Simulation and Mathematical Modeling Core

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Organization of Aims

Challenges

1. **Barriers to mechanistic modeling**
   - Many elements well developed, others missing, especially for multiple scales
   - Access difficult for biomedical scientists

2. **Methods/algorithms for diagnostic inverse solutions**
   - Methods incomplete, clinical success marginal

3. **Lack of integrated software**
   - Different programs, files, platforms

4. **Support for verification and validation**
   - Does the code work? Does it reflect reality?
#1: Barriers to mechanistic modeling

Aim 1: Create simulations of myocardial ischemia in realistic geometric models of dog hearts

Aim 2: Create tissue models of myocardial and neural cells to investigate the relationship between cellular and tissue level electrical, mechanical, and transport properties
1. Ischemia modeling progress

**Electrophysiology Experiments**

**Cardiac Imaging**

- T1
- T2

- Fiber Angle
- Diffusion Tensor
1. Ischemia modeling plan

Geometric models

- Have Auckland heart
- Create subject specific (segmentation and model pipeline)
- Assign ischemic zones

Simulation

- Bidomain source model (Henriquez collaboration)
- Compare with experiments
Aim 3. Investigate parametric formulations of bioelectric source problems that can form the basis of electrocardiographic and electrical impedance tomography inverse solutions. …

Aim 4. Investigate inverse solution approaches that make use of multiple information sources. …

Aim 5. Investigate the role of errors and uncertainty in volume conductor geometry and conductivity parameters on inverse problem accuracy. …
3. Parametric formulations: I

Wavefront-based inverse electrocardiography
- Parameterized curve model
- Two-level image as Tikhonov constraint / mean of statistical prior
- Ghodrati et al, IEEE TBME, in press (Sep?)

BEM-based EIT
- Known-geometry inverse solutions (FEM too)
- Babaeizadeh et al, IEEE TM, IEEE TBME in press
- Shape-based inverse solutions
- Babaeizadeh et al, submitted to IEEE TMI
3. Parametric formulations: II

Improved Dipole formulations

Physiological source

Computational equivalent

Wolters et al., Biomag, 2006
3. Parametric formulations: III

E/MEG with parameterized conductivity

Geometric model

- Optimize solution for source location and skull conductivity
- Showed best localization with accurate conductivity

Lew et al., Biomag, 2006
Multiple information sources in inverse solutions

Inverse electrocardiography: Using all available information

- Forward model and torso measurements
- Statistical information from database
- Catheter-based measurements

Place in Bayesian prior setting

- Enables incorporation of prior and catheter information
- Bayes error and Bayes evidence provide useful metrics
- Serinagaoglu et al, IEEE TMBE, May 2005 and in press (Oct?)

Combine EIT with Inverse ECG: future
Effect of errors and uncertainties on inverse solutions

Study of “reduced” lead-sets in inverse electrocardiography
- How to choose good lead in “inverse sense”?  
- How to apply fewer leads in denser model?  
- Ghodrati et al, IEEE TBME (in press and in preparation)

Study of effects of uncertainty of electrode position on known-geometry EIT
- High sensitivity of measuring voltage on current-carrying electrodes  
- Developed statistical methods to detect and in some cases correct position error  
- Babaeizadeh et al, (ISBI, ICASSP)

Stochastic variations in model parameters
- Use polynomial chaos to model variations in ECG with stochastic error in torso geometry/conductivity  
- Kirby, Genser, MacLeod (NFSI, EMBS)
#3: Lack of integrated, flexible, easy-to-use software

Aim 1. **Expand existing suite** of cardiac and neural bioelectric modules

Aim 2. **Integrate** simulation with the image and geometry processing

Aim 3. Add simulation tools for **cellular electrophysiology**

Aim 4. Create **PowerApps**

Aim 5. Develop **CCA support**

Aim 6. **Standards** for data and models
1. Expand existing modules

Forward problems

- Auckland heart geometry as SCIRun module
- Interactive setting of spatial parameters
- FEM core has complete element type coverage, higher order basis functions

Inverse electrocardiography

- Create combined endo-epicardial geometry
- Compare activation, potential, and wavefront-based solutions
  - Under way in collaboration with Oostendorp and van Oosterom
2. Integrate simulation with geometry and image processing

Segmentation and Model Building pipeline near completion

• Will be of service to many collaborations
3. Tools for cellular electrophysiology

Leveraging/bridging

- Cardiowave tools
  - > 20 cell models implemented
  - need extensions for pathophysiology
- CSES (http://cese.sourceforge.net/)?
- kaTools?
4. PowerApps and 5. CCA support

PowerApps:

- Light-weight stand-alone app for segmentation and model building
- See BioPSE for more...

CCA

- Standards still maturing
6. Standards for data and models

- **Data standards**
  - NRRD (developed initially at SCI by Kindlemann et al.) becoming broader standard
    - used for communication between 3DSlicer and SCIRun in Friedman collaboration

- **Model standards**
  - CellML model?
  - Performance concerns
#4: Verifying and validating simulations

**Aim 7.** Develop and implement **verification and validation schemes** to ensure quality and robustness of the BioPSE simulation

**Code verification**
- Regression testing with cmake/DART

**Data based validation**
- CVRTI tank, etc. for cardiac applications
- RPI tank (Isaacson collaboration) for EIT applications (note joint support with NSF ERC CenSSIS)
- Data repository on web site

**Computers in Cardiology Challenge**
- Collaboration with PhysioNet (P41 Center)