Overview

Electrophysiology

Tension development

Anatomy

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

Dr.-Ing. Gunnar Seemann
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

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

Preprocessing
Segmentation
Classification
Filtering
Visible Female Heart

Additionally segmented atrial tissue classes

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

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

Atrial Cell Models


\[ \frac{dV_m}{dt} = - \frac{1}{C_m} \left( \sum I_x - I_{\text{inter}} \right) \]
Ventricular Cell Models

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

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

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

Institute of Biomedical Engineering
Universität Karlsruhe (TH)
Research University • founded 1825

G. Seemann EFCM Meeting 2005 9

Heterogeneous Ventricle Model

<table>
<thead>
<tr>
<th></th>
<th>$\text{APD}_{\text{Endo}}$</th>
<th>$\text{APD}_{\text{Mid}}$</th>
<th>$\text{APD}_{\text{Epi}}$</th>
<th>$V_{\text{Rest}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experiment</td>
<td>263±17 ms</td>
<td>376±31 ms</td>
<td>271±14 ms</td>
<td>-81±3 mV</td>
</tr>
<tr>
<td>Simulation</td>
<td>272 ms</td>
<td>343 ms</td>
<td>265 ms</td>
<td>-80 mV</td>
</tr>
</tbody>
</table>

Measurement
Simulation

Transmural ECG

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


Institute of Biomedical Engineering
Universität Karlsruhe (TH)
Research University • founded 1825

G. Seemann EFCM Meeting 2005 10
Electromechanical Coupling

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

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

Tension Model

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

Measurement  Simulation

Peterson et al. 1991 AJP
260:H1013-H1024
**Conduction: Bidomain Model**

\[ \nabla \cdot (\sigma_i \nabla \Phi_i) = \beta I_m \]

\[ \nabla \cdot (\sigma_e \nabla \Phi_e) = -\beta I_m \]

\[ V_m = \Phi_i - \Phi_e \]

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

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

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

- **V_m** Transmembrane voltage
- **Intracellular potential**
- **Extracellular potential**
- **Intracellular conductivity**
- **Extracellular conductivity**
- **C_m** Membrane capacitance
- **I_x** Ion current of type X
- **I_{\text{inter}}** Interacellular current
- **Surface/Volume**

**Elliptical PDE**

**Parabolical PDE**

---

**Schematic Right Atrium**

**Conduction velocity (m/s)**

<table>
<thead>
<tr>
<th>Area</th>
<th>Measured</th>
<th>Simulated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrium</td>
<td>0.68 – 1.03</td>
<td>0.6</td>
</tr>
<tr>
<td>Crista Terminalis (CT)</td>
<td>1 – 1.2</td>
<td>1.18 – 1.2</td>
</tr>
<tr>
<td>Pectinate muscle (PM)</td>
<td>1.5 – 2</td>
<td>1.54 – 1.58</td>
</tr>
</tbody>
</table>

---

Institute of Biomedical Engineering
Universität Karlsruhe (TH)
Research University • founded 1825

G. Seemann EFCM Meeting 2005

---
Atrial Simulation

<table>
<thead>
<tr>
<th>Activation times (ms)</th>
<th>measured</th>
<th>simulated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bachmann</td>
<td>23</td>
<td>26</td>
</tr>
<tr>
<td>right atrium</td>
<td>81</td>
<td>83</td>
</tr>
<tr>
<td>left atrium</td>
<td>80</td>
<td>79</td>
</tr>
<tr>
<td>complete atrium</td>
<td>120</td>
<td>103</td>
</tr>
</tbody>
</table>

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

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

Simulation in the ventricular wall

Institute of Biomedical Engineering
Universität Karlsruhe (TH)
Research University • founded 1825

G. Seemann EFCM Meeting 2005
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**
- Reduction of $I_{Ks}$
- Defect in gene KCNQ1

**LQT2**
- Reduction of $I_{Kr}$
- Defect in gene KCNH2

**LQT3**
- 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


---

**$I_{K1}$ 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

Multi-channel ECG analysis

Forward and inverse problem

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