Bidomain modeling at PTB: From validation of animal experiments to the reconstruction of the human magnetocardiogram (MCG)

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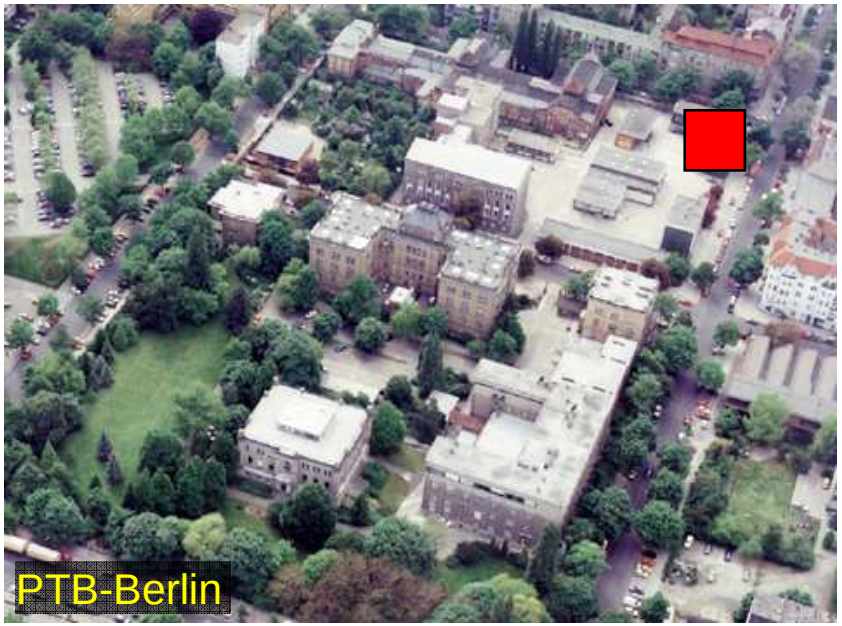
Mathematical Modeling and Data Analysis
Physikalisch-Technische Bundesanstalt (PTB), Berlin

European Cardiac Simulation Group Meeting, Manchester, Nov. 11th - 12th, 2005

PTB = German National Institute of Metrology
(like NPL, NIST…)

PTB Braunschweig

- Approximately **1200** members of staff
- 6 scientific divisions



PTB Berlin

- Approximately **300** members of staff

2 scientific divisions:

Division 8 of Medical Physics and Metrological IT

contains

Dept. 8.4 Mathematical Modeling and Data Analysis (15 staff members)

PTB Dept. 8.4 – Topics

Task: Support experimental PTB groups with mathematical expertise in a wide range of applications

- WG 8.41: Modelling and Simulation (M. Bär)

- Partial differential equations
- Inverse methods (heat conduction, optics)
- Modeling for cell biology and medicine
- Pattern formation

- WG 8.42: Data Analysis and Uncertainty (C. Elster)

- Methods of data analysis in metrology
- Determination of measurement uncertainty
- Signal processing for applications in medical physics
- Analysis of key comparisons

Heart Modeling at PTB

2002: Initiated by Hans Koch inside Dept. of Biosignals, project funded by BMBF ,,Myocarditis´´ - idea: combine MCG, numerical modeling and clinical studies to improve understanding

2002-2003: R. Weber dos Santos, S. Bauer (Ph. D. since 2005) join project

2004: Topic transferred to new mathematics department (head M. Bär)

Development of Bidomain Solver Package with U-Graz (G. Plank) and U-Calgary (E. Vigmond)

Systems studied (dimension, ionic model):

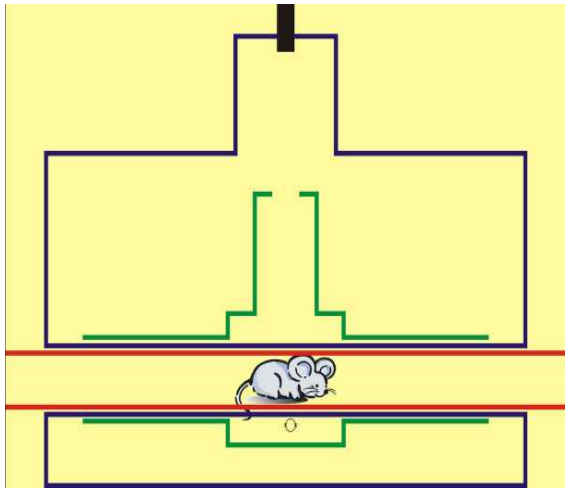
- Rat (2D, Luo-Rudy-II), Human (3D, ten Tusscher et al.)

- Mouse, rabbit (3D, mod. Beeler-Reuter)

Motivation:

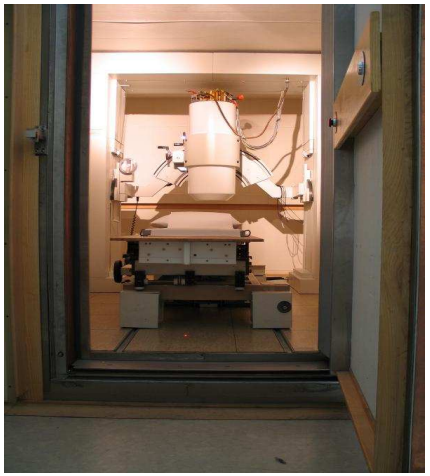
- Mathematical support of PTB research in measuring of biomagnetic fields (MCG)

- Goal 1: Computer model supports medical research by validation of animal experiments, drug testing, hypotheses on pathologies



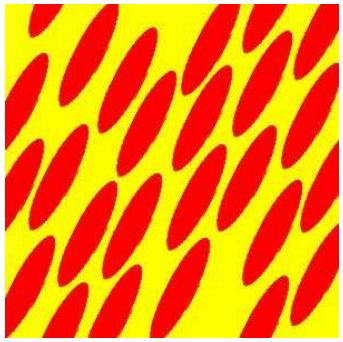
„animal scanner´´

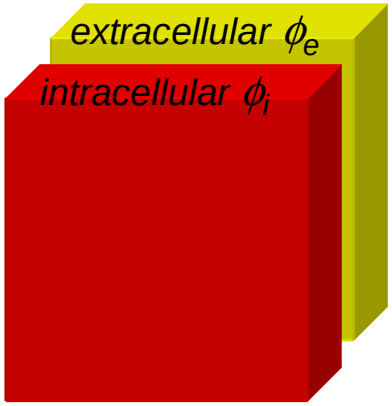
- Goal 2: Development of a computer model of the human heart in order to reproduce magneto- cardiograms (MCG)



PTB-MCG@Charite

Bidomain model for ventricular tissue





$$-\nabla(\sigma_e \nabla \phi_e) = \chi(C_m \frac{\partial \phi}{\partial t} + \frac{1}{R_m} f(\phi, \vec{h}))$$

$$\nabla(\sigma_i \nabla \phi_i) = \chi(C_m \frac{\partial \phi}{\partial t} + \frac{1}{R_m} f(\phi, \vec{h}))$$

10^{10} individual cells

two continuous domains for intra- and extracellular space

$$\phi = \phi_i - \phi_e \qquad \frac{\partial \vec{h}}{\partial t} = g(\phi, \vec{h})$$

- System of coupled PDEs
- Solution methods semi-implicit Crank-Nicholson and algebraic multigrid preconditioner
- 100 ms cardiac activity at 2.5 µs time resolution

Available computing power

At the PTB, Berlin:

Currently:
8 node cluster, 64-bit dual-processor architecture, Linux

16 AMD Opteron 2 GHz processors,2 GB RAM per proc., 32 GB total

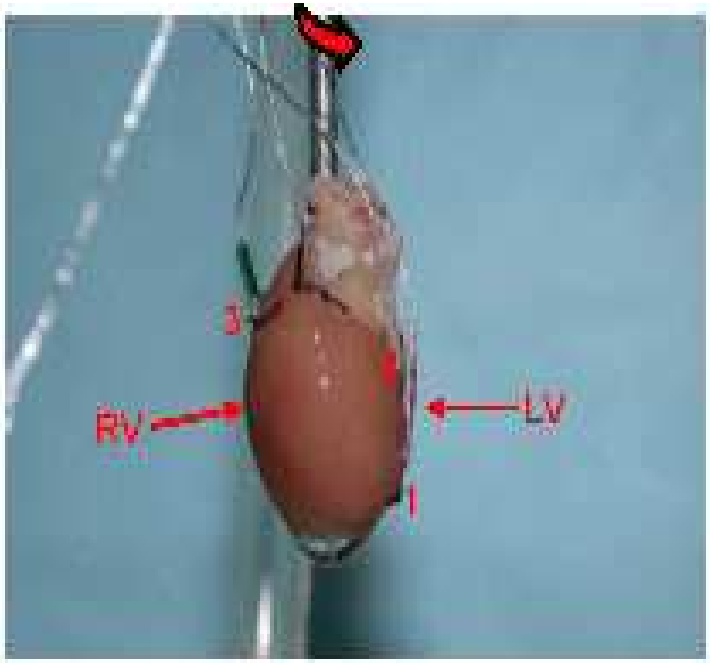
From 12/05:
48 AMD Opteron, 2.6 Ghz processors 4 GB RAM per proc., 192 GB total

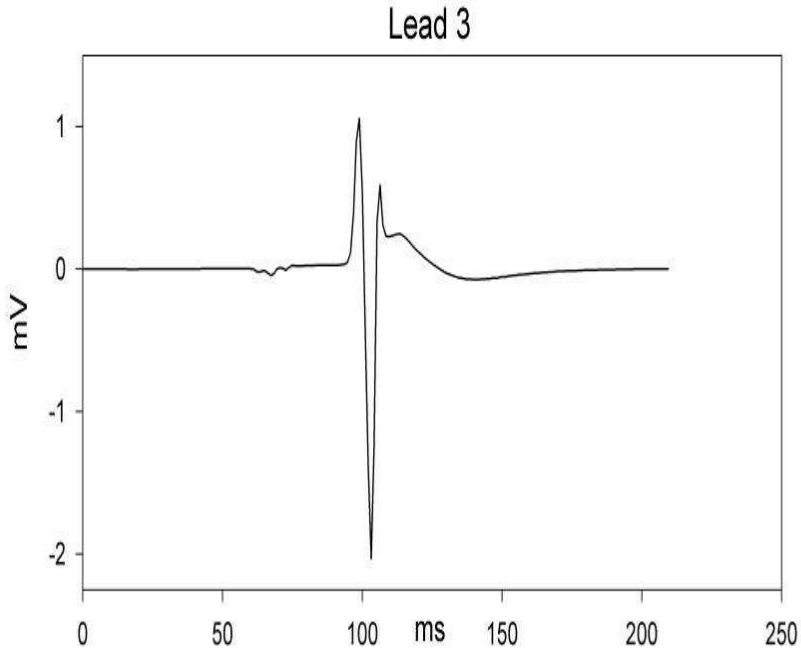
-> 3D-Human heart simulation

Model validation: Rat ECG measurement

Measurements were done in collaboration with A.Nygren, Department of Physiology and Biophysics, University of Calgary

ECGs shown are E1 – E2



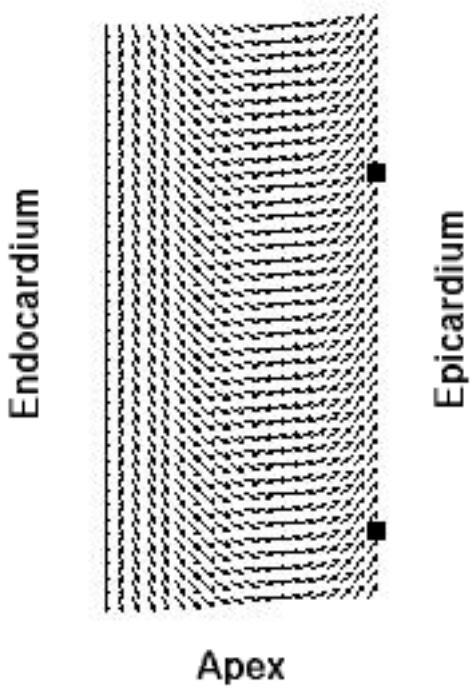


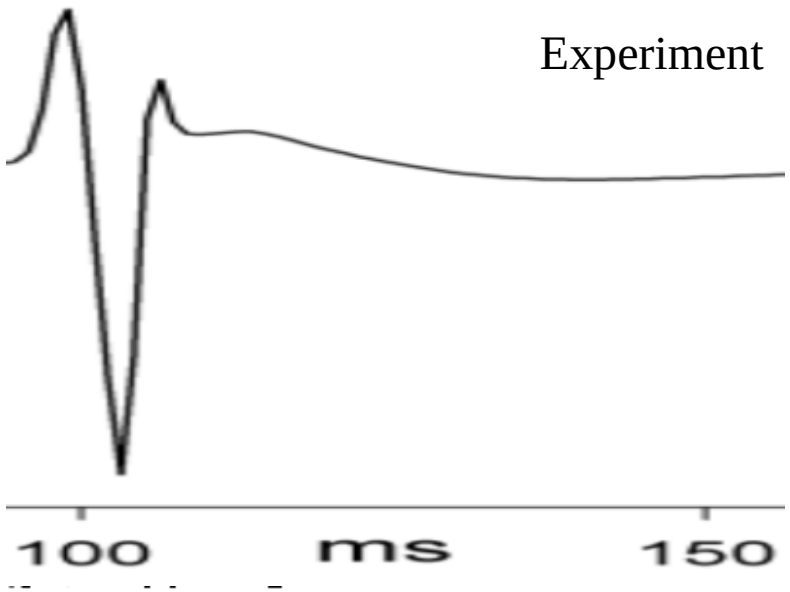
R. W. Santos, A. Nygren, H. Koch, W. Giles, J. Cardiovasc. Electr., in press (2005).

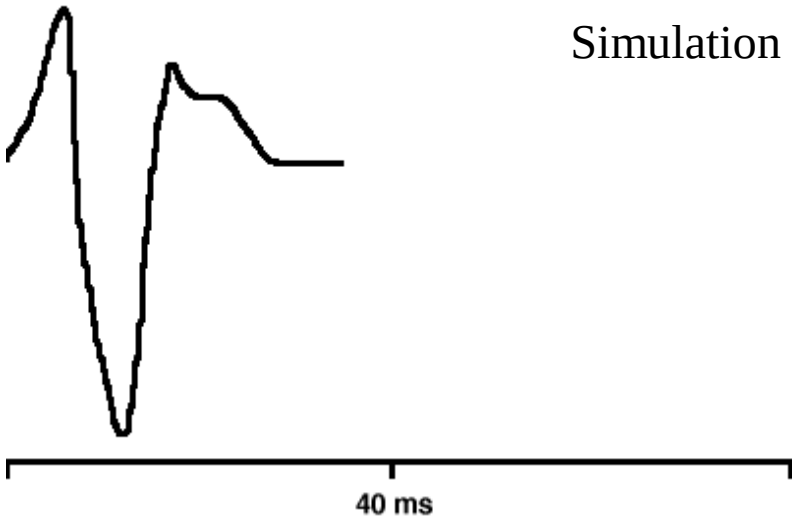
Rat 1, 2003-05-30

Model validation: Rat ECG simulation

- **A rat ventricular slice (4mm x 8mm) was modelled with varying sheet orientation**
- **Experimental ECG data matches with numerical simulation data**

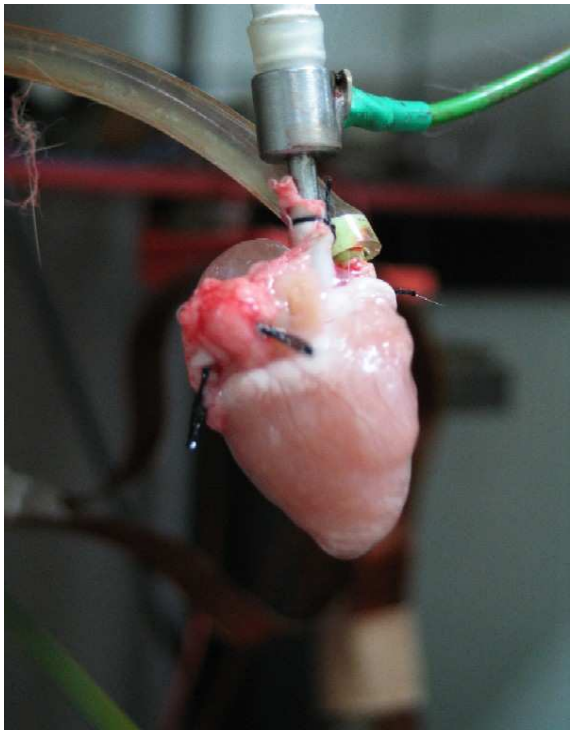


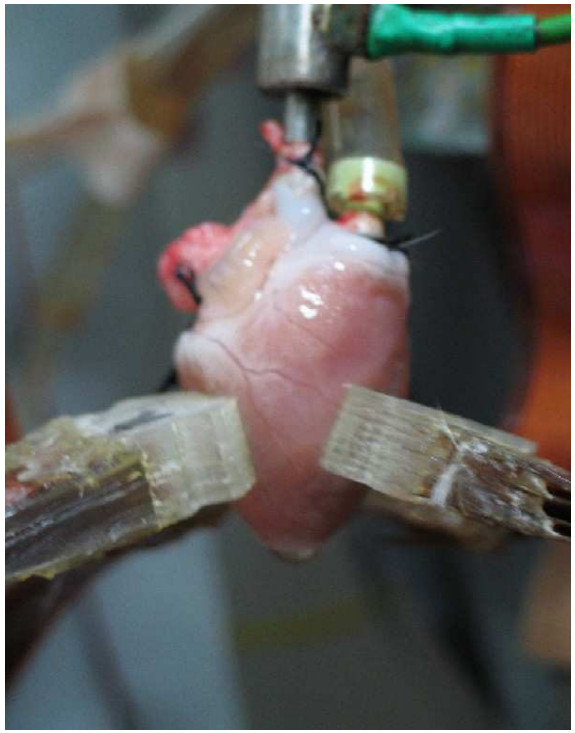




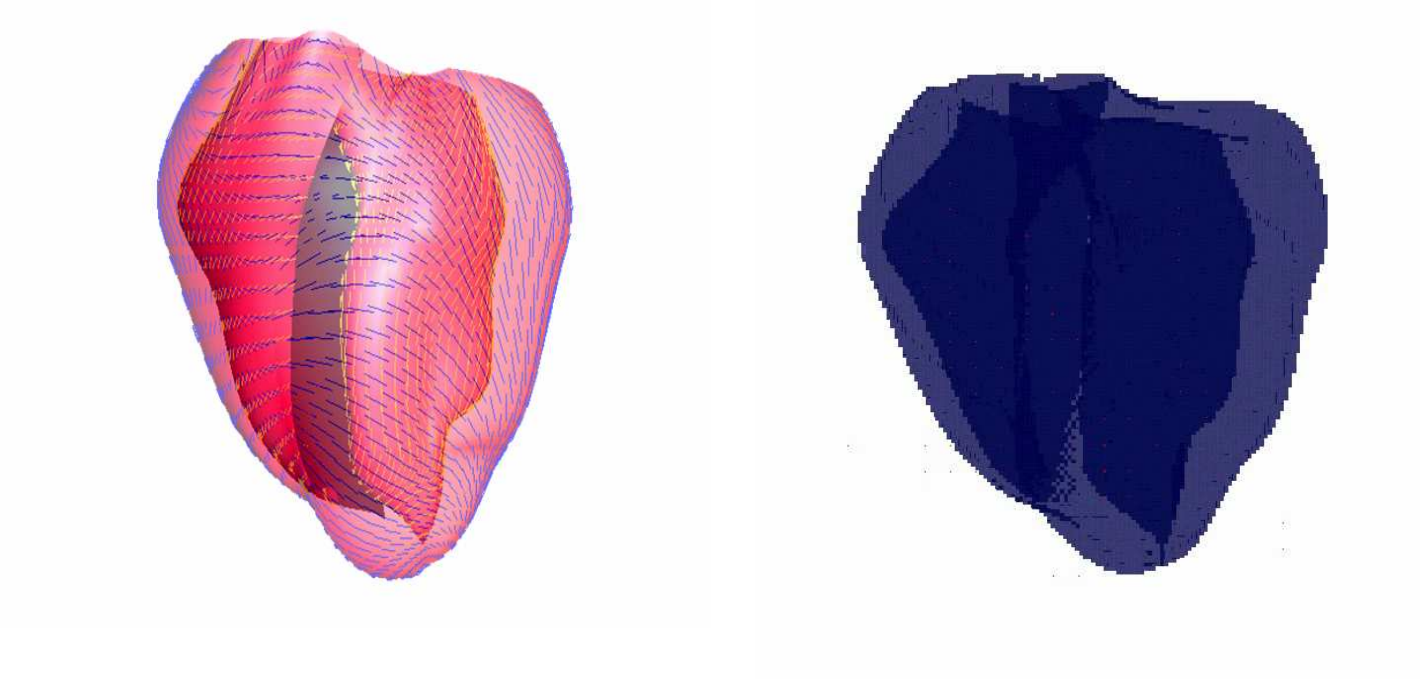
Project: Rabbit Heart (with U-Leipzig Cardiology)

- Electrogram measurements for hearts in Langendorff perfusion
- Comparison to MCG/ ECG
- Influence of Channel & gap junction blockers on propagation





Simulation of the Rabbit Heart



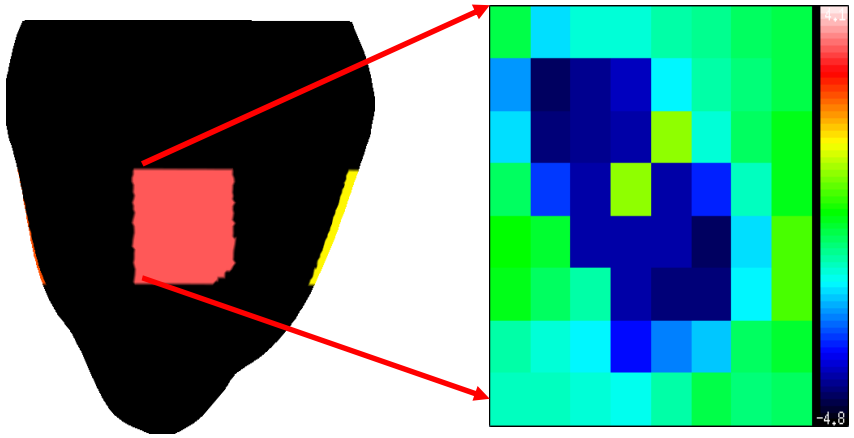
-Ventricle model, (San Diego rabbit heart),
2 million nodes (compare human heart: 10-20 million nodes)

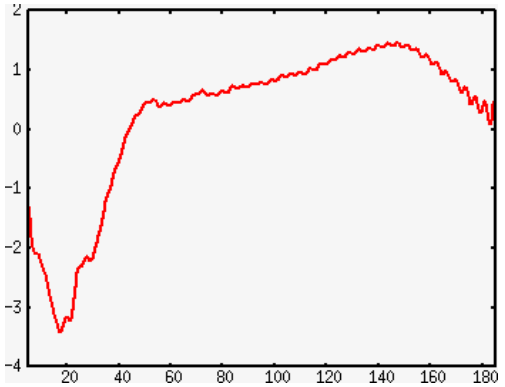
-Simulation of one heartbeat takes 10 hours on a 16-CPU computer

Experiment and Simulation of Electrogram

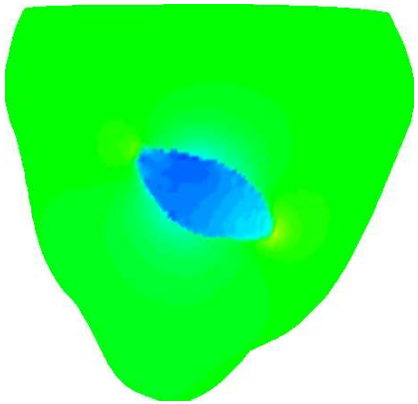
Rabbit heart in Langendorff-perfusion

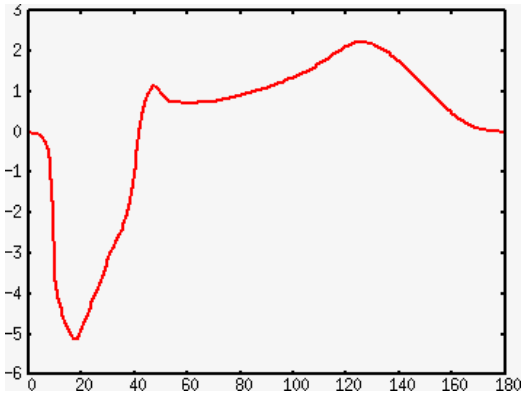
Experiment





Model

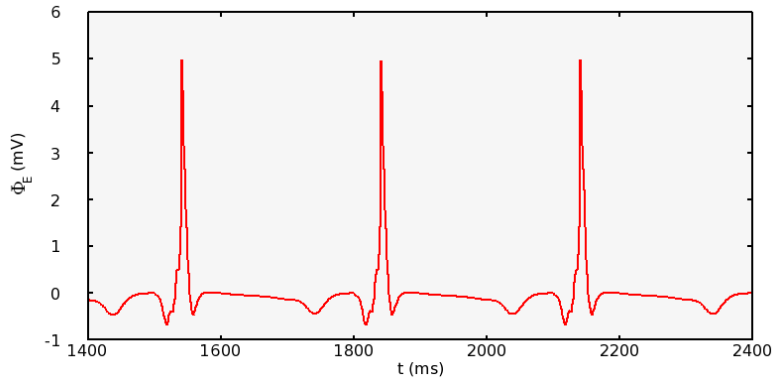


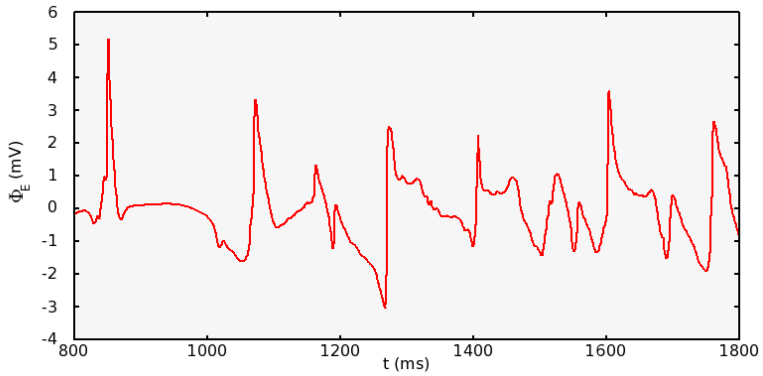


Periodic Pacing of Rabbit Ventricle

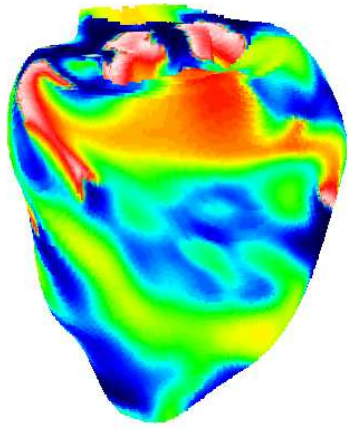
period: τ = 300 ms (regular heart beat) τ = 200 ms (fibrillation)

ECG



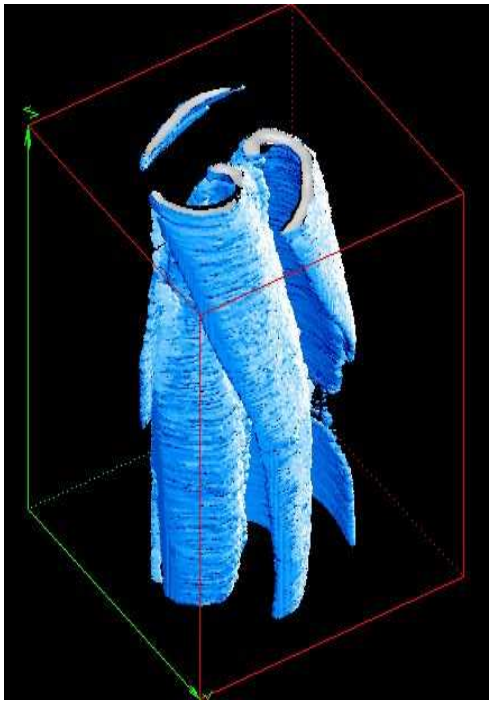


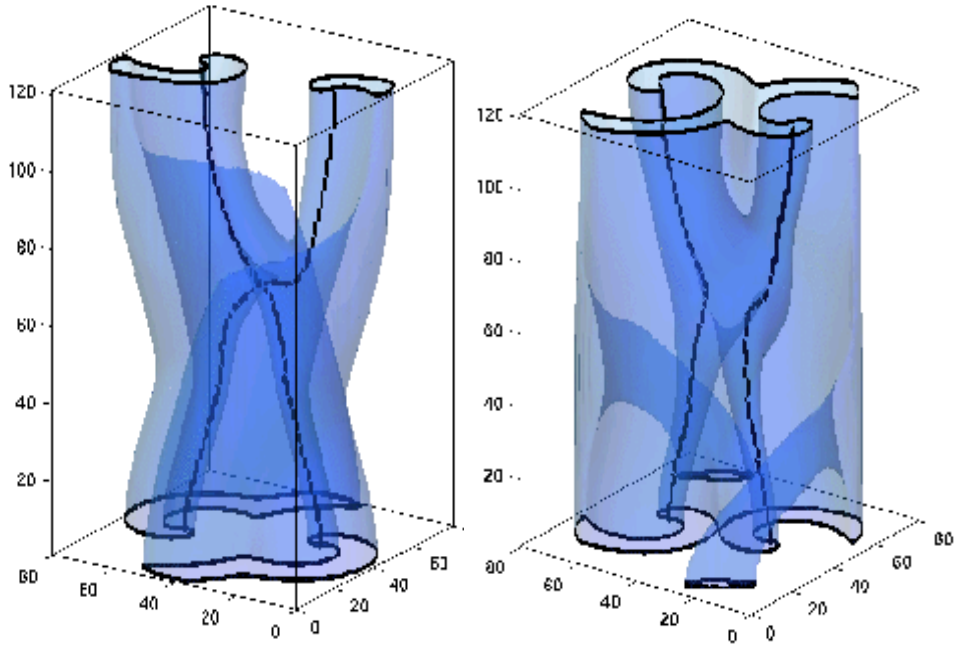
snapshot



Dynamics & Instabilities of Spirals and Scrolls

Example: 3D chemical reaction (optical tomography) and model simulation (with S. Müller, Magdeburg) – interaction of two scroll waves



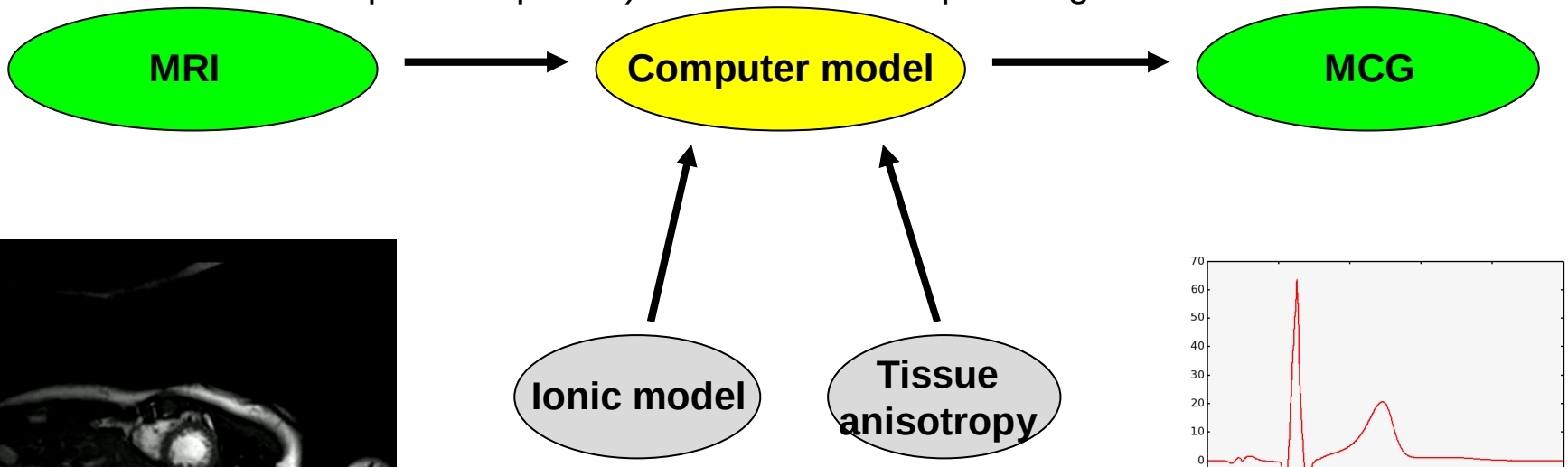


Since 1993: Work on spiral (a lot) and scroll (a little) stability
See also: http://ib.ptb.de/8/84/841/_indexe.html

Towards a Human Heart Model

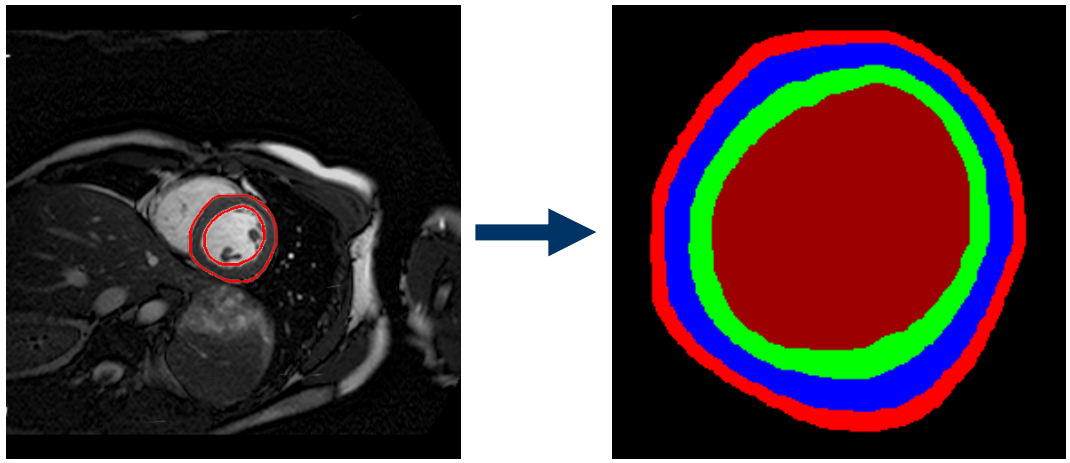
Provide geometrical base (general or patient-specific)

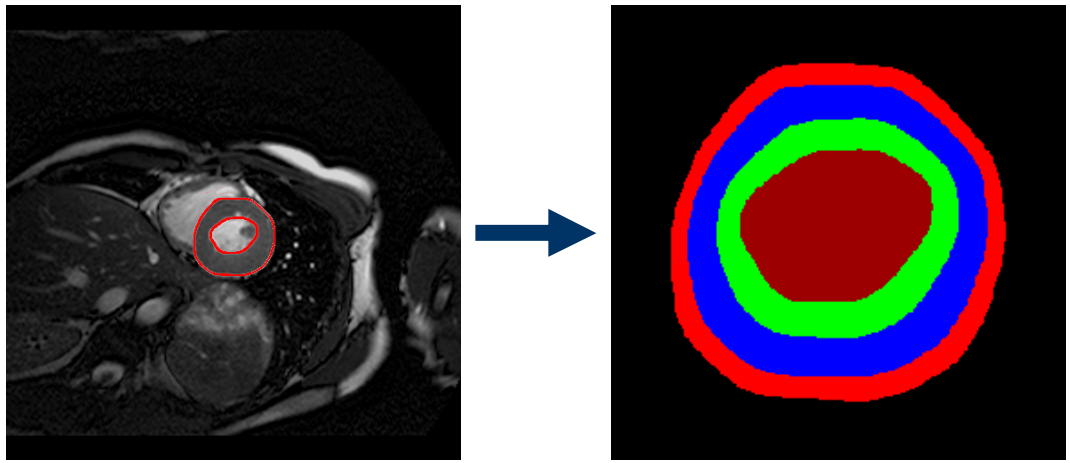
Model MCG / predict changes due to pathological conditions



Influence of Geometry Changes of Human Heart on ECG/ MCG

Geometry generation



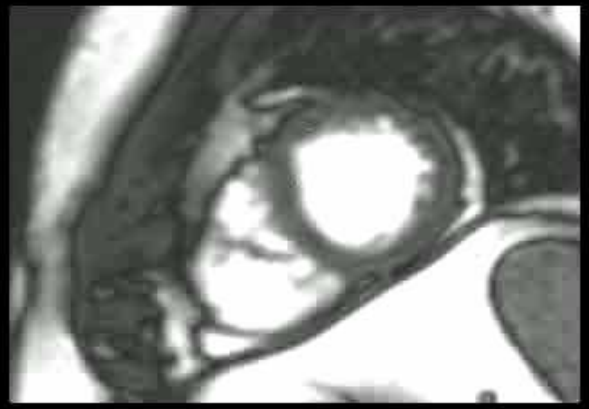


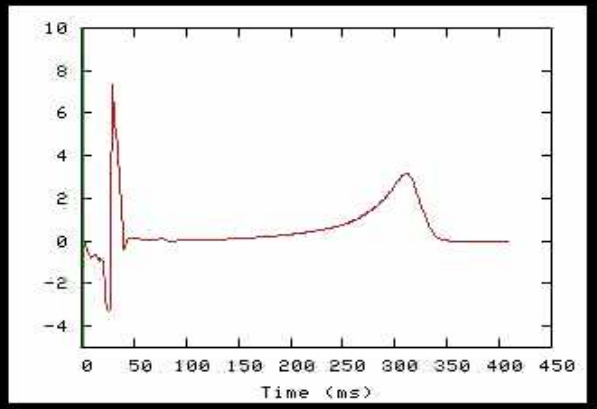
- Two geometrical extremes are investigated
- Geometry base for left ventricle extracted from MRI from 35-year old proband
- Differentiated geometries into 3 active and 2 passive regions
- Left ventricle geometries embedded into 30x15cm torso region
- Resulting mesh size $5{,}5 \cdot 10^4$ active, $1{,}4 \cdot 10^6$ passive voxels, regular FEM grid of hexahedral elements

Epicardial
M-Cell
Endocardial
Blood cavity
Torso

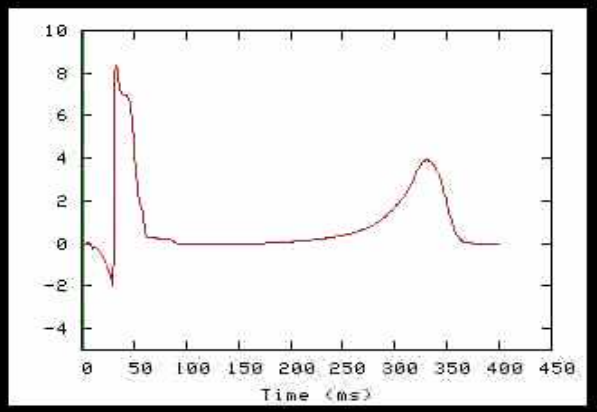
Results

Diastolic geometry

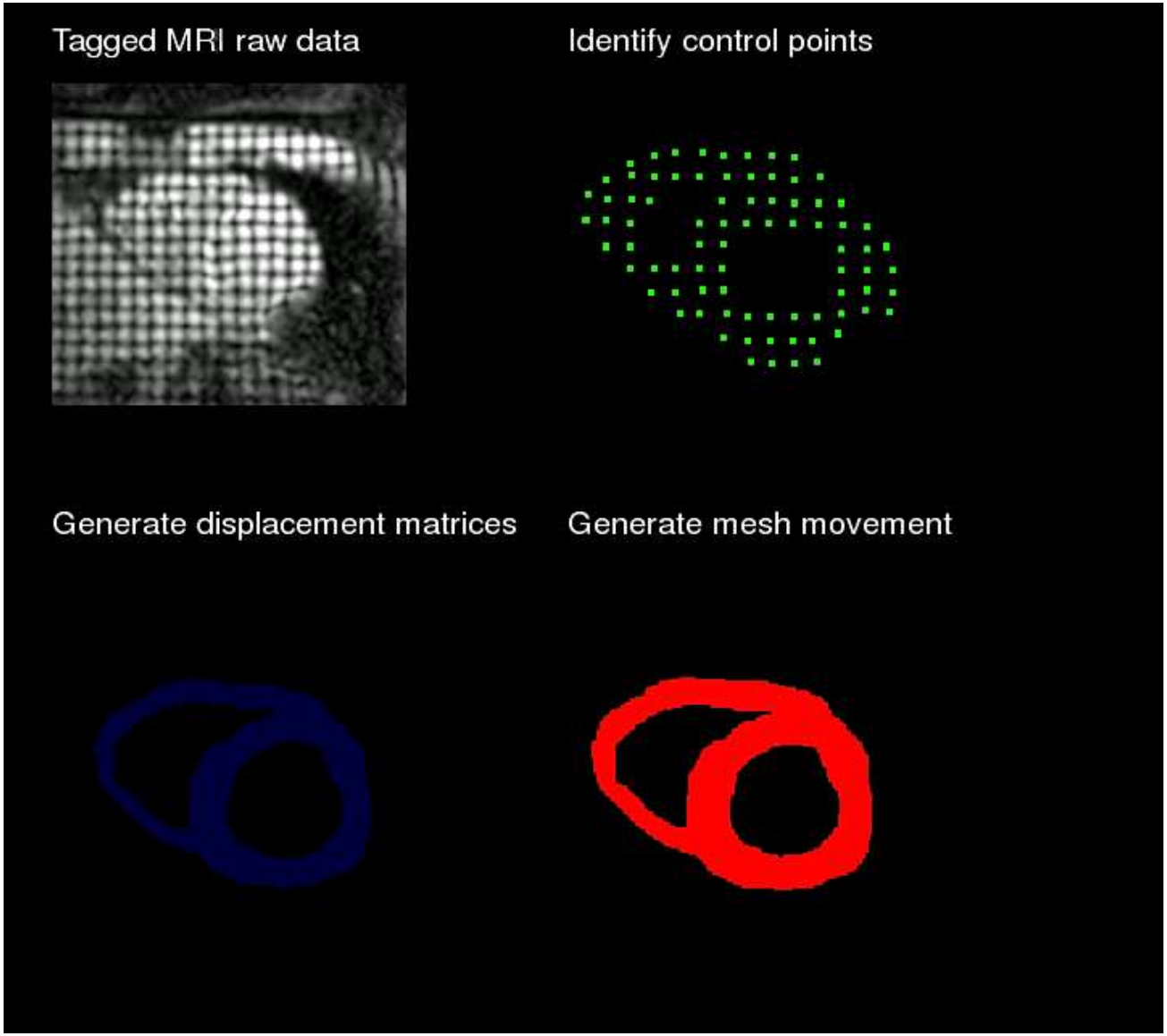




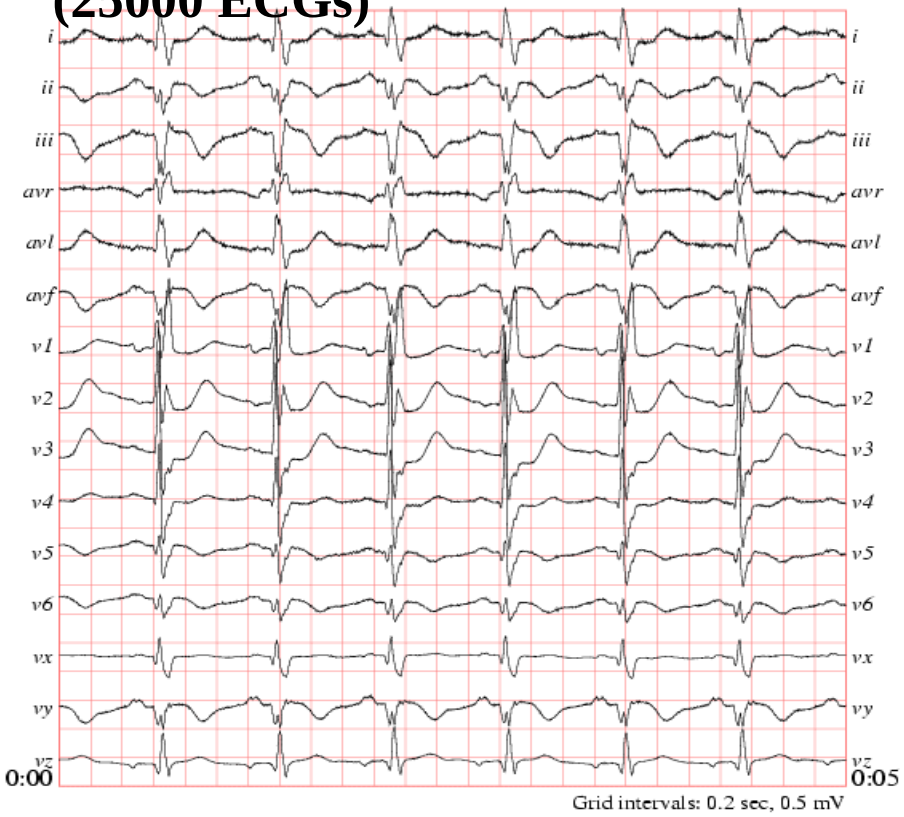
Systolic geometry



2D mechanical movement via Tagged MRI



The PTB Diagnostic ECG Database (25000 ECGs)



Diagnostic class	Number of subjects
Myocardial infarction	148
Cardiomyopathy/Heart failure	18
Bundle branch block	15
Dysrhythmia	14
Myocardial hypertrophy	7
Valvular heart disease	6
Myocarditis	4
Miscellaneous	5
Healthy controls	54

Name

Parent Directory
RECORDS
patient001/
patient002/
patient003/

Name

Parent Directory
s0015lre.dat
s0015lre.hea
s0015lre.xyz

http://ib.ptb.de/8/84/842/_indexe.html

PhysioNet/Computers in Cardiology Challenge 2006: QT Interval Measurement

(see http://www.physionet.org/challenge/2006/)

Acknowledgements:
Special thanks to …. PTB Berlin for proposing this Challenge, and to Michael Oeff, Hans Koch, Ralf Bousseljot, and Dieter Kreiseler of PTB Berlin for their generous contribution of *the excellent PTB Diagnostic ECG Database* used in this Challenge.

Summary: Heart modeling @ PTB

❖ **So far:**

- Implementation of bidomain model solver
- 3D simulations of mouse and rabbit hearts
- 2D simulations of human heart for different geometries
- Validation of electrograms for rat heart
- MCG computation, ,,drug´´´ testing

❖ **In the future:**

- Combined exptl. & modelling study of rabbit heart
- 3D human heart model with changing geometry
- Model validation from electrograms, ECG, MCG, ... ?
- Model incl. tissue structure from histological data