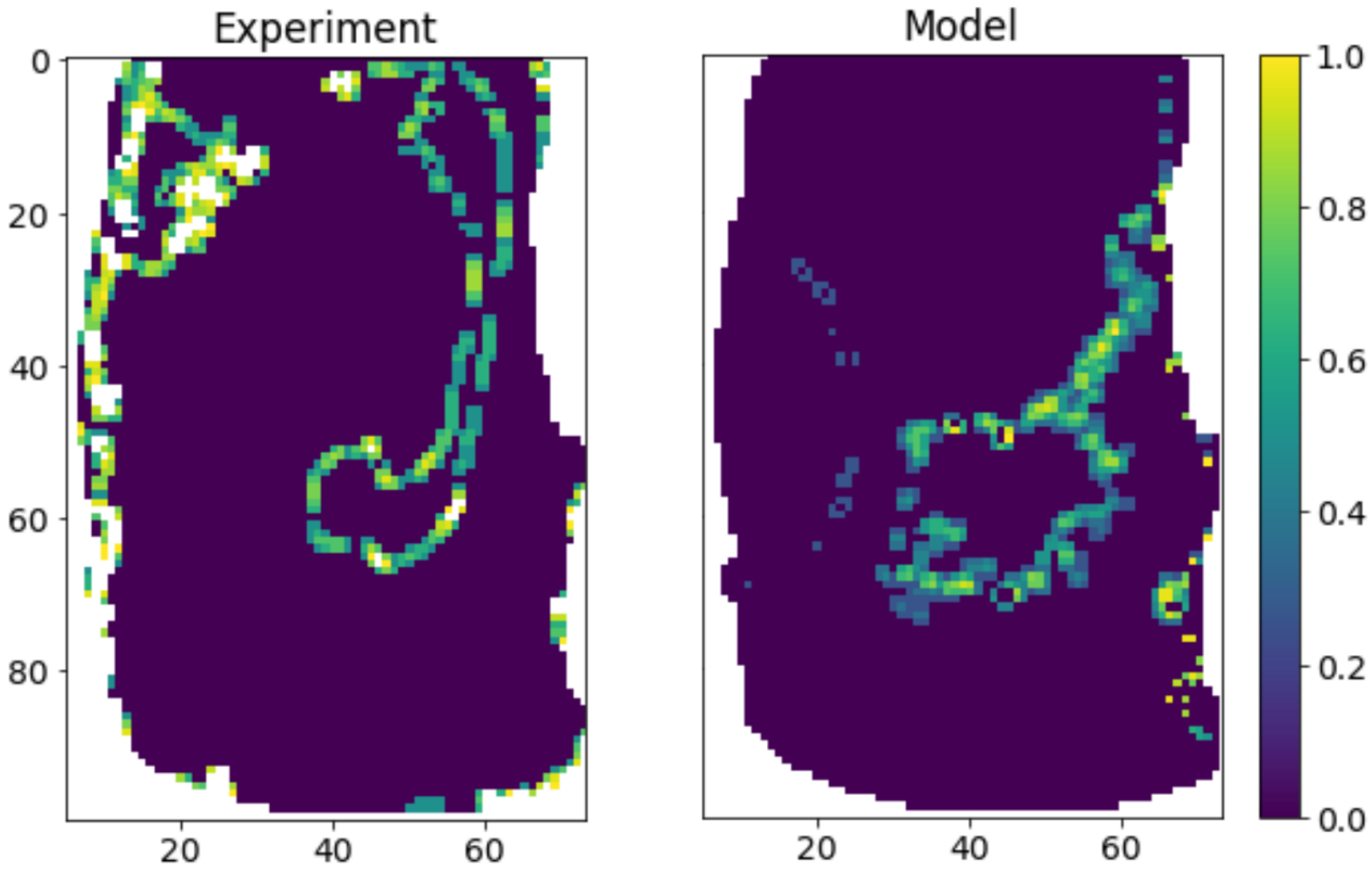
Endocardium. Stimulation period - 100ms

Activation maps



Endocardium. Stimulation period - 100ms

Phase singularities



Endocardium. Stimulation period - 100ms

Conclusions

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- New 3D electrophysiological parallel computational framework presented
- Model of IK_{ATP} corresponds to experimental data for APD
- We found heterogeneity areas on endocardium (different APD, maybe different ATP concentration)
- More pinacidil and higher frequency $\rightarrow$ wave break and arrhythmia
- 2D model makes good prediction of arrhythmia and singularities location

Current work

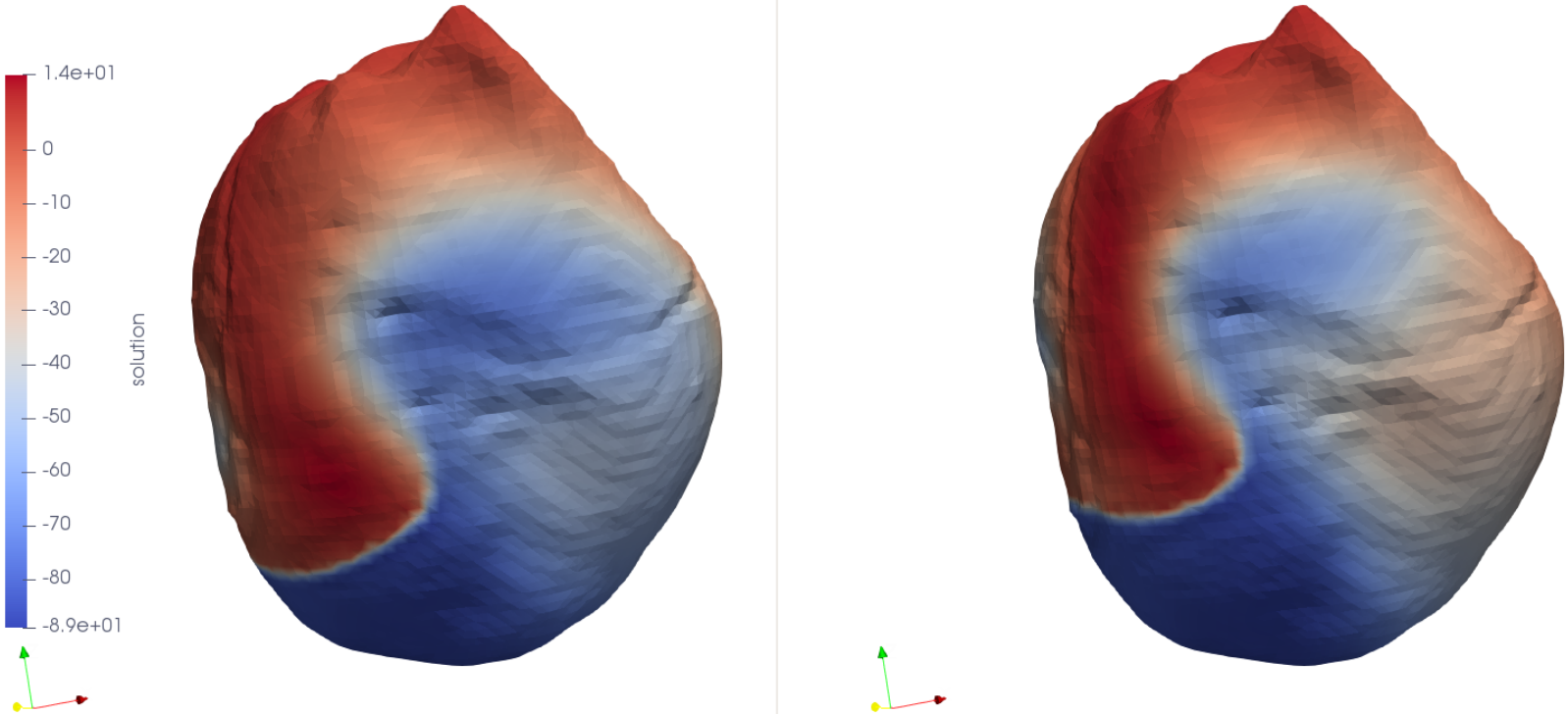
- Study the influence of IK_{ATP} activation on arrhythmia in 3D
- Electromechanics (linear elasticity already done)
- ECG validation
- More speedup

Thank You for Attention!

Numerical experiments: 3D Rabbit Heart

- "Oxford Rabbit Heart" (MR-based mesh of the rabbit heart)
- Reentry is induced by the S1–S2 protocol
- Monodomain problem with $v_0 = -85.4485\ mV$, $\chi = 140\ mm^{-1}$, $C_m = 0.01\ \mu F/mm^2$, $\sigma = 0.093\ mS/mm$.
- Ionic cell model is the Mahajan *et al.* rabbit cell model

Numerical experiments: 3D Rabbit Heart



Epicardial voltage at different time instances: 400 ms. Ani3D solution (left), Chaste solution (right).