European Functional Cardiac Modeling Meeting

Modeling of Anatomy, Electrophysiology and Tension Development in the Human Heart

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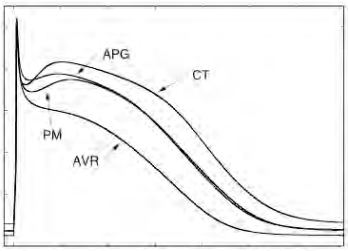
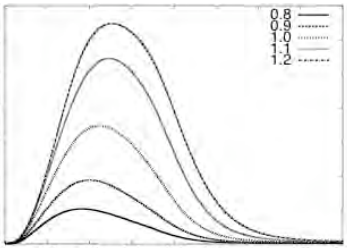
Universität Karlsruhe (TH)
Research University • founded 1825

Overview

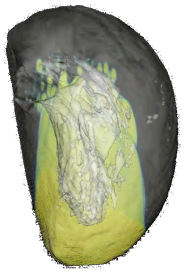
Electro-physiology

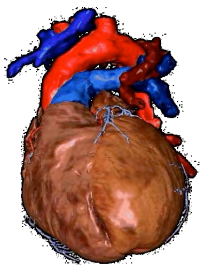


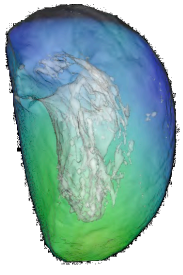
Tension development



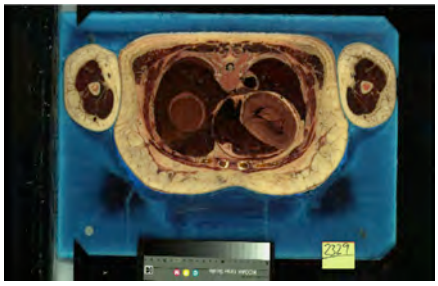
Anatomy







Anatomical Modeling



Visible Human Project
National Library of Medicine

Thin section photos

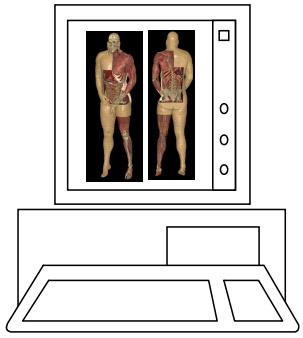
~ 1800 (male) and 5000 (female) cross-sectional digital images
1 mm (male) and 0.33 mm (female) distance between images
1280 x 2048 pixels per image
0.33 mm x 0.33 mm x 3 colors x 8 bit per pixel

Preprocessing

Segmentation

Filtering

Classification

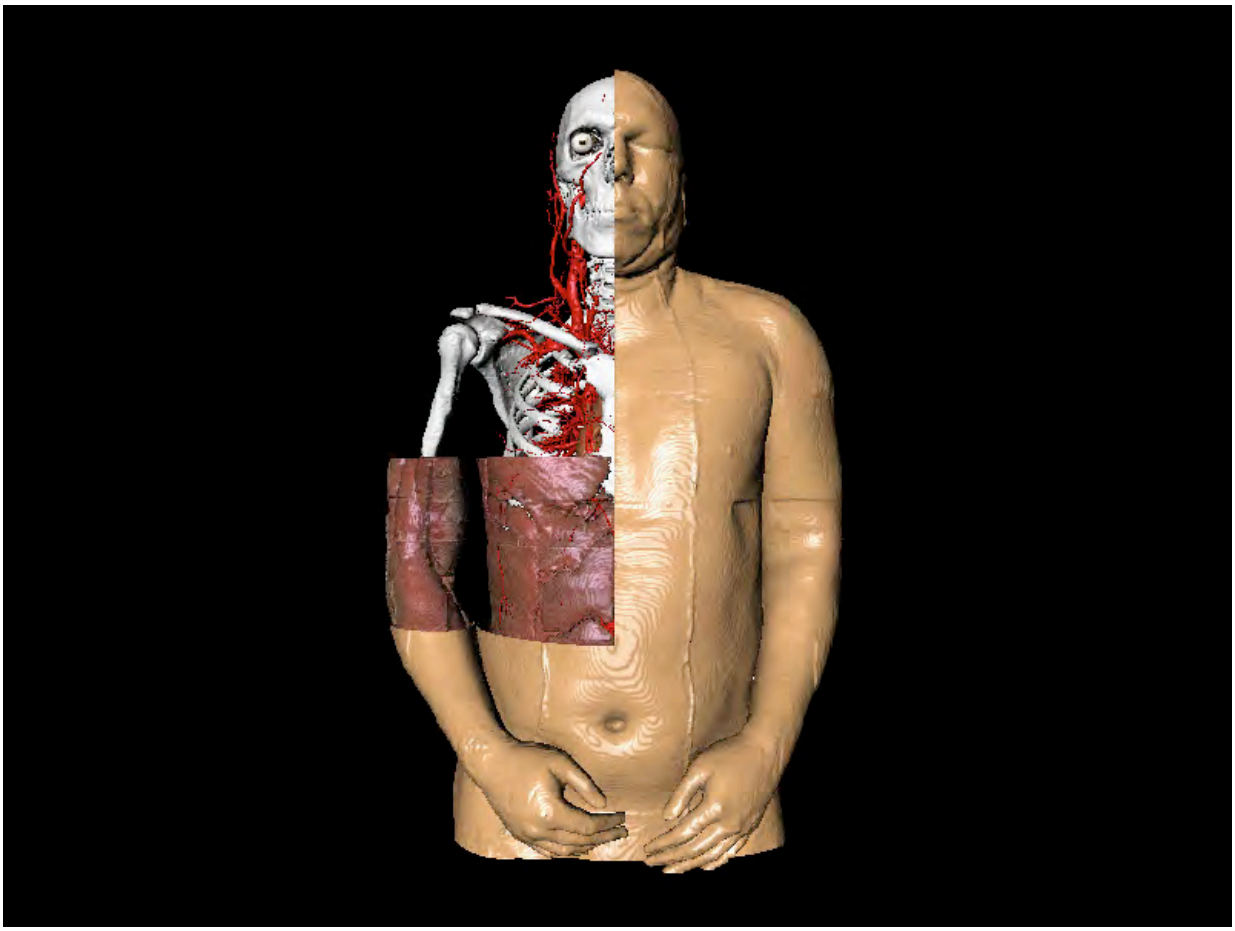


Anatomical Models

Cubic voxel representation

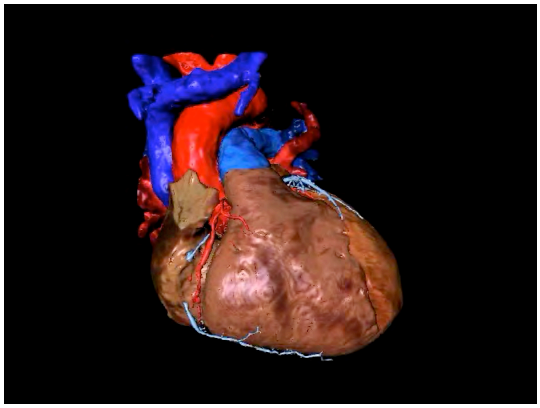
1 mm x 1 mm x 1 mm (male) and
0.33 mm x 0.33 mm x 0.33 mm
(female) per voxel

70 tissue classes
Orientation of muscle fibers



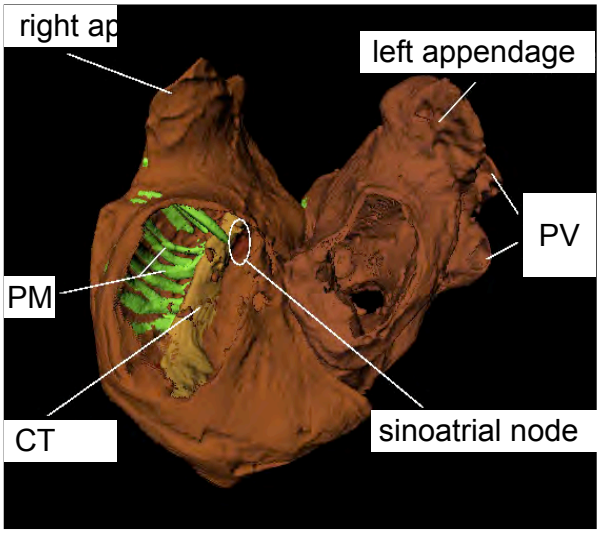
Visible Female Heart

Visible Female Heart



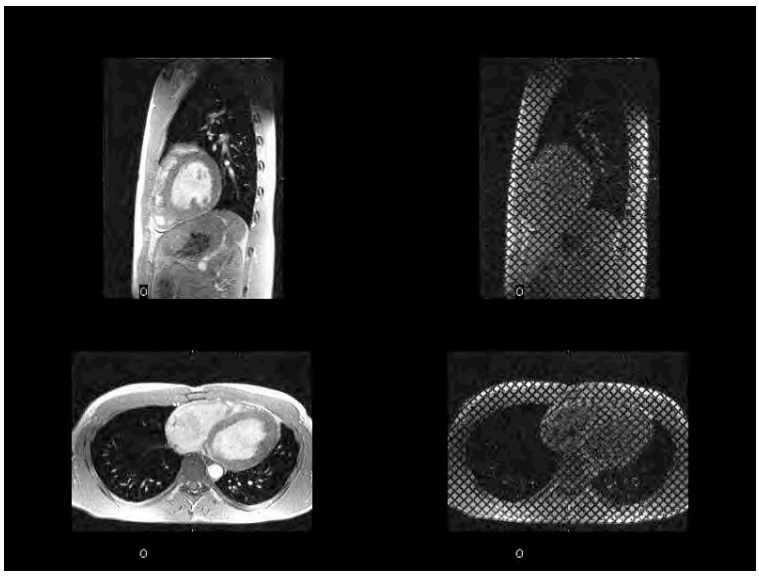
CT: Crista Terminalis
PM: Pectinate muscle
PV: Pulmonary veins

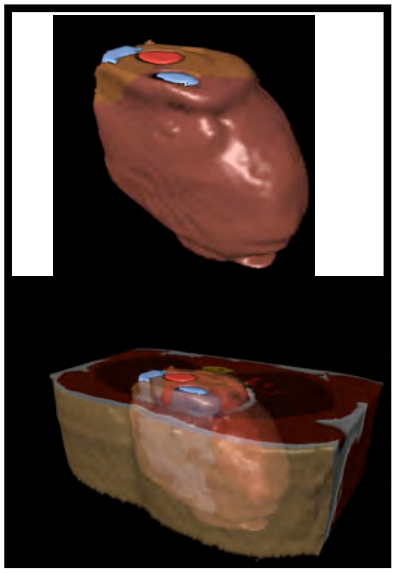
Additionally segmented atrial tissue classes



Seemann et al. 2005 Phil. Trans. Roy. Soc. in press

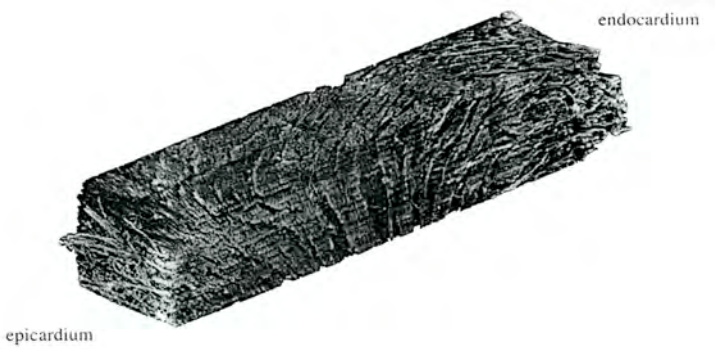
Individual MR Data and Model



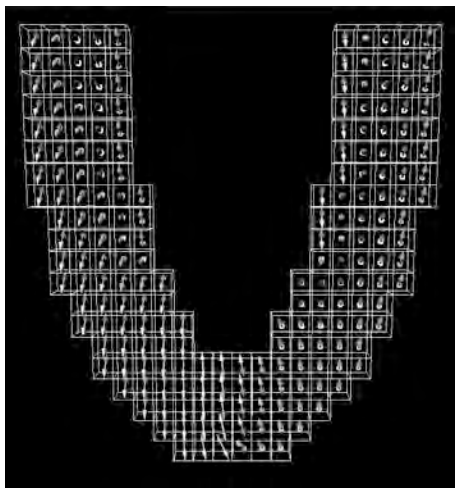


Fiber Orientation in Cardiac Tissue

Rat – left ventricle

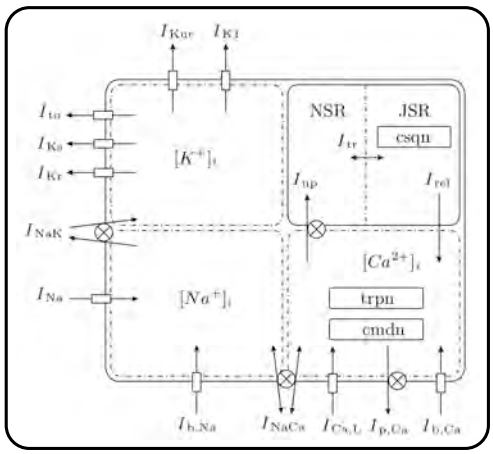


Young et al., 1998, J. Micros. 192: 139-150



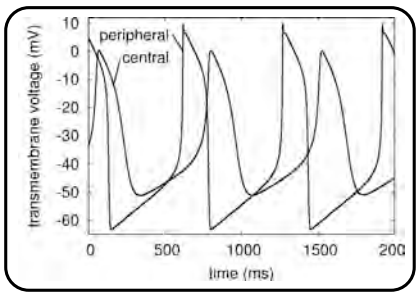
Model

Atrial Cell Models

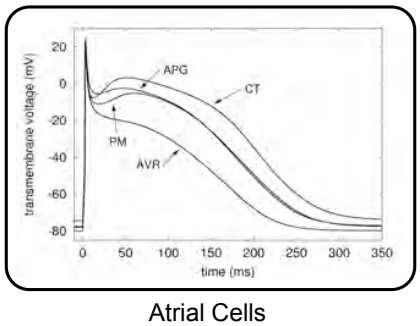


Courtemanche et al., 1998, Am. J. Physiol. 275(44): H3301-H321

$$\frac{dV_m}{dt} = -\frac{1}{C_m}\left(\sum I_x - I_{inter}\right)$$

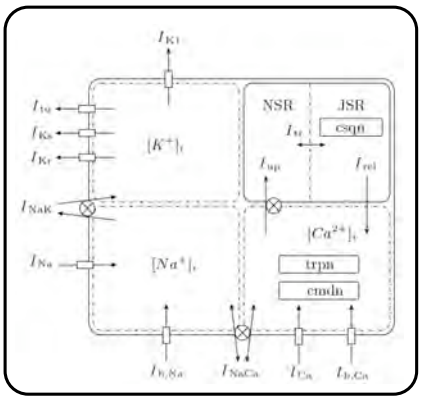


Sinoatrial Node

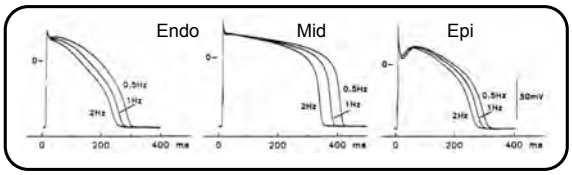


Atrial Cells

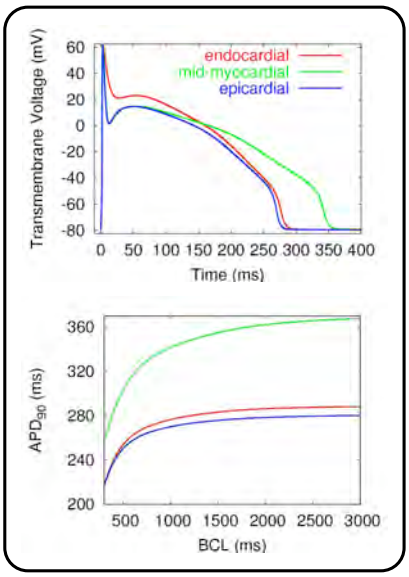
Ventricular Cell Models



Priebe & Beuckelmann 1998 Circ Res. 82:1206-1223



G.-R. Li et al. 1998 Am. J. Physiol. 275: H369-H377



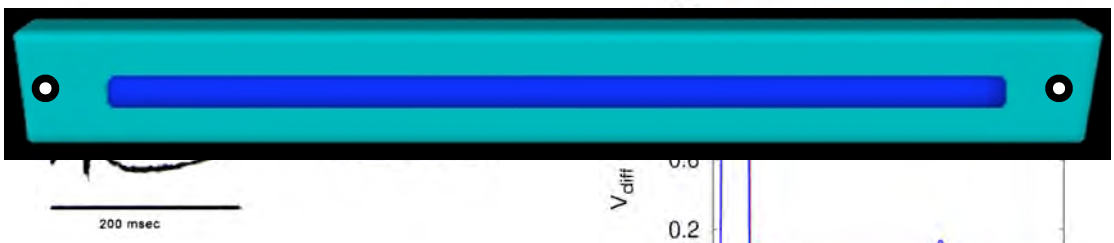
Seemann et al. 2003 J Cardiovasc Electrophysiol. 14(S10):S219-S228

Heterogeneous Ventricle Model

	APD_{Endo}	APD_{Mid}	APD_{Epi}	V_{Rest}
Experiment	263±17 ms	376±31 ms	271±14 ms	-81±3 mV
Simulation	272 ms	343 ms	265 ms	-80 mV

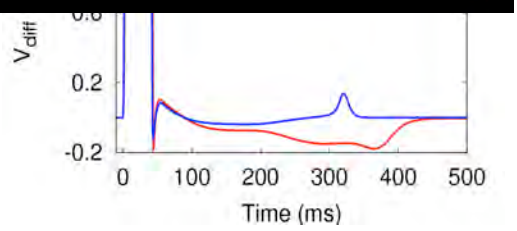
Transmural ECG

Measurement



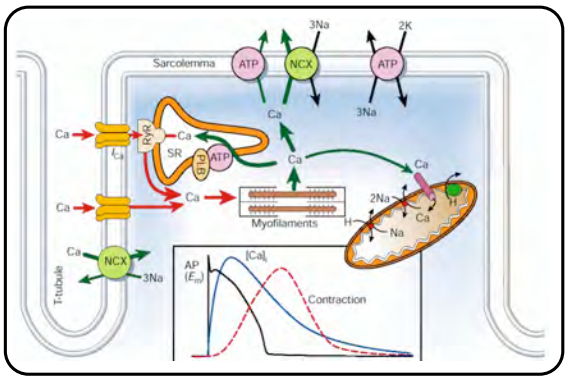
Shimizu et al. 2000 Circ. 102:706-712

Simulation

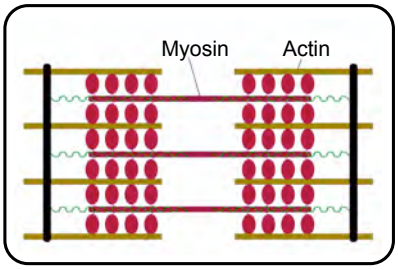


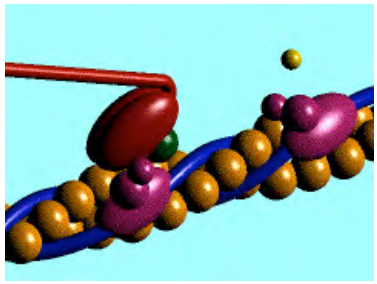
Seemann et al 2003 J Cardiovasc Electrophysiol. 14(10):S219-S228

Electromechanical Coupling



Bers 2002 Nature 415:198-205



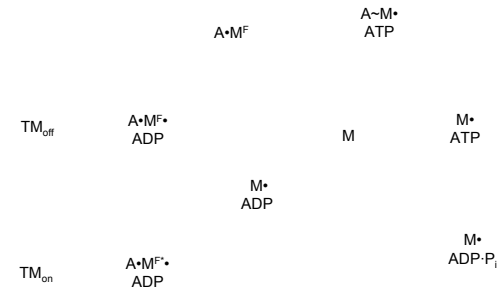


http://www.sci.sdsu.edu/movies/actin_myosin.html

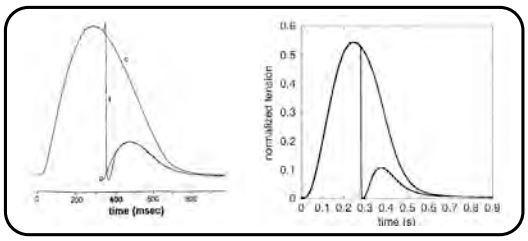
- Calcium binds to troponin C
- Shifting of tropomyosin opens myosin binding site of actin
- Interaction of actin and myosin
- Contraction of myofilaments

Tension Model

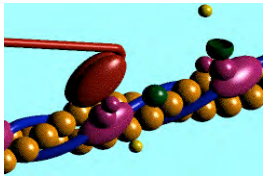
A	Actin
M	Myosin
TM	Tropomyosin
T	Troponin
ATP	Adenosintriphospate
ADP	Adenosindiphosphate
P_i	Phosphate
	Stress
v	Velocity
-	Weak Binding
•	Strong Binding



Measurement Simulation



Peterson et al. 1991 AJP 260:H1013-H1024



Conduction: Bidomain Model

$$\nabla \cdot (\sigma_i \nabla \Phi_i) = \beta I_m$$

$$\nabla \cdot (\sigma_e \nabla \Phi_e) = -\beta I_m$$

$$V_m = \Phi_i - \Phi_e \qquad \frac{dV_m}{dt} = -\frac{1}{C_m}\left(\sum I_x - I_{inter}\right)$$

$$\nabla \cdot ((\sigma_e + \sigma_i)\nabla \Phi_e) = -\nabla \cdot (\sigma_i \nabla V_m)$$

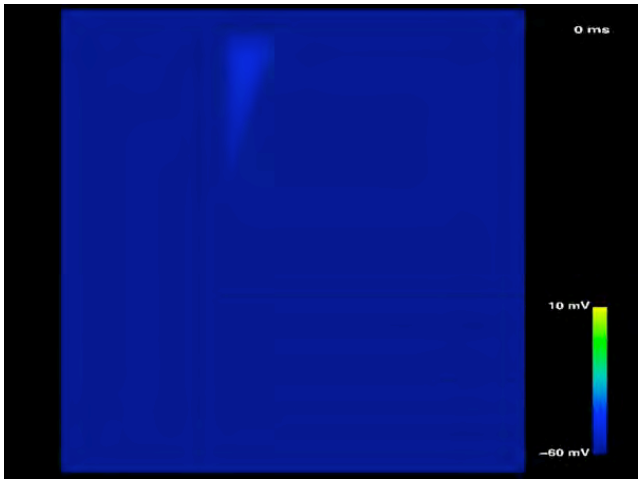
$$\nabla \cdot (\sigma_i \nabla V_m) + \nabla \cdot (\sigma_i \nabla \Phi_e) = -\beta\left(C_m \frac{dV_m}{dt} + \sum I_x\right)$$

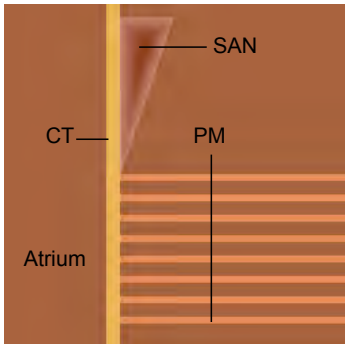
V_m Transmembrane voltage
Φ_i Intracellular potential
Φ_e Extracellular potential
σ_i Intracellular conductivity
σ_e Extracellular conductivity
C_m Membrane capacitance
I_X Ion current of type X
I_{inter} Intercellular current
β Surface/Volume

Elliptical PDE

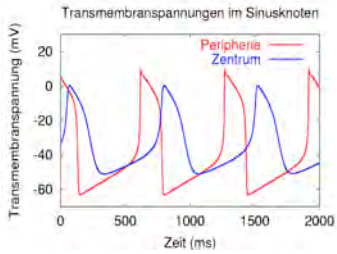
Parabolical PDE

Schematic Right Atrium



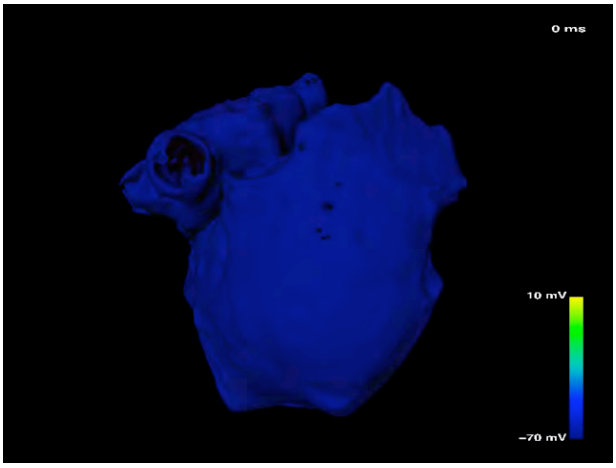


single cell simulation



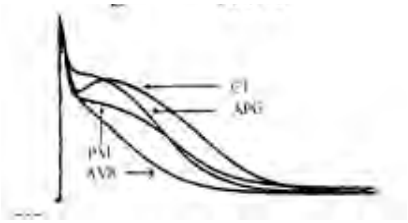
conduction velocity (m/s)	measured	simulated
atrium	0,68 – 1,03	0,6
Crista Terminalis (CT)	1 – 1,2	1,18 – 1,2
Pectinate muscle (PM)	1,5 – 2	1,54 – 1,58

Atrial Simulation



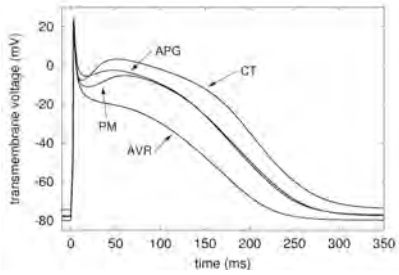
Activation times (ms)	measured	simulated
Bachmann	23	26
right atrium	81	83
left atrium	80	79
complete atrium	120	103

Measurement



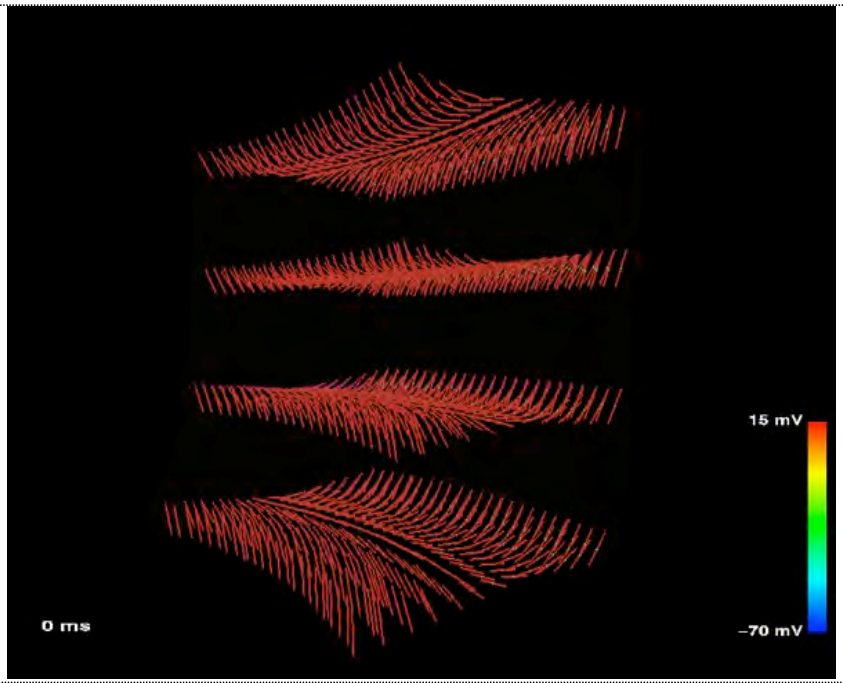
Feng et al.1998 Circ Res. 83:541-551

Simulation



Seemann et al. 2005 Phil. Trans. Roy. Soc. in press

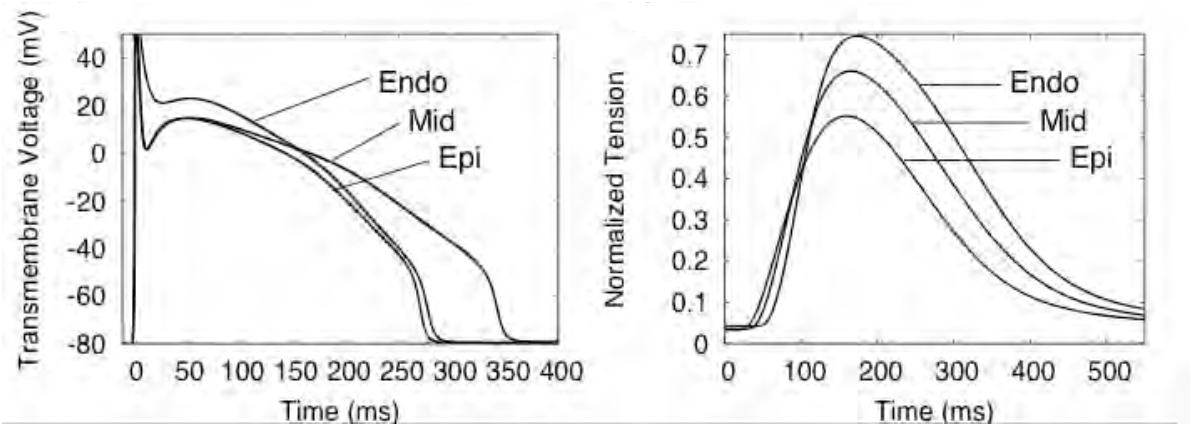
Simulation in the ventricular wall



Ventricular Electromechanics

Transmembrane voltage

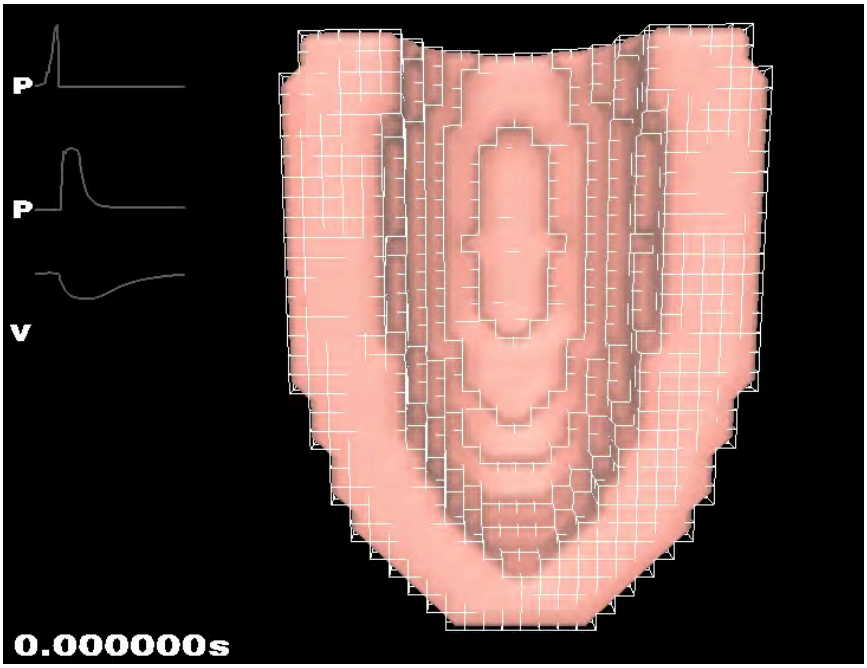
Tension development



Seemann et al. 2005 LNCS FIMH:312-319

Electrophysiological heterogeneity is one mechanism to homogenize the mechanical process

Deformation with Spring Mass System

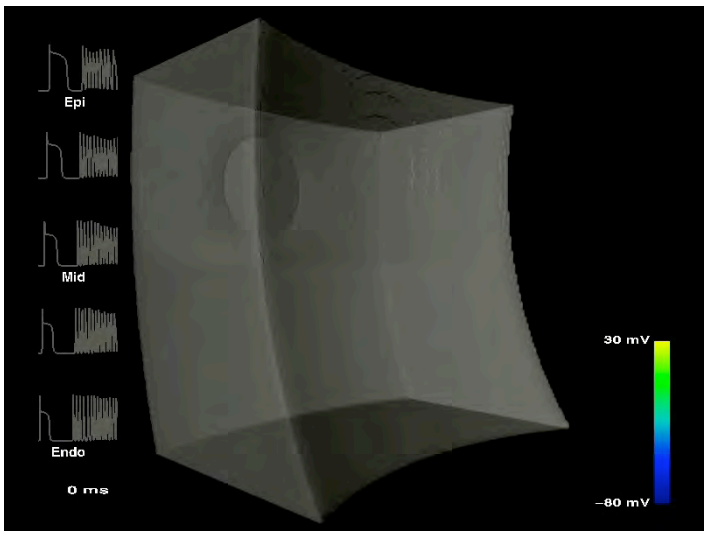


Pathological Modeling: Overview

- Atrial Flutter
- Atrial Fibrillation
- Atrial Electrophysiological Remodeling
- Ventricular Tachycardia
- Ventricular Fibrillation
- Mutations
  - Familial Atrial Fibrillation
  - Long QT Syndromes
  - Short QT Syndrome
  - I_{Ks} Mutations
  - I_{K1} Mutation
- ...

Ventricular Fibrillation

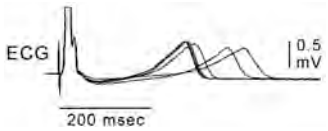
Section of the Left Ventricle

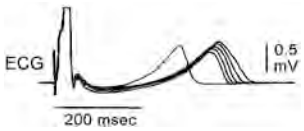


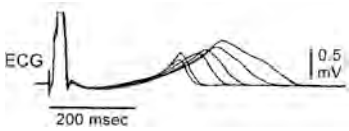
Seemann et al. 2003 Biomedizinische Technik 48-1:226-227

Mutation: Long QT Syndrome

LQT1	LQT2	LQT3
Reduction of I_{Ks} Defect in gene KCNQ1	Reduction of I_{Kr} Defect in gene KCNH2	Late inactivation of I_{Na} Defect in gene SCN5A

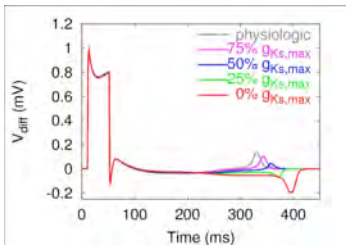


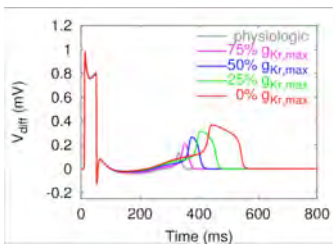


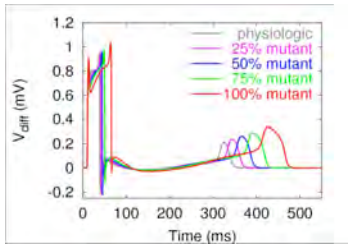


Shimizu et al.1998 Circ. 98: 2314–2322

Shimizu et al.1997 Circ. 96: 2038–2047



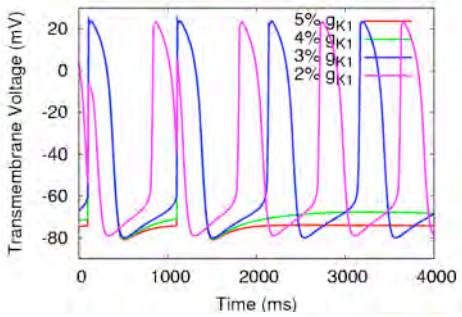


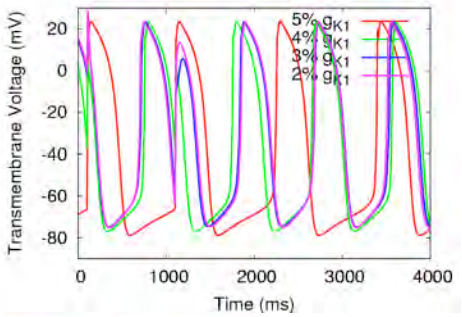


Seemann et al. 2003 IEEE Computers in Cardiology 30:287-290

I_{K1} Mutation in ten Tusscher Model

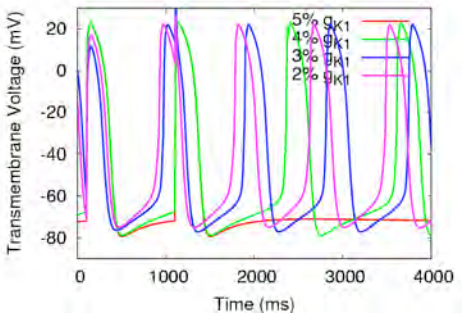
Endo AP





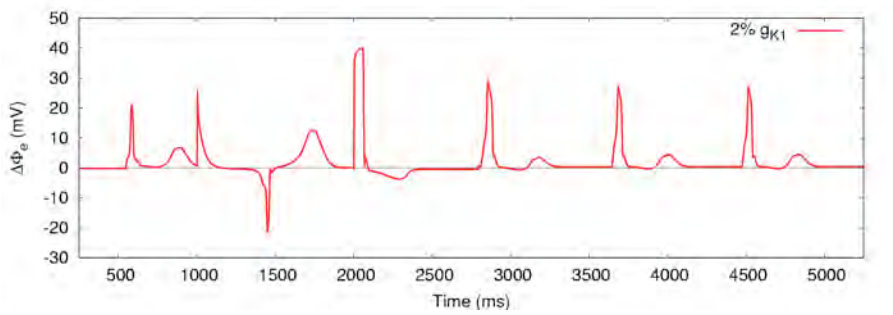
Mid AP

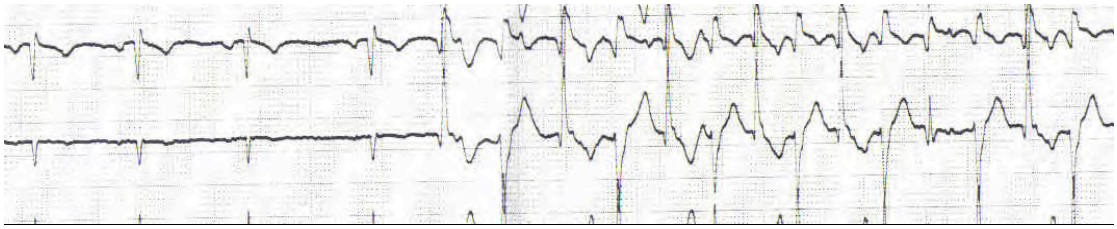
Epi AP



Mutation: I_{K1}

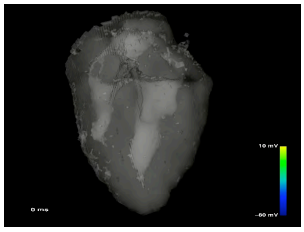
Transmural ECG in heterogeneous ten Tusscher et al. Model



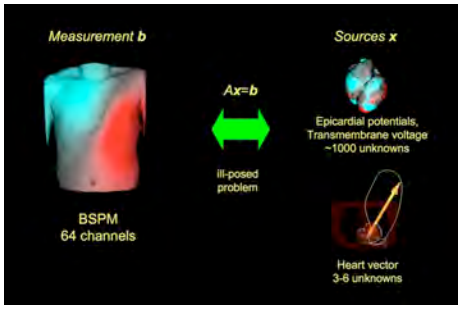


Other Research Activities

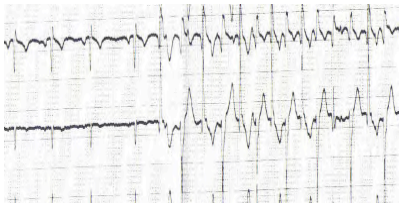
Cellular Automaton for clinical studies



Forward and inverse problem

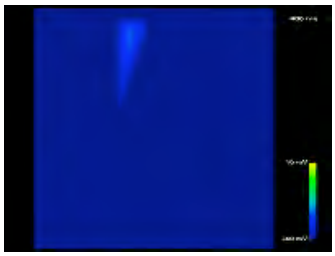
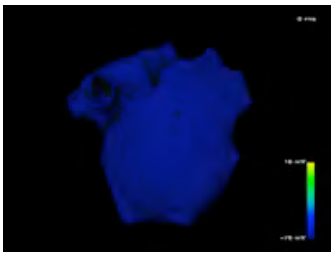
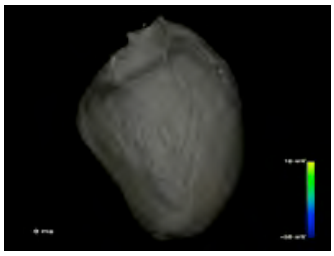


Multi-channel ECG analysis



Optical mapping of electrical activity + tension and deformation mapping

Perspectives

- Further heterogeneities (apico-basal)
- Further Pathologies esp. arrhythmia
- Individual complete heart geometry
- Forward calculation on body model
- Detailed mechanics and blood flow
- Support of drug development
- Therapeutical applications