Utah CIBC EAB Meeting 2008

Mathematical Modeling and Simulation of Bioelectricity

Overview

I. Forward modeling

II. Inverse solutions

III. Software

IV. Current / Future Initiatives
Crosscutting themes

- Images to models to forward simulations
  - Our software tools allow increasingly efficient expansion of application domains

- Common framework for forward / inverse solutions
  - Our software tools allow increasing ease of comparison of formulations and methods

- Integrated visualization key component for development

Forward modeling

**Major projects:**

A. Defibrillation simulation at the macroscopic scale  
B. Multiscale cardiac propagation modeling  
C. Whole heart anisotropic modeling of cardiac ischemia

**Secondary projects:**

D. Modeling fibrillation wavefront behavior  
E. Modeling effect of defibrillation shocks on 2nd implanted device  
F. Electrical stimulation of the brain
A. Simulation of defibrillation

Collaborators: J. Triedman, M. Jolley, T. Pilcher

Problem: ICD challenges: children, non-standard anatomy, subcutaneous leads

Goal: *in silico* subject-specific defibrillation

Results:
- Anatomical models / FE mesh from CT scans
- Realistic library of electrodes
- Mesh refinement as electrodes are moved
- Studying both clinical and technical aspects
- Progress: automated pipelines, new analyses
- Details to follow in DBP talk

B. Multiscale cardiac propagation modeling

Collaborator: C. Henriquez

Problem: Scale gap exists between continuum (bidomain) and discrete (cell-level) models

Goal: Build 3D tissue-level model using realistic histological parameters without tweaking

Results:
- Compared results to bidomain simulations
- Used results to derive bidomain parameters
- Results show:
  - Realistic conduction speeds obtained
  - Conductivity tensors from tissue model work in bidomain
  - Under ischemic conditions discrete model is needed
  - Utilizes both SCIRun and Cardiowave

B. Multiscale cardiac propagation modeling

Simulation

C. Anisotropic modeling of ischemia

Internal CIBC research: (Swenson/Stinstra/MacLeod)

Problem: Subject specific geometry may determine electrocardiographic manifestations of ischemia

Goal: MR-based customized computational model

Results:

- Canine electrical recordings under ischemia
- MR anatomical, DT imaging of excised hearts
- FE model based on reconstructed geometry
- Heavy reliance on Seg3D, SCIRun
  - Model building: months→weeks
- Comparison with experimental measurements coming soon….
C. Anisotropic modeling of ischemia

D., E. Secondary projects: Cardiac

- D. Whole heart modeling of fibrillation wavefront behavior, including body surface potentials
  
  A. Zaitsev / J. Stinstra, separate NIH support
  
  - Rapid prototyping with new tools: One week to customize pipeline using modeling and integration tools


- E. Modeling of effect of defibrillation shock on second implantable stimulation device

  Boston Scientific contract
F. Secondary project: Brain Stimulation

Deep Brain Stimulation: for treatment of Parkinson’s Disease: Macintyre/Butson:

Transcranial DC cortical stimulation: Oostendorp

Progress: rapid prototyping with new tools

Inverse solutions

A. Brain source localization
B. Forward modeling for inverse electrocardiography
C. Inverse methods for inverse electrocardiography
D. Electrical impedance tomography
A. Brain source localization: I

Collaborators: S. Lew, C. Wolters, S. Warfield

Problem: Subject discrimination / surgical planning for intractable epilepsy

Goal: Develop patient specific models with maximally extensive information and accurate conductivities

Results:
- Direct estimation of conductivities
- Inclusion of DT-based anisotropy
- Evaluation of FE meshes
- Dynamic inverse solutions
- Builds on forward model tools

A. Brain source localization: II

Direct estimation of conductivities (Lew Ph.D. thesis): combine low-resolution EEG with MEG in iterative approach:


S. Lew, C. Wolters, A. Anwander, S. Makeig, R. MacLeod, “Improved EEG source localization using low resolution conductivity estimation in a realistic head model”, Human brain mapping (in review)

S. Lew, C. Wolters, T. Dierkes, C. Roer, R.S. MacLeod. “Accuracy and run-time comparison for different potential approaches and iterative solvers in finite element method based EEG source analysis,” submitted to Applied Numerical Mathematics (in review)


Meshing pipeline with multiple information types: initial meshes obtained

Epilepsy Foundation grant (2nd submission): Warfield, Johnson, et al.
A. Brain conductivity estimation

**Simulation**

- MEG dipole fit: $x, \sigma_1, m_1$
- EEG LRCE ($x, \sigma_1, m_1$): $\sigma_1$
- EEG dipole fit ($x, \sigma_1$): $\sigma_2, m_2$
- Least Square Fit to MEG ($x, \sigma_2$): $m_2$
- EEG LRCE ($x, \sigma_2, m_2$): $\sigma_2$
- Accept $\sigma_2$

Significant improvements in simulation
Realistic results on measured data

B. Inverse ECG: forward model

**Internal CIBC research:**

**Problem:** Inverse ECG is badly ill-conditioned problem

**Goal:** Determine effect of sampling and discretization on inverse problem

**Results:**
- Lead selection for inverse ECG: *(Ghodrati, Brooks, MacLeod)*
- Mesh optimization for inverse ECG: *(Wang, Johnson, Kirby)*
  - Typically mesh optimization carried out for forward model accuracy
  - Optimizing information transfer for inverse solution is not the same
  - Results to date show meshing of interior elements is of great importance
C. Inverse ECG: inverse solutions: I

Simulation

Internal CIBC research (Erem / Keely / Ghodrati / MacLeod / Tadmor / Brooks)

Problem: Inverse ECG still not as reliable as needed
Goal: Use as many constraints as feasible

Results:
- Idea 1: incorporate sparse measurements close to heart surface
  - Used epicardial catheter model in Bayesian formulation
  - Obtained prior estimate of variance
  - Intracardiac catheter easily included


C. Inverse ECG: inverse solutions: II

Simulation

Idea 2: Use dynamic modeling as effective constraint

- Standard approaches
  - Activation-based: one free parameter per node
  - Potential-based: difficult to incorporate physiologically meaningful constraints

- Wavefront-based inverse ECG
  - Use wavefront-specific temporal model
  - Incorporate more realistic physiological constraints
C. Inverse ECG: inverse solutions: III

- Recent progress: integrated platform for comparisons
  - Activation and potential BEM forward models
  - Comparison of inverse methods using Matlab
  - Use of ECGSim and ForwardEDL tools

Publications


C. Inverse ECG: Example result

- ECGSim geometry, data
- SCIRun control of inverse solutions in Matlab
- Map3d visualization
- We have also ported CVRTI data to ECGSim geometry
D. Other inverse solution projects: EIT

Internal research in collaboration with Impedance Imaging Lab RPI (Isaacson / Newell)

Results:
- Developed new methods for known and unknown anatomy EIT
- Tested vs phantom tank measurements
- Developed method for identifying / correcting mislocated electrodes


Software

A. Improved Boundary Element Method support
B. Improved Finite Element Method support
C. Integration with external simulation packages
D. Integration of inverse electrocardiography methods
A., B. Improved BEM and FEM support

- A. BEM: in two stages:
  - Solid angle approach for potential surfaces (completed)
  - More general infinite medium + corrections approach (first stage completed, 2nd stage underway)
- B. FEM:
  - Support for periodic FE models (tissue modeling)
  - Support for “floating” electrodes
  - Better handling of boundary condition insertions
  - Related infrastructure improvements

C. Integration with simulation packages

- Expanded capabilities for bioelectric field simulations
  - Cardiowave for propagation modeling
  - NeuroFEM for forward modeling for brain source problems
  - ECGSim for geometry, forward modeling, and inverse solutions
  - ForwardEDL code for activation-based cardiac forward modeling
D. Integration with inverse ECG methods

- Extensive use of Matlab Interface
- Test results against externally-developed methods
- Current instantiation: Greensite potential-based methods
- Test and develop internally developed methods
- Current instantiation: Wavefront-Based Potential Reconstruction

Current / Future Directions

A. Defibrillation
B. Brain source localization
C. Inverse electrocardiography
D. Bone growth modeling
E. Ischemia modeling
F. New apps for brain stimulation?
G. Optical tomographic imaging?

Ongoing Bioelectric Field Projects
Newer Initiatives

Future directions?
A. Defibrillation project: status and plans

- Manuscripts in progress based on extensive clinically-relevant results (Triedman / Jolley)
- Initial experiments with body surface measurements during clinical implantations (Pilcher)
- New collaboration with N. Trayanova to incorporate active cardiac model
- Imaging, modeling cadaver hearts: CHB, UU, JHU together
- Opportunity for inverse solution approach
- Major emphasis on BRP proposal (210 score from May submission)
- Details in DBP talk

B. Brain source localization: status and plans

- Warfield collaboration under active development
  - D. Hyde, former NU Ph.D student, new hire postdoc in Warfield lab on this project
  - Epilepsy Foundation grant resubmitted
- Reviving G. Worrell collaboration
  - Recent visit to Utah
- Planning collaboration with Don Tucker, U. of Oregon / EGI
C. Inverse ECG: future directions

- Complete suite of forward / inverse models in SCIRun
- Validate wavefront-based solutions in wider set of scenarios
- Develop more powerful dynamic models, based on
  - Dynamical modeling methods from control theory (NU colleagues Tadmor, Sznaier)
  - Manifold discovery / optimization methods (NU colleagues Dy / Erdogmus)
- Optimized electrode placement

D. Bone growth modeling: new initiative

**Collaboration with VA and Utah Orthopedics**

**Problem:** Metal implants for amputees slow to attach to existing bone

**Goal:** Model use of electrical stimulation to enhance and speed attachment

**Results:**
- Synergistic modeling with existing CIBC bioelectric field technology
- Useful to study electrode placement, design, stimulation protocols
- Potential high impact for injured veterans
- Initial simulations carried out on 3 subjects

D. Bone growth modeling: initial results

Simulation

Schematic

Label Map

Field histograms: 2 band electrode

FEM Result

E. Ischemia modeling: future directions

Comparison to experimental measurements

Experimentally-based source models

Tailor mesh geometry to myocardial structure

Simulate body surface potentials

Parameterized inverse problem
  - Ischemic zone location parameters
  - Ischemic zone shape parameters
F. Brain stimulation: status and possibilities

Current proposal included (secondary) collaboration on deep brain stimulation (Macintyre / Butson)
  - Dr. Butson now Asst. Prof. at Medical College of Wisconsin

Growing suite of technologies and applications
  - Technology: Cortical arrays, transcutaneous, DC, AC, ...
  - Applications: Parkinson’s, pain, tinnitus, motor control and rehab ...

Fits well with bioelectric field focus
Need to identify additional collaborators
  - House (U. Utah)
  - Beth Israel / Spalding Rehab Boston (Fregni / Bonato)
  - VA ?

G. Optical tomographic imaging: outreach?

- Diffuse optical and fluorescence tomographic imaging
  - Breast cancer imaging (MGH)
  - Multimodal functional brain imaging (MGH, S. Lew postdoc with M. Hamalainen and D. Boas)
  - Small animal imaging (NU, V. Ntziachristos and new hire M. Niedre)

- Growing interest in multimodal subject-specific imaging
- Another type of diffusion equation
- Tradeoff: dilution of focus vs. expansion of influence
- Need to identify appropriate collaborators