Bioeng 6460
Electrophysiology and Bioelectricity

Modeling of Electrical Conduction in Cardiac Tissue IV

Frank B. Sachse
fs@cvrti.utah.edu

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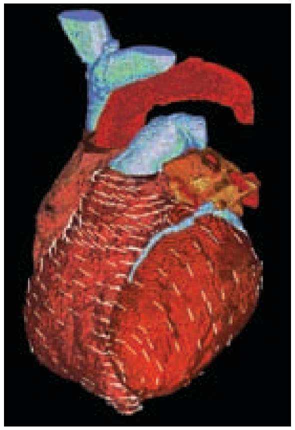
Overview

- ECG Simulation
  - Physiology and Pathophysiology
  - Arrhythmia
- Microscopic Modeling
- Multidomain Modeling
- Electro-Mechanical Modeling
- Summary

Group work

Group work

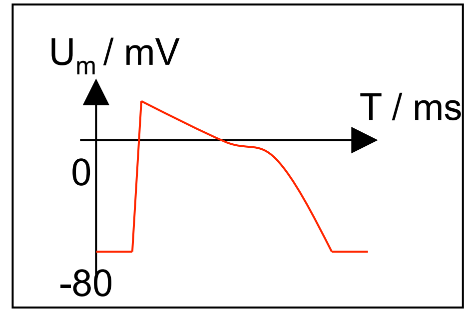
Cellular Automaton: Application in ECG/BSPM Simulation



Anatomie

Cellular Automaton

- Transmembrane voltages
- Membrane current densities

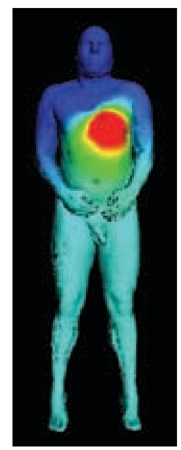


Electrophysiology

Numerical Field Calculation

- Volume and surface voltages
- Current densities

EKG



BSPM

Body
Surface
Potential
Map

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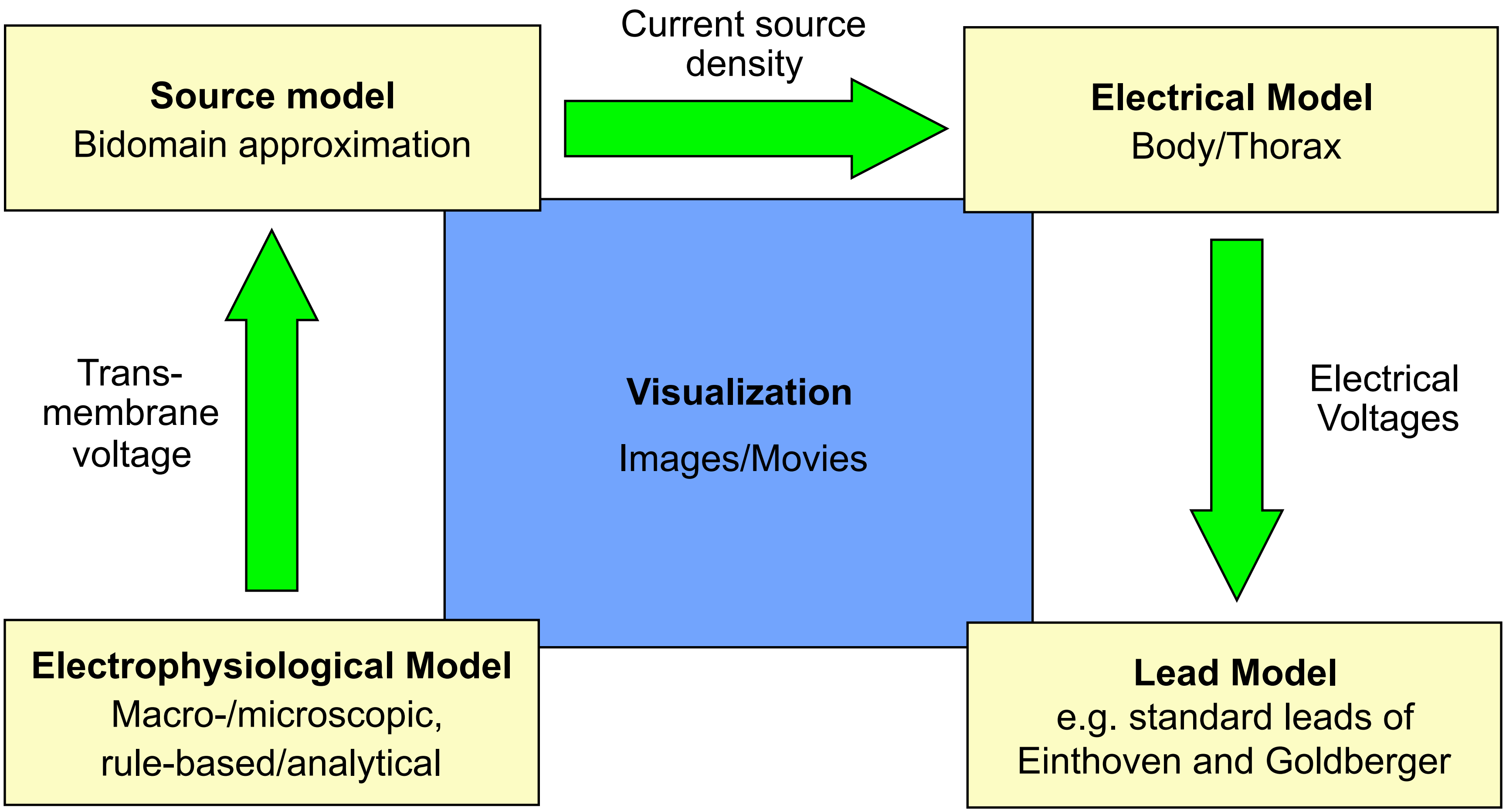
Simulation System: Overview



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Example: ECG Simulation

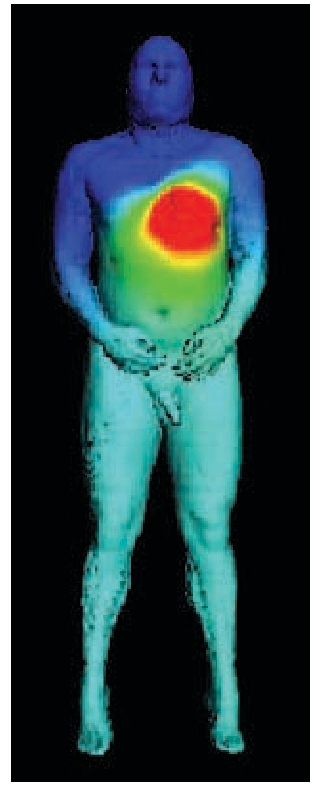
V_m

Trans-
membrane
voltage

Cellular automaton
of excitation propagation

f_e

Current
source
densities



Bidomain
model

ECG

BSPM

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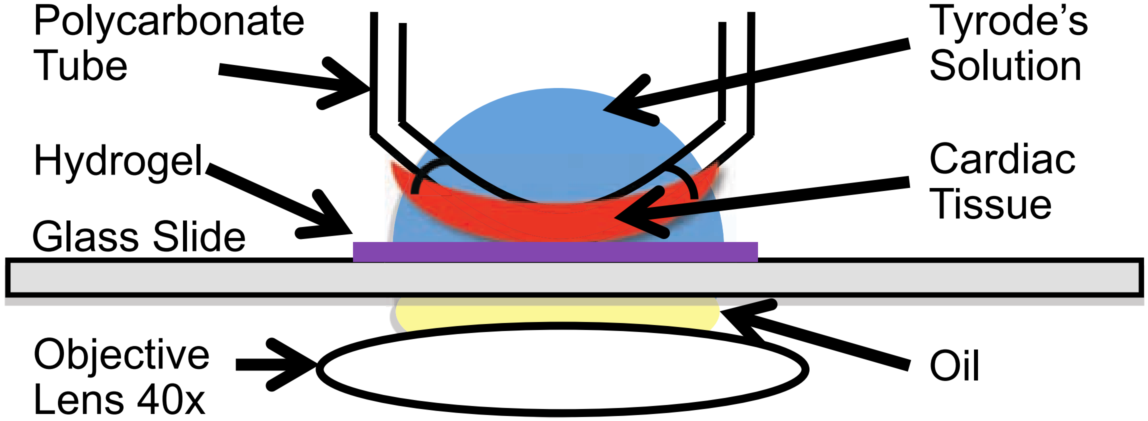
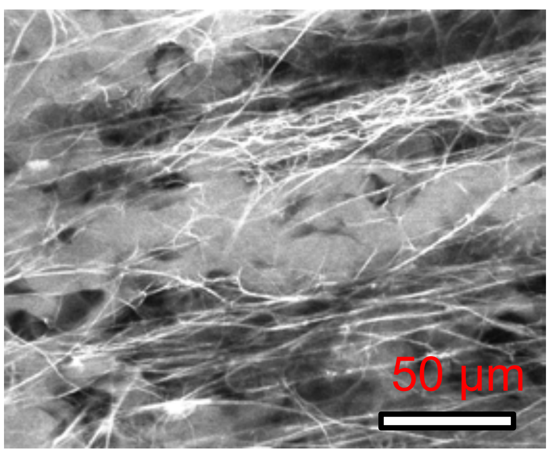
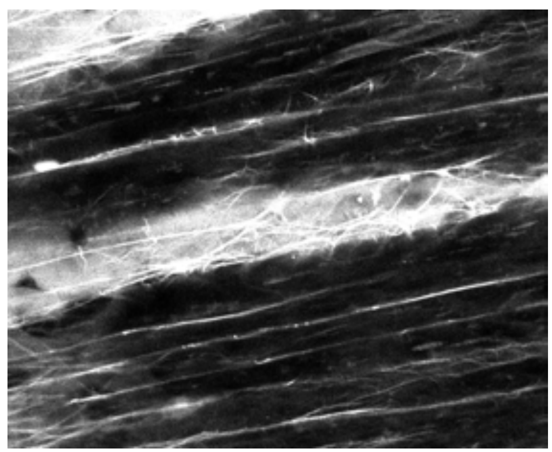
[redacted]

Microscopic Imaging

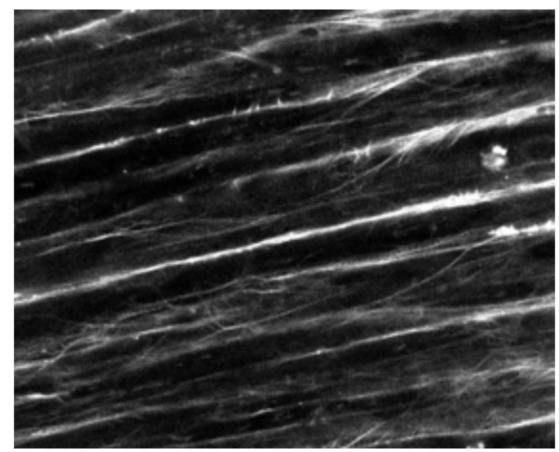




Epicardial surface



Depth: 5 µm



Depth: 15 µm

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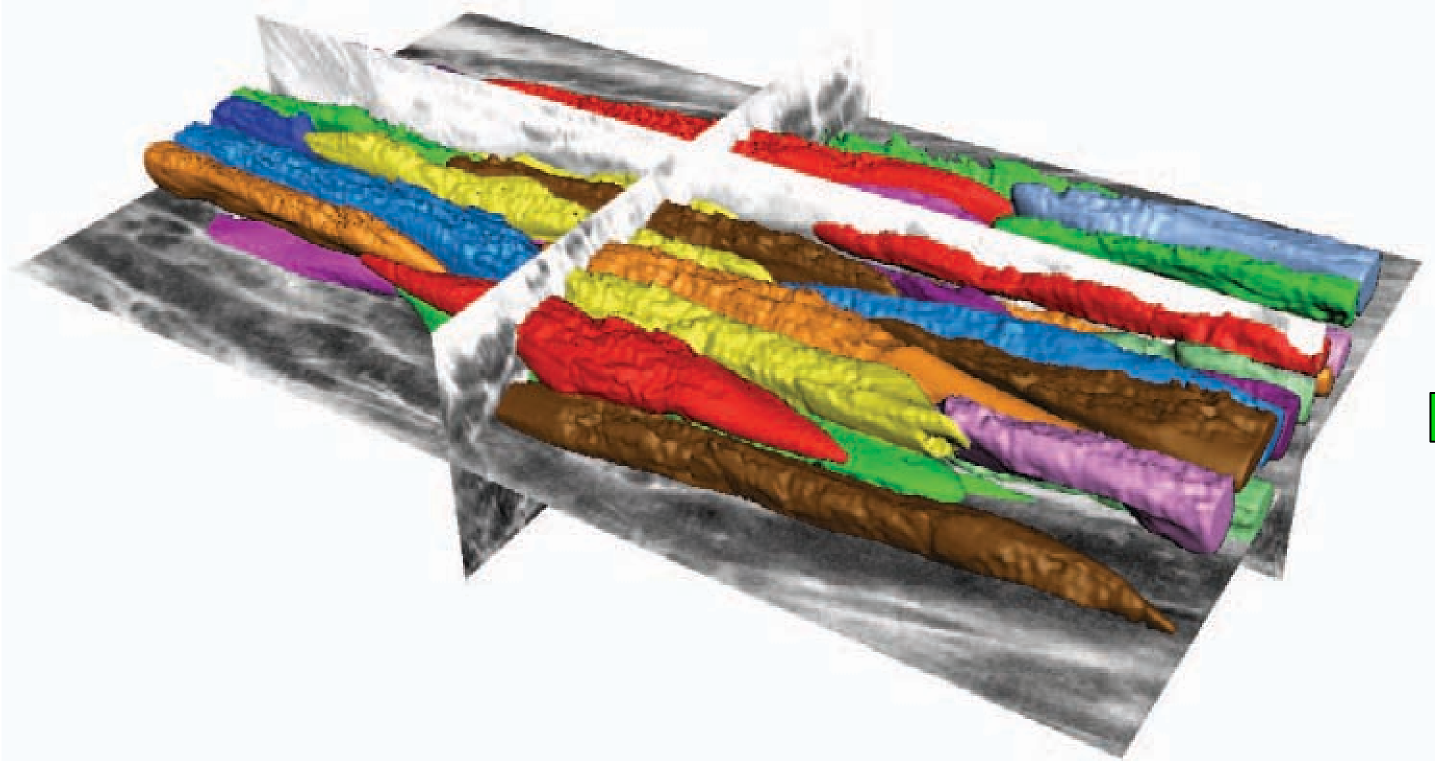
(Lasher et al, IEEE Trans Med Imaging, 2009)

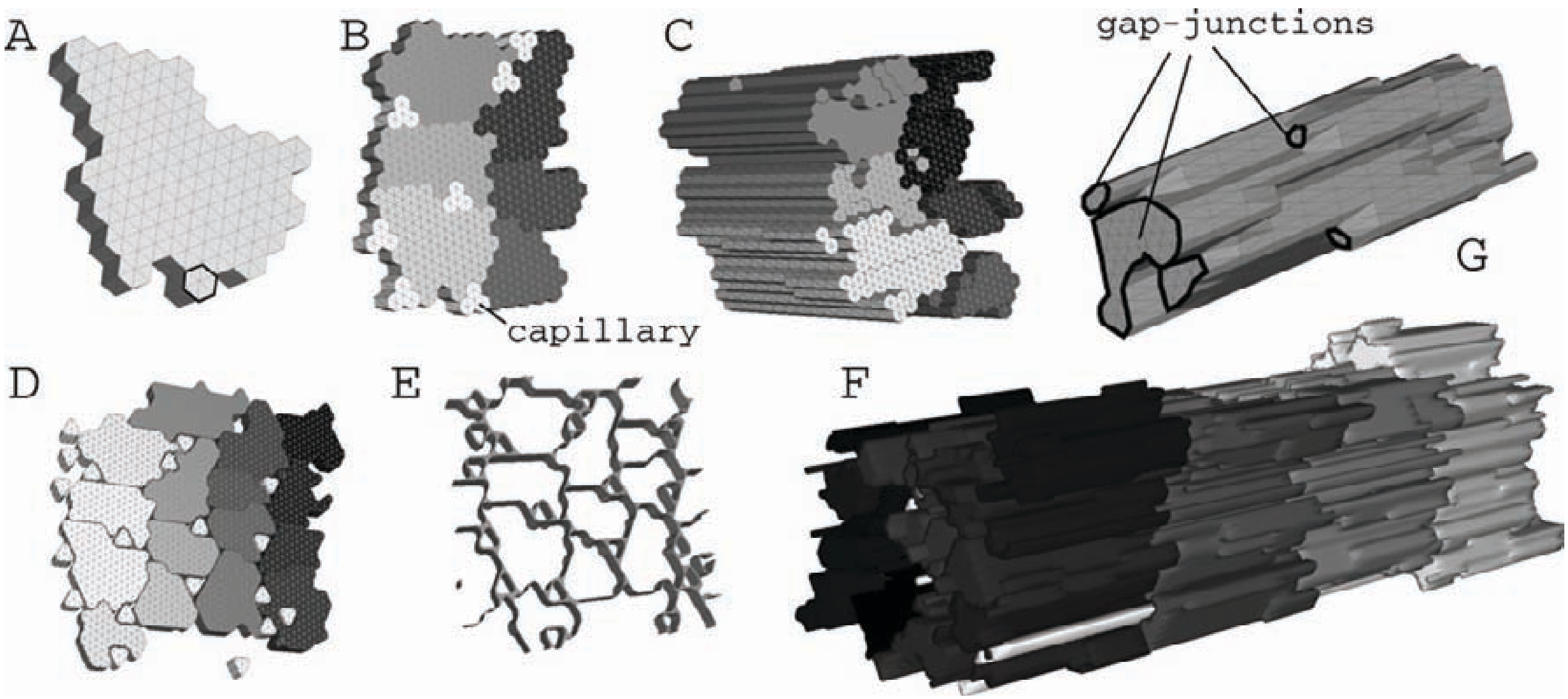
Imaging-Based 3D Model of Cardiac Tissue



Tissue	Length (µm)	Width (µm)	Height (µm)	Volume (μm^3)
Atrial (n=28)	105.0±10.6	13.1±1.7	9.7±1.6	4901±1713
Vent. (n=20)	112.3±14.3	18.4±2.3	14.1±2.7	10,299±3598

(Lasher et al, IEEE Trans Med Imaging, 2009)

CAD-Based 3D Model of Cardiac Tissue



(Stinstra et al, Ann Biomed Eng, 2005)

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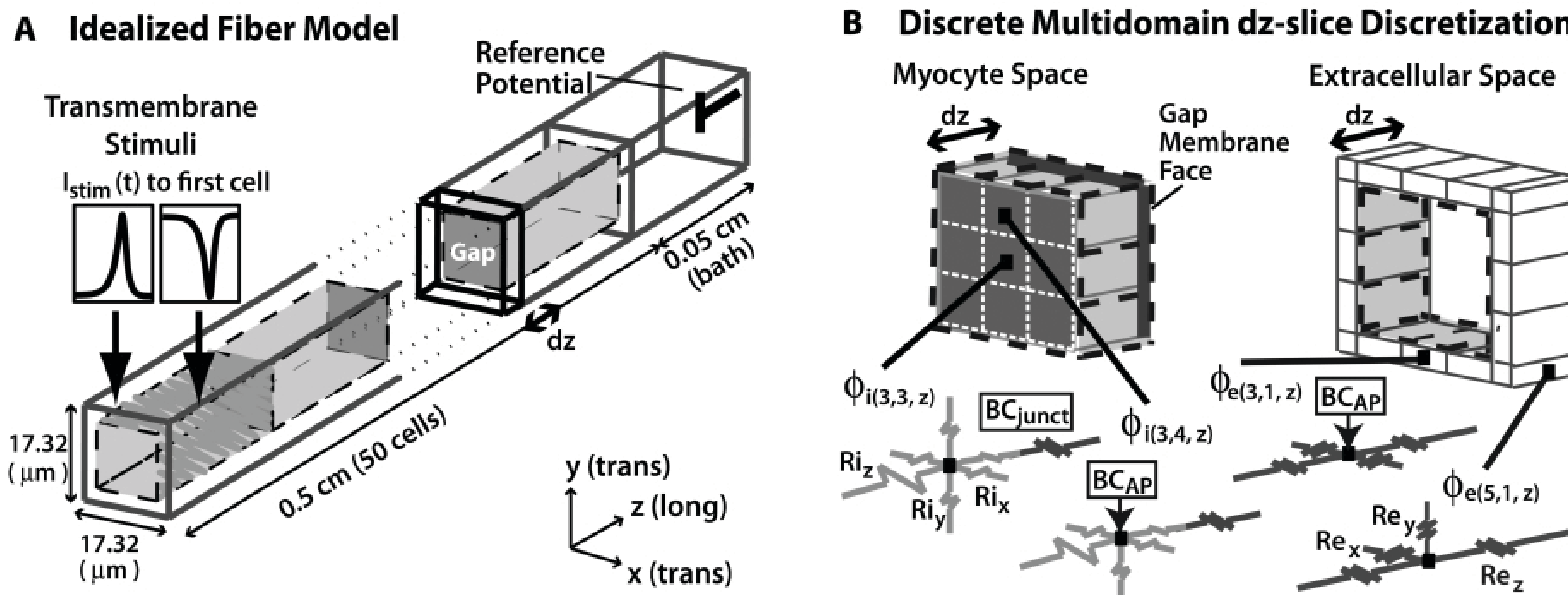
Microscopic Modeling of Conduction

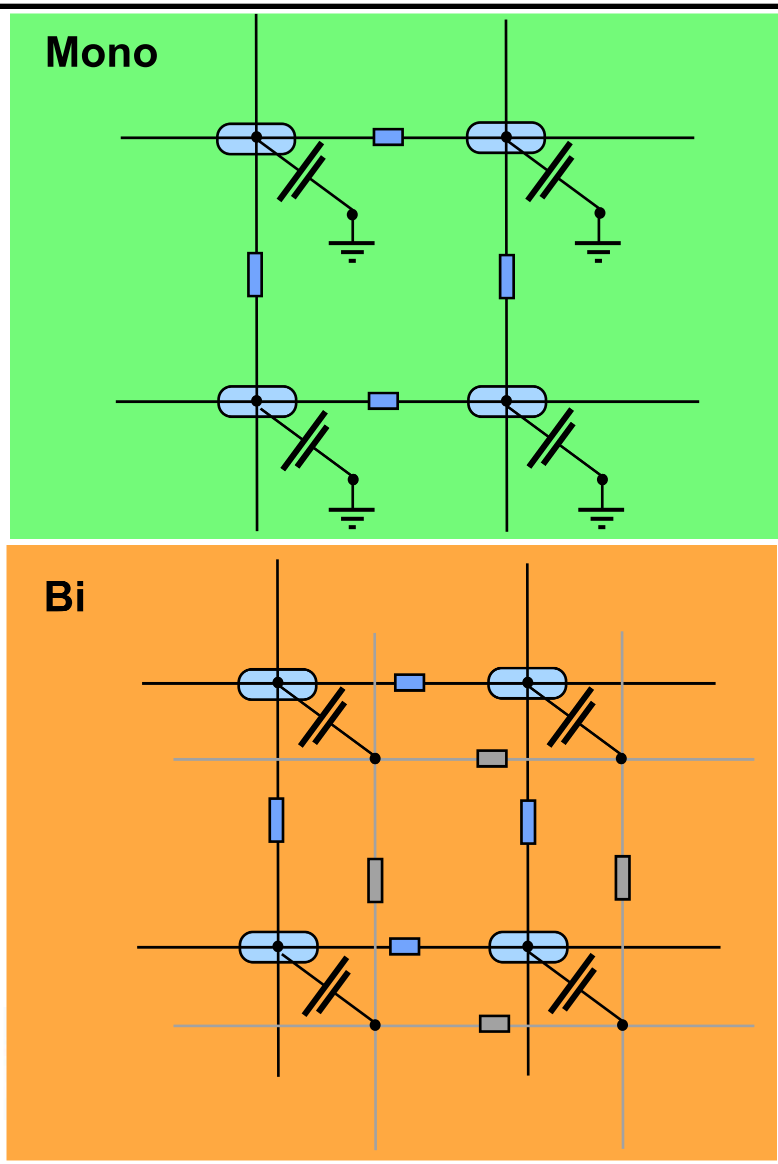


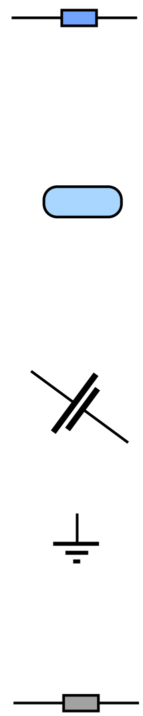
(Roberts et al, Biophys J, 2008)

Group Work

Compare discrete microscopic models with bidomain models. List model parameters and types of simulation results.

Mono- and Bidomain Models of Cardiac Conduction





Resistor of intracellular space
(including gap junction channels)

Myocyte
intracellular space
surrounded by sarcolemma

Membrane Voltage Source

Ground

Resistor of extracellular space

Multidomain Modeling of Conduction

Cardiac tissue is composite of various cell types

- major cell type by volume: myocyte
- major cell type by number: fibroblast
- other types: endothelial, vascular smooth muscle and neuronal cells

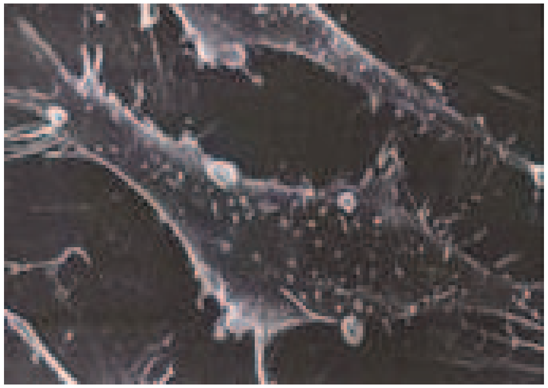
Numbers of these cells vary

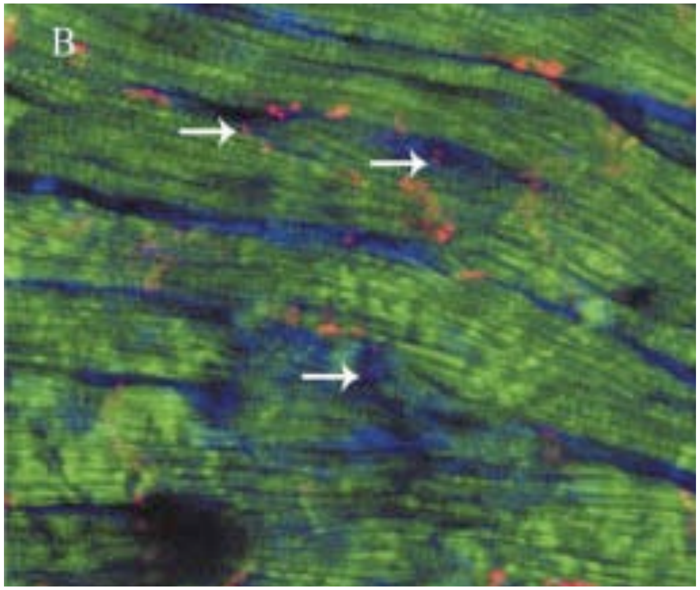
- for tissue types
- during development
- among species
- in disease

Common approaches for modeling of electrical conduction in tissue involve only myocytes

Fibroblasts

- fibroblasts are the most numerous cells in myocardium
- electrically inexcitable, but coupled via gap junction channels to myocytes and fibroblasts
- electrical bridging of myocytes over distances up to 300μm (G. Gaudesius et al, Circ Res 2003)





Fibroblast organization in rat neonatal tissue
(E. C. Goldsmith et al, Develop Dyn 2004)

Discoidin domain receptor (DDR) - Fibroblasts

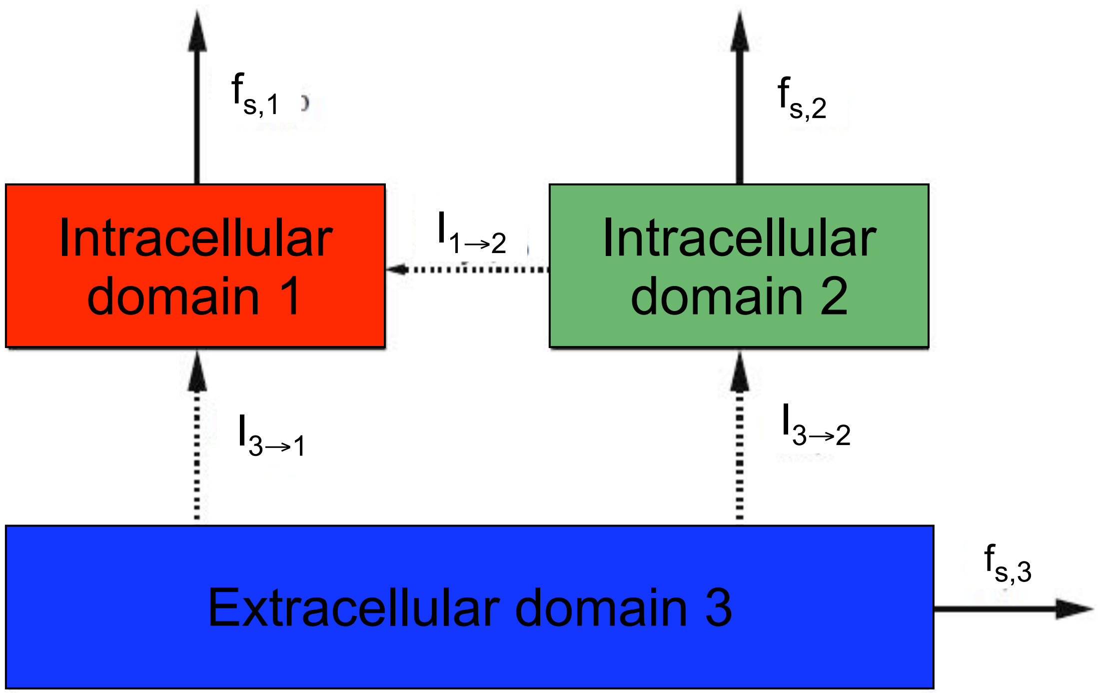
Actin - Myocytes

Cx43 - Gap Junctions

Arrows indicate gap junctions of fibroblasts

Multidomain Model: Schematics

- Multidomain model allows for description of electrophysiology in composite tissue
- Example: Fully coupled 3-domain model. Extension to n-domain model is straightforward
  - Domain 1: Myocytes
  - Domain 2: Fibroblasts
  - Domain 3: Interstitial



f_s: Current source density
$I_{\rightarrow}$: Membrane current

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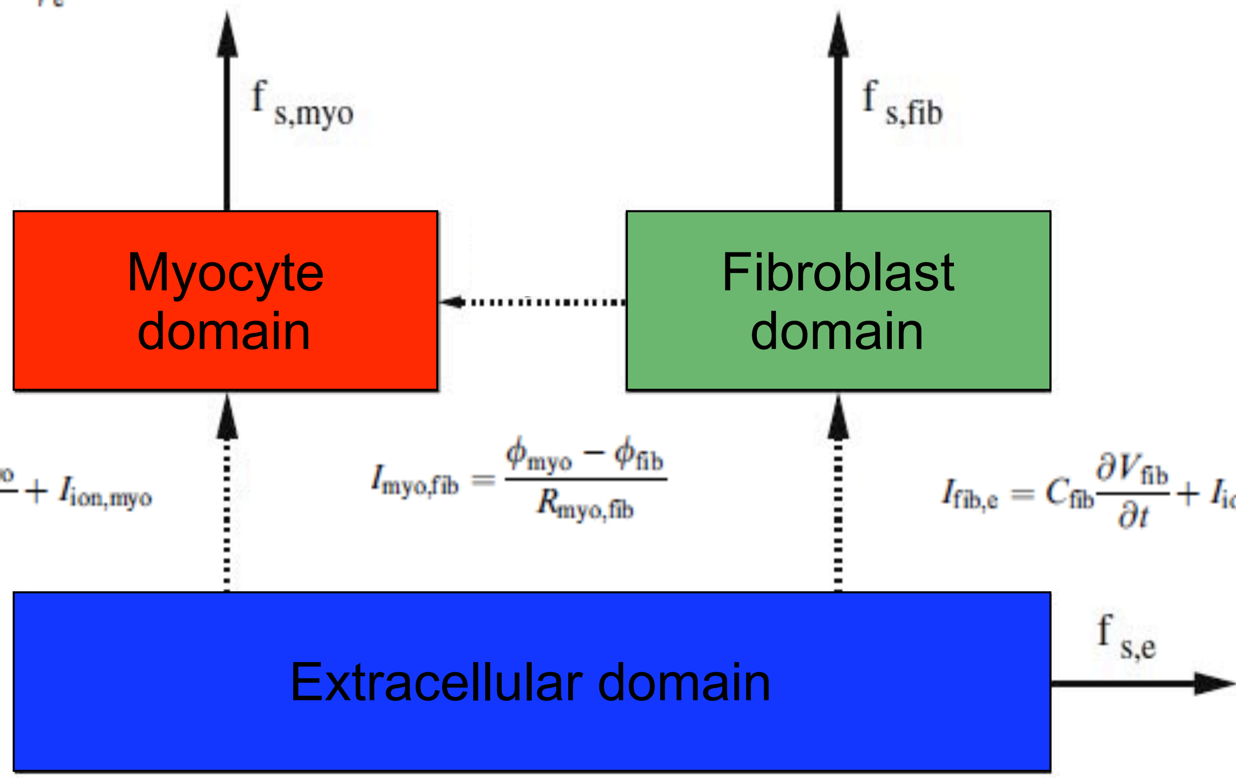
Fully Coupled 3-Domain Model

$$\nabla \cdot (\sigma_{myo} \nabla \phi_{myo}) = -f_{s,myo} + \beta_{myo} I_{myo,e} + \beta_{myo,fib} I_{myo,fib}$$

$$V_{myo} = \phi_{myo} - \phi_e$$

$$\nabla \cdot (\sigma_{fib} \nabla \phi_{fib}) = -f_{s,fib} + \beta_{fib} I_{fib,e} - \beta_{myo,fib} I_{myo,fib}$$

$$V_{fib} = \phi_{fib} - \phi_e$$



$$I_{myo,e} = C_{myo} \frac{\partial V_{myo}}{\partial t} + I_{ion,myo}$$

$$I_{myo,fib} = \frac{\phi_{myo} - \phi_{fib}}{R_{myo,fib}}$$

$$I_{fib,e} = C_{fib} \frac{\partial V_{fib}}{\partial t} + I_{ion,fib}$$

$$\nabla \cdot (\sigma_e \nabla \phi_e) = -f_{s,e} - \beta_{myo} I_{myo,e} - \beta_{fib} I_{fib,e}$$

Methods: Conductivities - Assumptions

- Extracellular space occupies 20% of total tissue volume
- Conductivities in myocyte and fibroblast domains scale linearly with their volume ratio

Variation of volume ratios can be described by number of fibroblasts per myocyte (*n*):

$$\frac{Vol_{\text{myo}}}{Vol} = \frac{80\%}{Vol_{\text{myo,single}} + n\,Vol_{\text{fib,single}}} Vol_{\text{myo,single}} \quad \blacktriangleright \quad \sigma_{\text{myo}} = \frac{Vol_{\text{myo}}}{Vol}\bar{\sigma}_{\text{myo}}$$

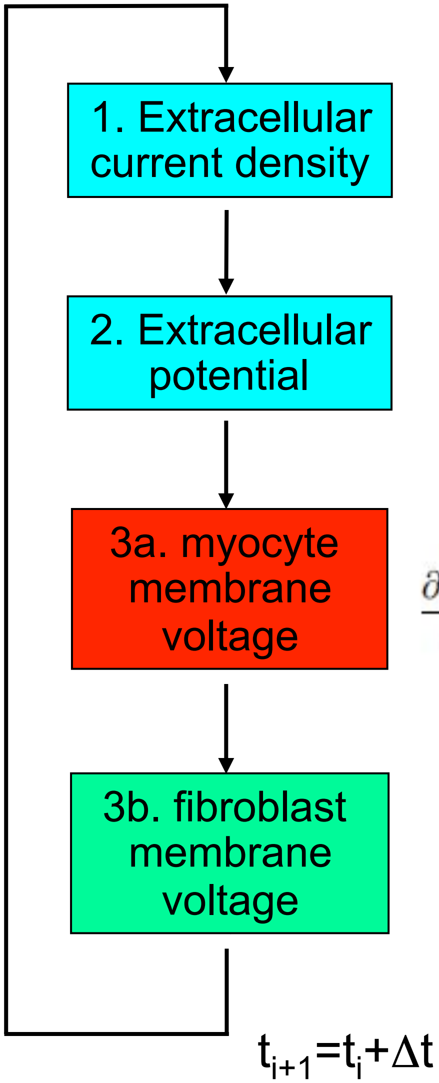
$$\frac{Vol_{\text{fib}}}{Vol} = \frac{80\%}{Vol_{\text{myo,single}} + n\,Vol_{\text{fib,single}}} n\,Vol_{\text{fib,single}} \quad \blacktriangleright \quad \sigma_{\text{fib}} = \frac{Vol_{\text{fib}}}{Vol}\bar{\sigma}_{\text{fib}}$$

Domain	Symbol	Volume fraction (%)	Longitudinal conductivity (S/m)	Transversal conductivity (S/m)
Extracellular	σ_e	20	0.375	0.214
Intra-myocyte	$\bar{\sigma}_{\text{myo}}$	100	0.469	0.047
	σ_{myo}	60,…, 80	0.281,…, 0.375	0.028,…, 0.038
Intra-fibroblast (no coupling)	$\bar{\sigma}_{\text{fib}}$	0	0.000	0.000
	σ_{fib}	0,…, 20	0.000	0.000
Intra-fibroblast (high coupling)	$\bar{\sigma}_{\text{fib}}$	100	1.000	1.000
	σ_{fib}	0,…, 20	0.000,…, 0.200	0.000,…, 0.200

Reference bidomain conductivities from Roth, Circ, 1991

Numerical Solution and Implementation

Decomposition approach similar as for bidomain model (Hooke et al, Crit Rev Biomed Eng, 1992):



$$f_{\mathrm{sum,e}} = \nabla\cdot\left(\sigma_{\mathrm{myo}}\nabla V_{\mathrm{myo}}\right) + \nabla\cdot\left(\sigma_{\mathrm{fib}}\nabla V_{\mathrm{fib}}\right) + f_{\mathrm{s,myo}} + f_{\mathrm{s,fib}} + f_{\mathrm{s,e}}$$

$$\nabla\cdot\left(\left(\sigma_{\mathrm{e}}+\sigma_{\mathrm{myo}}+\sigma_{\mathrm{fib}}\right)\nabla\phi_{\mathrm{e}}\right) = -f_{\mathrm{sum,e}}$$

$$\frac{\partial V_{\mathrm{myo}}}{\partial t} = \frac{1}{C_{\mathrm{myo}}}\left(\frac{f_{\mathrm{s,myo}}+\nabla\cdot\left(\sigma_{\mathrm{myo}}\nabla V_{\mathrm{myo}}\right)+\nabla\cdot\left(\sigma_{\mathrm{myo}}\nabla\phi_{\mathrm{e}}\right)-\beta_{\mathrm{myo,fib}}I_{\mathrm{myo,fib}}}{\beta_{\mathrm{myo}}} - I_{\mathrm{ion,myo}}\right)$$

(Pandit et al, Biophys J, 2001)

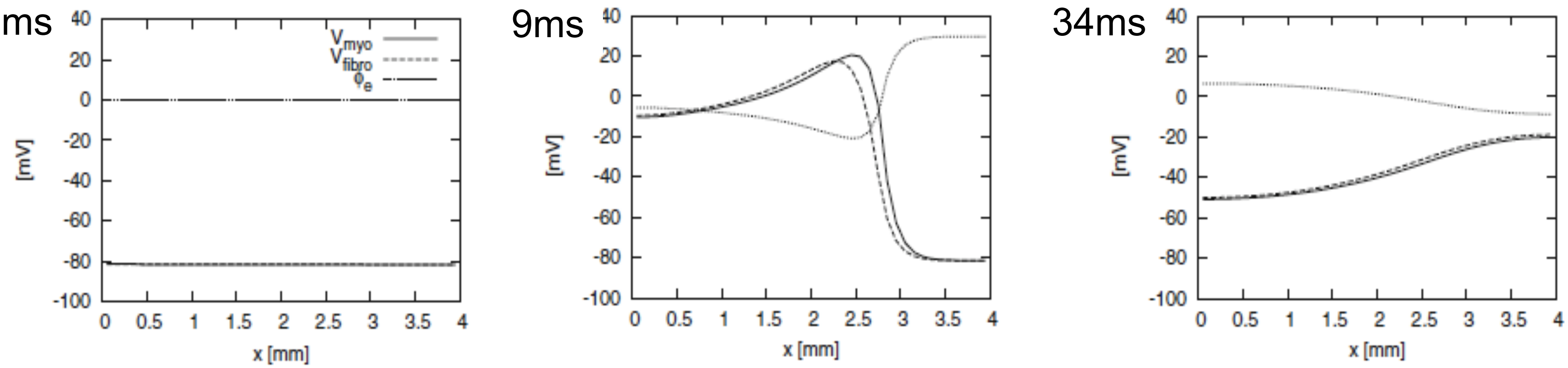
$$\frac{\partial V_{\mathrm{fib}}}{\partial t} = \frac{1}{C_{\mathrm{fib}}}\left(\frac{f_{\mathrm{s,fib}}+\nabla\cdot\left(\sigma_{\mathrm{fib}}\nabla V_{\mathrm{fib}}\right)+\nabla\cdot\left(\sigma_{\mathrm{fib}}\nabla\phi_{\mathrm{e}}\right)+\beta_{\mathrm{myo,fib}}I_{\mathrm{myo,fib}}}{\beta_{\mathrm{fib}}} - I_{\mathrm{ion,fib}}\right)$$

(F. B. Sachse et al, Ann Biomed Eng, 2008)

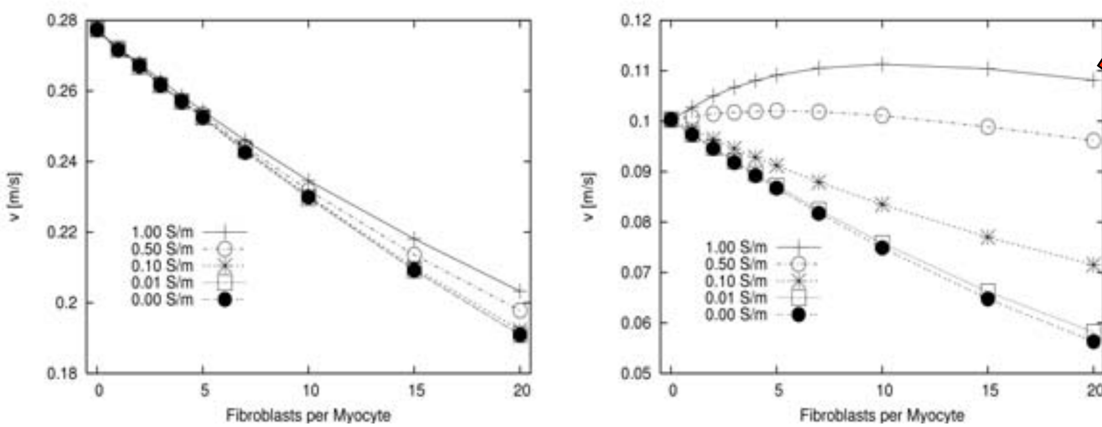
Propagation in Tissue (1D)

Example: Fibroblasts per myocyte=1, $R_{myo,fib}$=100 MΩ, intra-fibroblast coupling σ_{fib}=0 S/m

0ms 9ms 34ms



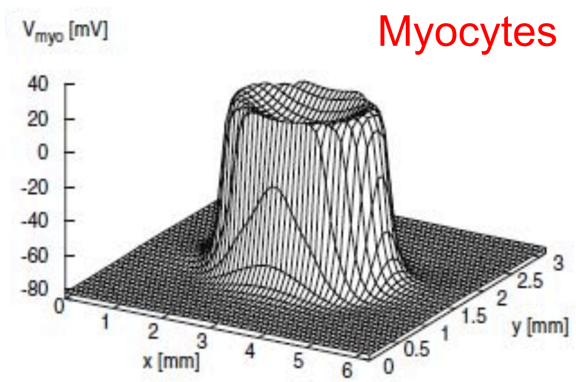
Longitudinal Transversal

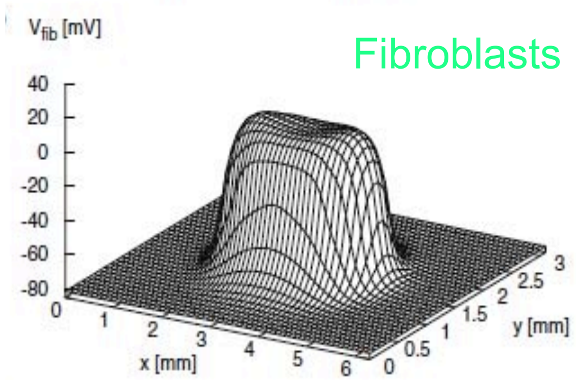


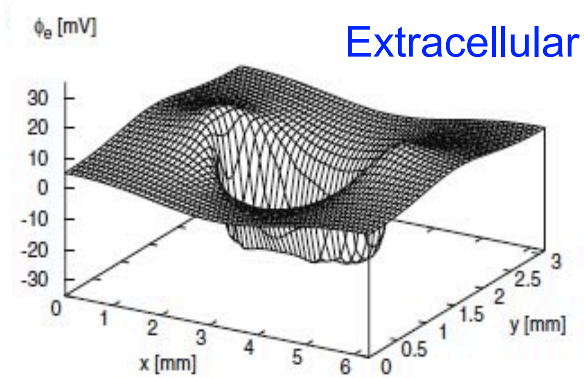
High intra-fibroblast coupling

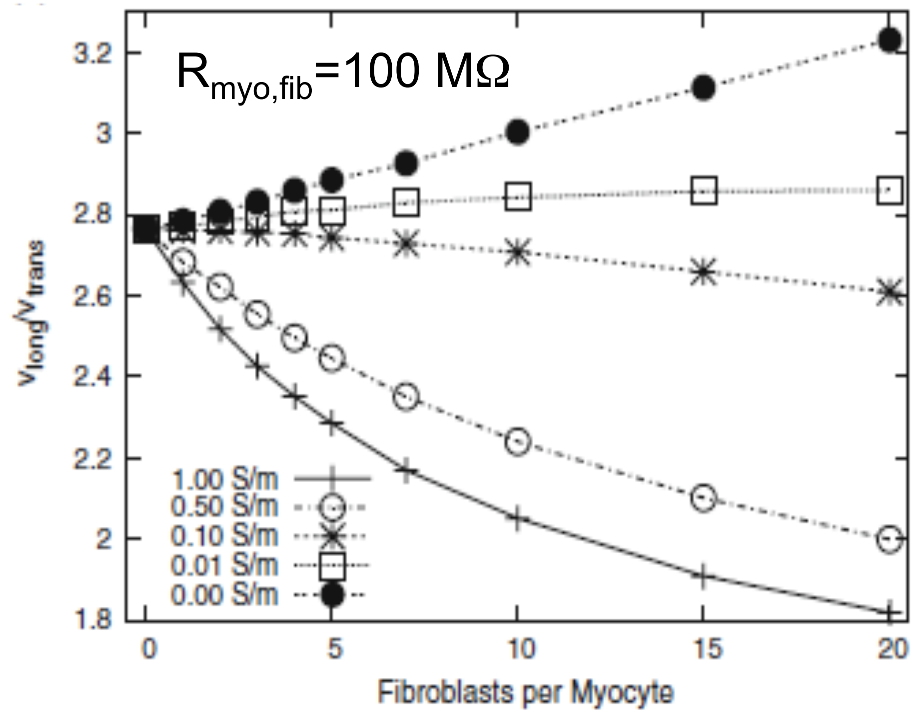
Effects of fibroblasts more significant on transversal conduction and with high intra-fibroblast coupling!

Propagation in Thin Tissue Slice (2D)



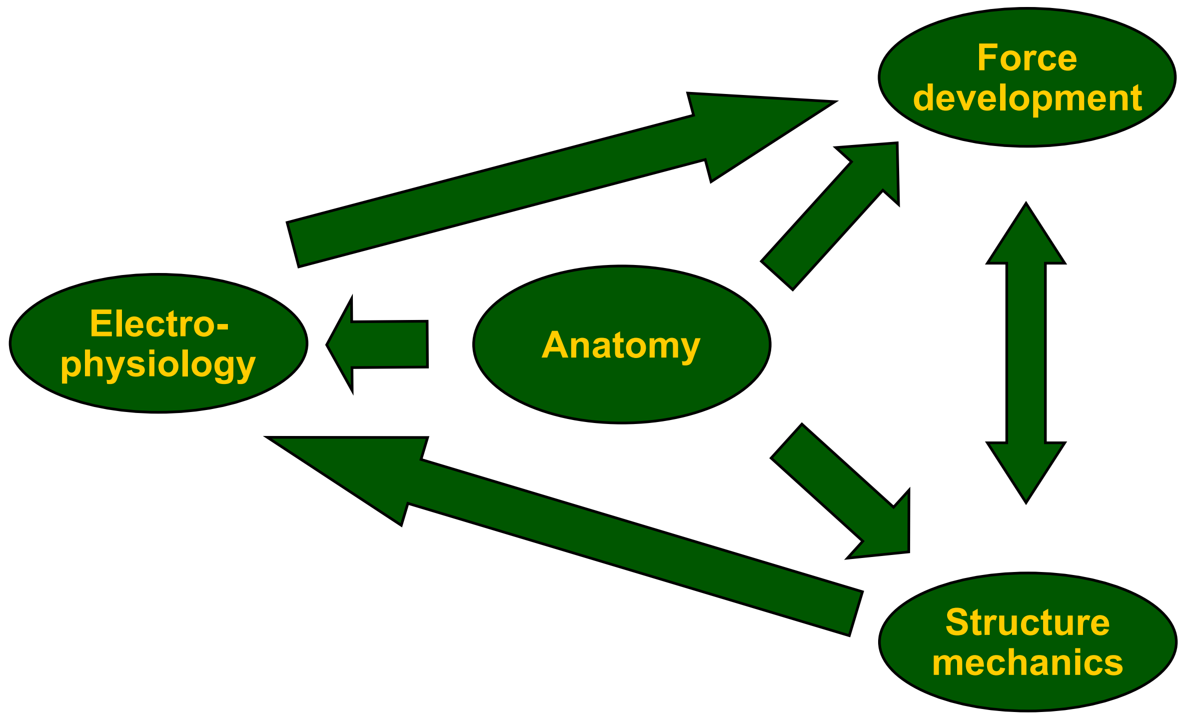






Intra-fibroblast coupling affects anisotropy ratio of conduction velocity strongly dependent on the number of fibroblasts per myocyte!

Coupled Electro-Mechanics



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Example: Electro-Mechanics of Myocardium

Array of myocytes

Volume:2^3 mm^3
Elements: 20^3
with fiber orientation
and lamination

Electrophysiology

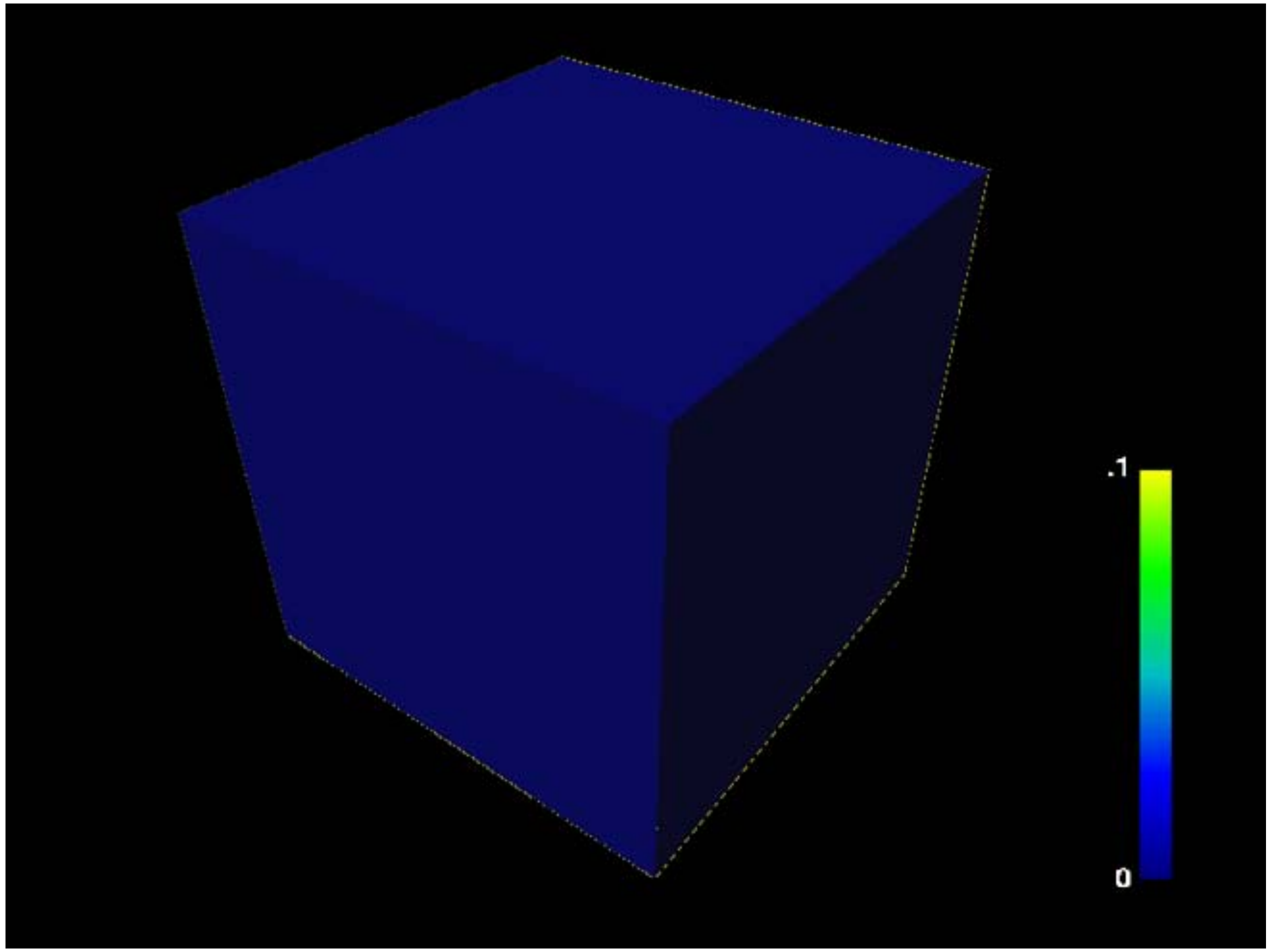
Noble et al. 98
Bidomain model

Force Development

Six-state model of
Rice et al. 99

Structure Mechanics

Constitutive law of
Hunter et al. 95



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(Sachse, Seemann, Werner, Riedel, and Dössel, CinC, 2001)

Example: Electro-Mechanics in Ventricular Model

Anatomy

Lattice of elements
Volume: 273.6 mm^3
Fiber orientation:
-70°, 0°,70°

Electrophysiology

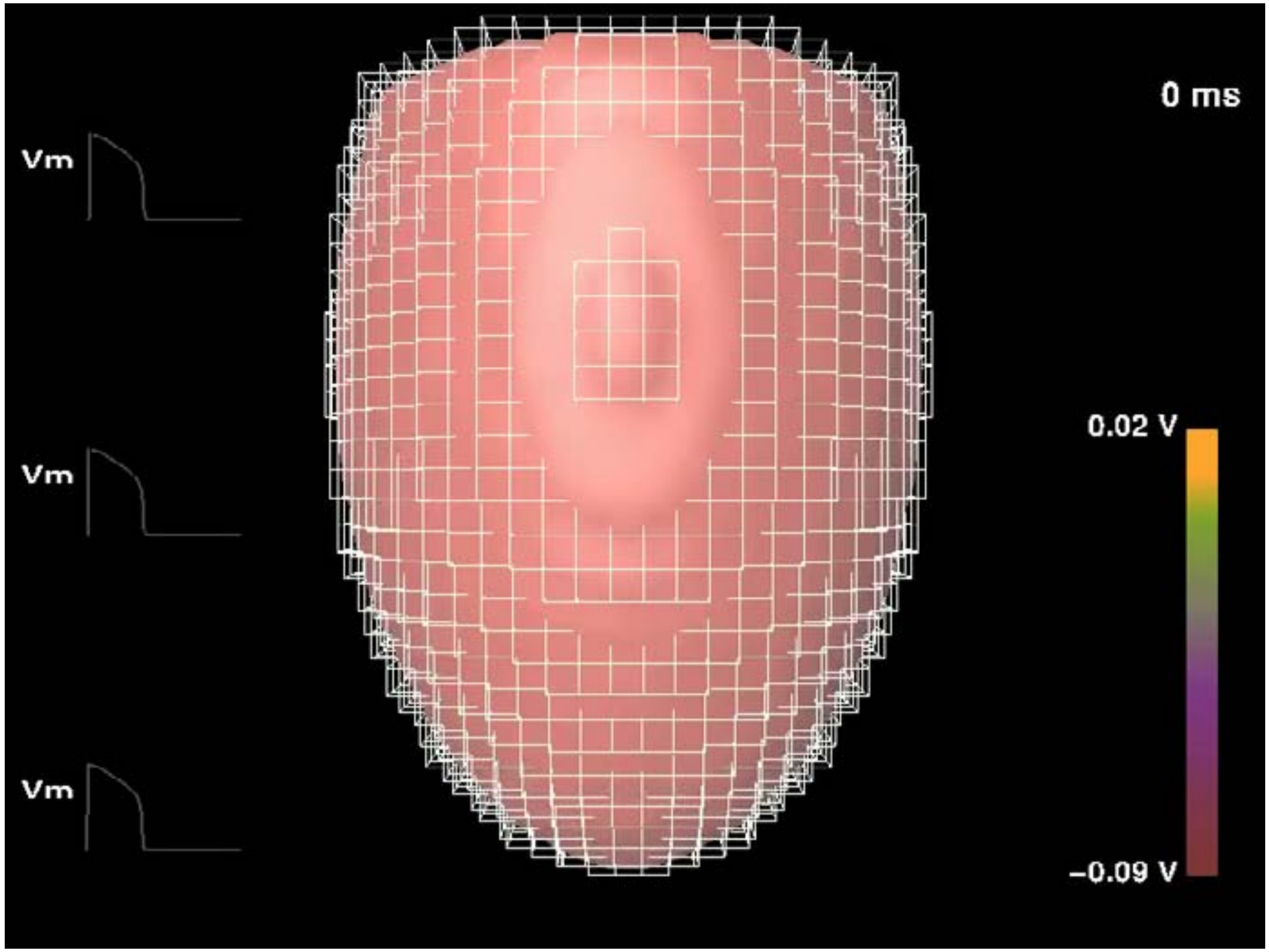
Noble et al. 98
Monodomain model
Elements: 46x46x58
Step-length: 20 μs

Tension

Glänzel et al. 02
Elements: 46x46x58
Step-length: 20 μs

Structure Mechanics

Constitutive law of
Guccione et al. 91
Elements: 23x23x29
Step-length: 5 ms



(Sachse, Seemann, and Werner, CinC, 2002)

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Example: Electro-Mechanics in Biventricular Model

Anatomy

Lattice of elements
Volume: 273.6 mm^3
Fiber orientation:
-70°, 0°,70°

Electrophysiology

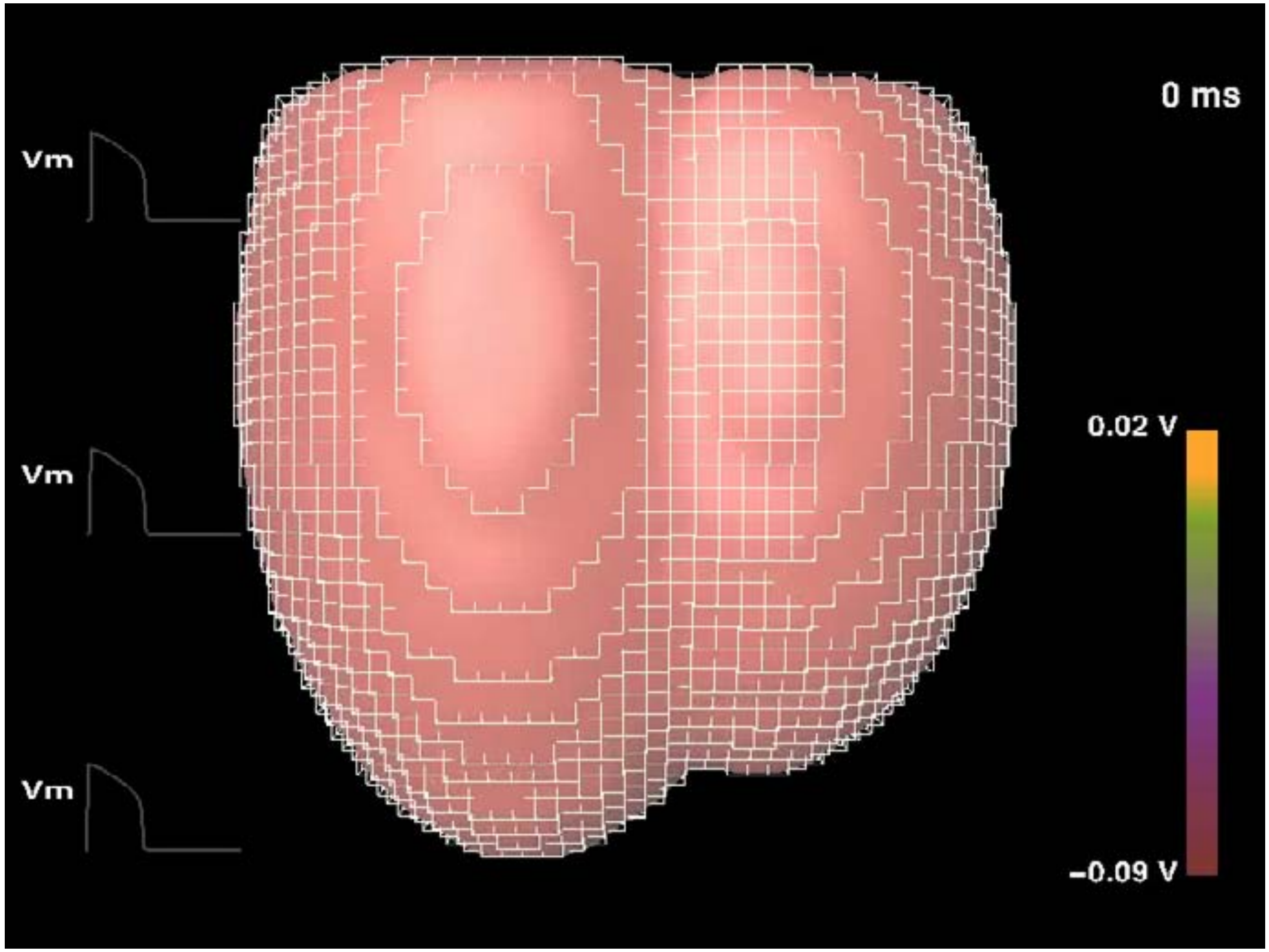
Noble et al. 98
Monodomain model
Elements: 40x30x38
Step-length: 20 μs

Tension

Glänzel et al. 02
Elements: 40x30x38
Step-length: 20 μs

Structure Mechanics

Constitutive law of
Guccione et al. 91
Elements: 20x15x19
Step-length: 5 ms



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Group Work

List potential clinical applications of models of tissue electrophysiology.
What will be necessary for this purpose?

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Overview

- ECG Simulation
  - Physiology and Pathophysiology
  - Arrhythmia
- Microscopic Modeling
- Multidomain Modeling
- Electro-Mechanical Modeling

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