Modelling heart attacks and therapeutical treatment regimes with supercomputers

G. Plank
Overview

- Crash Introduction into Cardiac Electrophysiology
- Heart Attacks and Therapeutical Options
- How to model the heart
  - Single Cell Modelling
  - Tissue and Organ Models
  - The Bidomain Equations
  - Numerical Techniques
- The Future of Cardiac Modelling
  - „Virtual Tissue/Heart“ Simulators
  - Imaging, Image Processing and Mesh Generation
  - Applications
Crash Introduction into Cardiac Electrophysiology
How the Heart works

Atria

Sinus Node
Primary Pacemaker

AV Node

HIS-Bündel

PVJ

Ventricles

Heart is an electrically controlled Pump

Electrical activation precedes mechanical action following a well defined pattern

Disturbances of the electrical activation impair mechanical function

Severe Disturbances lead to SCD
Activation Sequences

Normal

Healthy: Ventricles activated from Apex to Base and transmurally

Right Bundle Branch Block

Bundle Block: Right Ventricle activated in a lateral Direction

Ventricular Tachycardia

VT: disorganized Activation Sequence >> Impairment of Pumping Function
Properties of Cardiac Cells

- **Resting Potential**
  - negative around -75 mV
  - No Resting Potential with Pacemaker Cells

- **Excitability**
  - Linear-Passiv (subthreshold)
  - Nonlinear-Active (suprathreshold)
  - Triggers **Action Potential**
  - **AP Propagation**

- **Refractoriness** **ARP**
  - No AP can be triggered
Induction of Arrhythmias

Phase Singularities arise at Intersection of Critical Recovery Isoline with Critical Stimulation Strength
Therapeutical Options to prevent/terminate Cardiac Arrhythmias
Therapeutical Options

- **Defibrillation**
  - Only effective Therapy to prevent SCD
  - Highly effective, but suboptimal Therapy
    - Causes severe tissue Damage
    - Pain related psychological Problems
  - **Application:** Optimization to reduce Pain

- **Pharmacological Treatment**
  - Not reliable to prevent SCD
  - Studies (SWORD, etc):
    - Improve Classification, Increase SCD
  - **Application:** Pharmacological Testing

- **Catheter Ablation**
  - Curative Therapy
  - Atria mainly (AF, etc)
  - **Application:** Where and howto create Lesions?
Defibrillation

Vulnerability Grid

Dose Response Curve

Strength S

Probability P

Tachycardia

Fibrillation

Pulse Shapes

Monophasic

Biphasic

Tr. Exp.

Multiphasic+Tr. Exp.
Modelling Techniques

Modelling Techniques
Cell and Tissue Modelling

- Cylindrical Shape
- 3 Spaces
- Model consists of:
  - Electrical Analogon
  - Kinetic Gating Model (ODEs)
  - Fluid Compartment
- Cells connected via Gap Junctions
  - Preferred Direction
  - Anisotropy
- Homogenization
The Bidomain Equations

Set of Equations

\[
\begin{align*}
\text{I} & \quad \nabla \cdot (\bar{\sigma}_i \nabla \Phi_i) = -\beta I_m \\
\text{II} & \quad \nabla \cdot (\bar{\sigma}_e \nabla \Phi_e) = \beta I_m \\
\text{II} & \quad \nabla \cdot (\bar{\sigma}_b \nabla \Phi_e) = I_e
\end{align*}
\]

Membrane Kinetics

\[
\begin{align*}
I_m &= C_m \frac{\partial V_m}{\partial t} + I_{ion}(V_m, \bar{\eta}) - I_{tr} \\
\frac{d\bar{\eta}}{dt} &= g(V_m, \bar{\eta}) \\
V_m &= \Phi_i - \Phi_e
\end{align*}
\]
Solving the Bidomain Equations

Temporal Discretization based on Operator Splitting

**Elliptic PDE:**

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

**Parabolic PDE:**

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

**ODE's:**

\[
\begin{align*}
V^{k+1} &= V^{k*} + \frac{\Delta t}{C_m} i_{ion}(V^{k*}, \eta^{k}) \\
\eta^{k+1} &= \eta^{k} + \Delta t g(V^{k+1}, \eta^{k})
\end{align*}
\]
Simulation of 4s Activity in a Rabbit Ventricle

- 870,000 unknowns, 500,000 timesteps
- Human Heart: at least 20 times bigger (20-100 Mio dofs)

Plank, Clayton, Vigmond, Boyd, HPCx Capability Computing, 2006
HPCx: good performance with CARP out of the box
Parallelization (PETSc, Elliptic and Parabolic)
Efficient Cache Usage (ODEs)
Large Scale Cardiac Applications perfectly feasible, also in the Context of a Human Heart
Acknowledgement: Michael Holden and Kevin Stratford
HPCx Benchmark

HPCx:

<table>
<thead>
<tr>
<th>Procs</th>
<th>Ell. Hours</th>
<th>Par. secs</th>
<th>ODE secs</th>
<th>Bid. Hours</th>
<th>Mono. secs</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>2.80</td>
<td>32.56</td>
<td>15.00</td>
<td>2.84</td>
<td>47.58</td>
</tr>
<tr>
<td>64</td>
<td>1.52</td>
<td>11.78</td>
<td>7.23</td>
<td>1.57</td>
<td>19.00</td>
</tr>
<tr>
<td>128</td>
<td>0.99</td>
<td>5.68</td>
<td>4.03</td>
<td>1.00</td>
<td>9.70</td>
</tr>
</tbody>
</table>

NGS with 32 Procs

<table>
<thead>
<tr>
<th>PC</th>
<th>Ell. h</th>
<th>Par. secs</th>
<th>ODE secs</th>
<th>Bid. h</th>
<th>Mono. secs</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILU</td>
<td>4.21</td>
<td>44.08</td>
<td>30.98</td>
<td>4.28</td>
<td>75.05</td>
</tr>
<tr>
<td>AMG</td>
<td>1.37</td>
<td>46.95</td>
<td>31.33</td>
<td>1.44</td>
<td>78.28</td>
</tr>
</tbody>
</table>

Puglisi+EP_RS+IA:

32 Procs → ODE: 217 s → × 7

- Ratio HPCx/NGS approximately 2 with 32 CPUs
- With AMG Preconditioner, NGS more than 2 times faster than HPCx
Basic Idea behind Multigrid

GMG as Preconditioner

Level 0, finest grid: 1 iteration Parallel CG with ILU(0) Preconditioner

Level 1: 1 iteration Parallel CG with ILU(0) Preconditioner

Level nlevels-1, coarsest grid: Sequential LU Direct Solver

Testcases

2D

N=160,000
K=10,000

3D

N=1,000,000
K=10,000

Typical Speedup over ILU-CG using between 1 and 16 Processors: 3
MG and Algebraic MG (AMG)

- MG-CG is more robust, converges faster than ILU-CG
- better suited for unstructured grids
- avoids explicit generation of coarser meshes
- avoids construction of transfer operators to prolong/restrict between grids
Parallel Scaling::ILU vs AMG

Opteron Cluster with IB interconnect
RVGM, Reentry and Pacing Sequence
Scaling very similar, but performance gain ~6 with AMG

AMG Preconditioner for the Cardiac Bidomain, Plank et al., IEEE-TBME, to appear.
The Future of Cardiac Modelling

„Virtual Heart“ Simulators
Image Sources – Gross Anatomy

Serial Histology

- Serial Histology: Higher Resolution, better Tissue Discrimination
- Destructive Method >> Registration Problem
„Best of both Worlds ...“

Burton, Plank, Schneider et al., Ann. NY Acad. Sci, to appear
Mesh Generation::TARANTULA

- **Unstructured Grids**
  - "Smooth"
  - "Adaptive"

- **Method**
  - Octree-based
  - Boundary-fitted
  - Locally refined
  - Conformal
  - Hybrid (tetralyzer)
  - hex-dominant
  - Resolution
  - **Fully automatic**

MRI Segmented -> Adaptive Hex-dominant Hybrid Mesh

Resolution adjustment
Testcases

<table>
<thead>
<tr>
<th></th>
<th>LV Wegde Preparation</th>
<th>Papillary muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Resolution</td>
<td>μm</td>
<td></td>
</tr>
<tr>
<td>Vertices</td>
<td>1.310.539</td>
<td>8.942.317</td>
</tr>
<tr>
<td>Elements</td>
<td>2.216.811</td>
<td>14.373.800</td>
</tr>
<tr>
<td>Mesh generation time</td>
<td>s</td>
<td>6.191</td>
</tr>
</tbody>
</table>

128 CPUs
Examples

Wedge

Papillary

Human Atria

Seemann et al
Further Applications

- BEM FEM Coupling (FEMBEM)
- Adaptivity (FEMBEM)

- Mechanical Contraction
- Fluid Dynamics (Kicking, Kunisch)

- Inverse Problems in electrical and optical Mapping (MGINV)

- Microanatomically realistic Human Atria (FREELEVEL, INVERSE)

- Couple Virtual Heart with lumped model of the cardiovascular system (HAMC)
Acknowledgements

Funding:
- Austrian Science Fund FWF
  (J-1916-INF, J-2132-INF, R21-N04)
- IB Project
- BBSRC (P. Kohl)
- MC-OIF 040190 (N. Trayanova)

Cooperations:
- University of Calgary (Vigmond)
- University of Oxford
  (Kohl, Gavaghan, Rodriguez, Schneider, Grau)
- Johns Hopkins University (Trayanova)
- Technische Universität Karlsruhe (Seemann)
- University of Badajoz (Sanchez-Quintana)
- Karl Franzens University Graz (Kunisch, Haase, Keeling)
Parallel Robustness

AIPC10  2.6.2006

Medizinische Universität Graz

RVGM-Pacing

RVGM-Reentry

A) 10 50 75 110 140 Time [ms] N_s-ILU

B) 2000 2100 2200 Time [ms] N_s-ILU