Largescale Cardiac Modelling using Bidomain Formulations

*Developing a “Virtual Heart" Simulator*

Gernot Plank
Research Interests

- **Cardiac Electrophysiology**
  - Electrical Mapping
    - Cardiac Nearfield Techniques
  - Defibrillation
    - Microscopic Effects
    - Level of Organization
    - Midmyocardial polarization and "Wedge" effects

- **Computer Modelling**
  - Numerical Techniques for Bidomain Models
  - Imaging and Image Processing
  - Mesh Generation Techniques
The Bidomain Equations
Core Conductor Equations

Voltage Drop:

\[
\frac{\partial \Phi_i}{\partial x} = -r_i I_i \\
\frac{\partial \Phi_e}{\partial x} = -r_e I_e
\]

Current Conservation:

\[
\frac{\partial I_i}{\partial x} = -i_m \\
\frac{\partial I_e}{\partial x} = i_m + i_e
\]

\[
I_i = -g_i \frac{\partial \Phi_i}{\partial x} \\
I_e = -g_e \frac{\partial \Phi_e}{\partial x}
\]

\[
\frac{\partial I_i}{\partial x} = - \frac{\partial}{\partial x} \left( g_i \frac{\partial \Phi_i}{\partial x} \right) \quad (1)
\]

\[
\frac{\partial I_e}{\partial x} = - \frac{\partial}{\partial x} \left( g_e \frac{\partial \Phi_e}{\partial x} \right) \quad (2)
\]
Homogenization

For each axis $x$, $y$ and $z$:

\[ A = A_i + A_e \]
\[ f_i = \frac{A_i}{A} \]
\[ f_e = \frac{A_e}{A} \]
\[ f_i + f_e = 1 \]

For instance, to keep the conductance along $x$ constant:

\[ \sigma_{ix} A_{ix} = \bar{\sigma}_{ix} A_x \quad \rightarrow \quad \sigma_{ix} = \bar{\sigma}_{ix} \frac{A_x}{A_{ix}} = \frac{\bar{\sigma}_{ix}}{f_{ix}} \]
\[ \sigma_{ex} A_{ex} = \bar{\sigma}_{ex} A_x \quad \rightarrow \quad \sigma_{ex} = \bar{\sigma}_{ex} \frac{A_x}{A_{ex}} = \frac{\bar{\sigma}_{ex}}{f_{ex}} \]

$\bar{\sigma}_i$, $\bar{\sigma}_e$: bidomain conductivities.
The Bidomain Equations

Equations - The Coupled System:

\[- \nabla \cdot (\bar{\sigma}_i \nabla \phi_i) = -\beta I_m \quad (3)\]
\[- \nabla \cdot (\bar{\sigma}_e \nabla \phi_e) = \beta I_m \quad (4)\]
\[- \nabla \cdot (\bar{\sigma}_b \nabla \phi_e) = I_e \quad (5)\]

with

\[I_m = C_m \frac{\partial V_m}{\partial t} + I_{ion}(V_m, \bar{\eta}) - I_{tr}\]
\[\frac{d\bar{\eta}}{dt} = g(V_m, \bar{\eta})\]
\[V_m = \Phi_i - \Phi_e\]
Decoupled Systems

Now the solution scheme can be broken down to three independent steps which have to be solved sequentially:

**Elliptic PDE**

\[
\begin{bmatrix}
- \nabla \cdot (\bar{\sigma}_i + \bar{\sigma}_e) \nabla \phi_e \\
- \nabla \cdot \sigma_b \nabla \phi_e
\end{bmatrix} = \begin{bmatrix}
\nabla \cdot \bar{\sigma}_i \nabla V \\
I_e
\end{bmatrix}
\]

**Parabolic PDE**

\[
\frac{\partial V}{\partial t} = \frac{1}{\beta C_m} \left( \nabla \cdot \bar{\sigma}_i \nabla V + \nabla \cdot \bar{\sigma}_i \nabla \phi_e \right)
\]

(6)

**Set of ODE’s**

\[
\frac{\partial V}{\partial t} = - \frac{1}{C_m} i_{ion}(V, \eta)
\]

(7)

\[
\frac{d\vec{\eta}}{dt} = g(V, \vec{\eta})
\]

(8)
Computing Scheme

\[ A_i = -\frac{\nabla \cdot (\bar{\sigma}_i \nabla V)}{\beta C_m}; \quad A_e = -\frac{\nabla \cdot (\bar{\sigma}_i \nabla \Phi_e)}{\beta C_m}; \quad t = k\Delta t \]

Elliptic PDE:

\[(A_i + A_e)\Phi_e^{k+1} = A_i V^{k+1} + I_e\]

Parabolic PDE:

\[
\begin{cases}
V^{k*} = (1 - \Delta t A_i) V^k - \Delta t A_e \phi_e^k & \Delta x > 100\mu m \\
[1 + \frac{1}{2} \Delta t A_i] V^{k*} = [1 - \frac{1}{2} \Delta t A_i] V^k - \Delta t A_e \phi_e^k & \Delta x < 100\mu m
\end{cases}
\]

ODE’s:

\[
V^{k+1} = V^{k*} + \frac{\Delta t}{C_m} i_{ion} (V^{k*}, \vec{\eta}^k)
\]

\[
\vec{\eta}^{k+1} = \vec{\eta}^k + \Delta t g (V^{k+1}, \vec{\eta}^k)
\]
Cardiac Simulation Environment
Electrical Mapping Techniques
Cardiac Nearfield Mapping

Experimental Setup

CNF Vector Loops

Hofer et al, Biosensors, 2005

- Local Conduction Velocity
- Direction of local Conduction
- Local Activation Time
Electrical Defibrillation
Why Defibrillation?

Facts
- The most effective therapy to prevent SCD (MADIT, AVID, etc)
- # of ICD implantations increased almost exp. over the last decade
- Underlying biophysical mechanism are still poorly understood

Optimization
- Reduce energy requirements (tissue damage, device lifetime, time to therapy, etc)
- Optimize waveforms, electrode geometry and position, shock timing, etc
- Develop smarter shocking strategies
  - “Control"
  - “Unpinning"
  - “Resonance Drift"
  - Adjust dose depending on type of arrhythmia
Activation Patterns

Induction of Reentrant Activation Patterns of different Level of Disorganization:

- Single Rotor (SR) with one PS
- Double Rotor (DR) with 2-3 PS
- Fibrillation (FB) with 6-10 PS

ACTIVATION SEQUENCES

SR  DR  FB
Activating Function and Micro-Heterogeneities

\[ \beta C_m \frac{\partial V_m}{\partial t} = \nabla (\bar{\sigma}_i \nabla V_m) - \beta i_{ion} + \nabla (\bar{\sigma}_i \nabla \phi_e) \]

\[ S = \bar{\sigma}_i : \nabla(\nabla \phi_e) + (\nabla \bar{\sigma}_i) \cdot \nabla \phi_e \]
Postshock VEP Patterns

Shown are typical Postshock VEP Patterns and Mechanism of Shock-Induced EG Erradication:

Shock Success or Failure depends on the timely Erradication of the Excitable Gap.
Fibrillation

- Research Interests
  - Bidomain Equations
  - Mapping
  - Defibrillation
    - Why?
    - Activation Pattern
    - Activating Function
    - Postshock VEP
    - Fibrillation
    - Dose Response
- Bidomain Models
- Multilevel Methods
- Imaging
- Mesh Generation

<table>
<thead>
<tr>
<th>Current Density (kA/cm²)</th>
<th>14 ms</th>
<th>21 ms</th>
<th>30 ms</th>
<th>42 ms</th>
<th>70 ms</th>
<th>100 ms</th>
<th>125 ms</th>
<th>290 ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>A) 5 kA/cm³</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B) 9 kA/cm³</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C) 15 kA/cm³</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Medical University of Graz
Dose-Response Relationship

Conclusions:

- Degree of Disorganization increases DFT
- Heterogeneities favour Shock Success

Microscopic Bidomain Models of the entire Heart
## Heart Size and Computational Complexity

### Mouse, Rabbit, Human Heart Sizes

<table>
<thead>
<tr>
<th>$\Delta x$ (µm)</th>
<th>Mouse</th>
<th>Rabbit</th>
<th>Human</th>
</tr>
</thead>
<tbody>
<tr>
<td>250</td>
<td>0.02</td>
<td>0.5</td>
<td>13 - 38 Mio</td>
</tr>
<tr>
<td>100</td>
<td>0.31</td>
<td>7.8</td>
<td>210-586 Mio</td>
</tr>
<tr>
<td>50</td>
<td>2.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Why Discretization matters

Conduction Velocity $v$

<table>
<thead>
<tr>
<th>$\Delta x$</th>
<th>100</th>
<th>200</th>
<th>250</th>
<th>333</th>
<th>500</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative Error</td>
<td>5%</td>
<td>10%</td>
<td>27%</td>
<td>50%</td>
<td>100%</td>
</tr>
</tbody>
</table>

$V_m(t)$ $V_m(x)$

- $90\%$ APA
- $0.2-0.8\text{ m/s}$
- $1\text{ ms}$
- $0.2-0.8\text{ mm}$

$V$ $0.67\text{ m/s}$
$V$ $0.65\text{ m/s}$
$V$ $0.49\text{ m/s}$

$10\%$ APA
$27\%$ Relative Error
$5\%$ Relative Error
$100\%$ Relative Error

Why Discretization matters
Multilevel Preconditioning Methods
**Basic Idea:** Iterative methods are efficient in removing high frequency Components of the Solution/Residual, but are inefficient with low frequency components

**Geometric Multigrid Preconditioner**

*Typical Speedup over ILU-CG using between 1 and 16 Processors: 3*

**Algebraic Multigrid Preconditioner**

**Unstructured Grids**
- **Adaptivity**: Degrees of freedoms can be reduced significantly without any negative side effects
- **Smooth Organ Surfaces**: Avoids artifactual current due to jagged boundaries.

**GMG vs AMG**
- No explicite geometric coarse mesh generation
- Avoids prolongation and restriction between unstructured grids

Adaptivity

Artifacts due to jagged Boundaries

Structured Hexahedral Grid

Unstructured Tetrahedral Grid
Sequential Benchmarks - Setup

Research Interests
- Bidomain Equations
- Mapping
- Defibrillation
- Bidomain Models
- Multilevel Methods
  - GMG
  - AMG
  - PC Sequential
  - AMG Residual
  - Convergence
  - PC Parallel
  - Parallel Scaling
- RHS
- Imaging
- Mesh Generation

RVS Setup

1 ms 20 ms 40 ms 60 ms 85 ms

120 ms 140 ms 160 ms 180 ms 200 ms

S1 S2 S1 S2

0 ms 85 ms 500 ms

Technical Data:
- Unknowns $\Phi_e$ 111.589
- Unknowns $V_m$ 59.292
- $\Delta t$ [$\mu$s] 20
- $T_{\Delta t}$ 25.000
- Ionic Model Puglisi+EP-RS+Ia

Medical University of Graz
ILU versus AMG: Iterations and Solver Time

<table>
<thead>
<tr>
<th>Method</th>
<th>Avg. # Its</th>
<th>Avg. Time/Step</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILU</td>
<td>212.83</td>
<td>12.27</td>
</tr>
<tr>
<td>BOOMER</td>
<td>4.80</td>
<td>1.89</td>
</tr>
<tr>
<td>PEBBLES</td>
<td>9.99</td>
<td>0.86</td>
</tr>
<tr>
<td>SLU</td>
<td>1.00</td>
<td>0.55</td>
</tr>
</tbody>
</table>
BoomerAMG: Average convergence rate is an order of magnitude per iteration.
Parallel Benchmarks - Setup

RCV Setup

RCV-Pacing

10 ms 50 ms 105 ms 140 ms 200 ms

RCV-Reentry

2000 ms 2070 ms 2130 ms 2160 ms 2190 ms

Technical Data:

- Unknowns $\Phi_e$: 862.515
- Unknowns $V_m$: 547.680
- $\Delta t$ [µs]: 20
- $T_{\Delta t}$: $10^4$
- Ionic Model: Puglisi+EP-RS+Ia

Medical University of Graz

March 2, 2006
Differences in parallel scaling between AMG and ILU were negligible, overall performance gain was constant for varying $N_p$ around 6.
AMG is both **more efficient** (execution time between 6-15 times shorter) and **more robust** (weaker dependency on righthand side)
Research Interests

Bidomain Equations

Mapping

Defibrillation

Bidomain Models

Multilevel Methods

Imaging

Multimodal

Histology

Segmentation

Registration

Mesh Generation

Imaging
There is no single **ideal** Imaging Modality ...

- MRI
- Histology
- Segmentation
- Registration

Specialized Conduction System

D. Sanchez-Quintana et al.

Strutural Details

J. Schneider, R. Rowland, P. Kohl

P. Kohl, R. Rowland
Image Processing

Research Interests
- Bidomain Equations
- Mapping
- Defibrillation
- Bidomain Models
- Multilevel Methods
- Imaging
  - Multimodal
  - Histology
  - Segmentation
  - Registration
- Mesh Generation

Registration
- S. Keeling
- Minimization of $\chi^2$
- Rigid Body
- Affine
- Optical Flow

Segmentation
- Object-Background
- Subobject Segmentation
- Mumford-Shah
- Levelset Methods
- Topological Gradients

Fiber Detection
- 2D Methods
- 3D Methods
  (Coherence Vector)
Segmentation

- Remove MRI Chamber
- Thresholding + Edge Detection
- Morphological Operations
- Segmentation
Registration

Optical Flow based Multilevel Registration Approach

Serial Histological Sectioning

After Sectioning

After Registration

Mesh Generation
Structured versus Unstructured Grids

Most imaging techniques provide anatomical information on a voxel based manner (Regular Grids).

Advantages of Unstructured Grids

- **Surface Representation**
  Smooth Surfaces are essential to avoid artefacts during extracellular injection of stimulation currents.

- **Adaptive Meshes**
  Decreasing the resolution with distance to the cardiac surfaces yields significant memory savings without affecting the solution.
NURBS based Surface Smoothing

The Choice of NURBS Order allows to control the Smoothness of the Surface
NURBS Parametrization of Cardiac Surfaces

- Research Interests
  - Bidomain Equations
  - Mapping
  - Defibrillation
  - Bidomain Models
  - Multilevel Methods
  - Imaging
  - Mesh Generation
    - Unstructured Grids
    - NURBS
    - NURBS
  - Triangulation
  - Meshing
  - Image2Mesh
  - Acknowledgements

Epicardial Surface  Endocardial Cavities

Hexahedral Contours vs. NURBS Surface
Surface Triangulation

- Discretization of Parameterspace $(u,v)$
  - Determine $\Delta u$ to obtain a desired $\Delta s$

- Determine Curve Length $L$

- Determine #Vertices $N(u_i)$
  - $N(u_i) \approx L/\Delta s$

- Triangulate Surface spanned by $u_i, u_{i+1}$
  - Shift vertices to obtain quadrilaterals of desired edge length
  - Insert triangles to account for
    $\Delta N = N(u_{i+1}) - N(u_i)$
Meshing using Unstructured Grids

Research Interests
- Bidomain Equations
- Mapping
- Defibrillation
- Bidomain Models
- Multilevel Methods
- Imaging

Mesh Generation
- Unstructured Grids
- NURBS
- NURBS
- Triangulation
- Meshing
- Image2Mesh
- Acknowledgements

Meshing using Unstructured Grids

Structured Grid → NURBS → Triangulation

San Diego Rabbit

Smooth Parametrized Surfaces

SPIDER

Unstructured Grid

Volume Mesh

Medical University of Graz

March 2, 2006
Image2Mesh

Research Interests
- Bidomain Equations
- Mapping
- Defibrillation
- Bidomain Models
- Multilevel Methods
- Imaging

Mesh Generation
- Unstructured Grids
- NURBS
- Triangulation
- Meshing
- Image2Mesh

Acknowledgements

MRI

MRI Segmented

Tarantula

March 2, 2006

M E D I C A L  U N I V E R S I T Y  O F  G R A Z
Acknowledgements

Computing
E. Vigmond
D. Gavaghan + IB people
R. Weber dos Santos
S. Bauer
G. Haase
K. Kunisch
M. Liebmann

Image Processing
V. Grau Colomer
S. Keeling
H. Ahammer
M. Hintermüller

Mesh Generation
A. Prassl
F. Kickinger (Spider)

Imaging
P. Kohl
R. Rowland
J. Schneider
E. Hofer
D. Sanchez-Quintana
V. Climent-Mata

Medical University of Graz