Integrative System Framework for Noninvasive Understanding of Myocardial Tissue Electrophysiology

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From patient observations to personalized electrophysiology

- Noninvasive observations on specific patient:
  - Structural: tomographic image
  - Functional: projective ECG/BSPM

- In clinical settings, it really has been a sophisticated pattern recognition process to decipher the information.

- How can models offer help?
  - Better models lead to more appropriate constraints in data analysis.
    - Physiological plausibility vs. algorithmic/computational feasibility
    - Volumetric?
  - Ultimately, models have to be personalized to be truly meaningful.
Integrative system perspective

Prior Knowledge: Models
- Built up over many years
- General population

Patient Observations
- Subject-specific information
- Noisy, sparse, incomplete

System Modeling
- System dynamics
- System observations

Individual

Personalized Information Recovery
- Electrical function
- Tissue property
- Latent substrate

Subject

Data Acquisition
- BSP sequence
- Tomographic images

Physiological model constrained statistical framework

- System perspective to recover personalized cardiac electrophysiology
  - (phenomenal) Model constrained data analysis: prior knowledge guides a physiologically meaningful understanding of personal data
  - Data driven model personalization: patient data helps to identify
Volumetric myocardial representation

- Ventricular wall: point cloud

- Fiber structure: mapped from Auckland model

Slice segmentation

Surface mesh

Volume representation

Surface registration

Surface fiber structure

3D fiber structure
Surface body torso representation

- (Isotropic and homogeneous volume conductor)
Cardiac electrophysiological system

Volumetric TMP dynamics model

Personalized 3D-BEM mixed heart-torso model

TMP-to-BSP mapping
System dynamics: volumetric TMP activity

- Diffusion-reaction system: 2-variable ordinary differential equation

\[
\begin{align*}
\frac{\partial u}{\partial t} &= \nabla \cdot (D \nabla u) + f_1(u, v) \\
\frac{\partial v}{\partial t} &= f_2(u, v)
\end{align*}
\]

- Meshfree representation and computation

\[
\begin{align*}
\frac{\partial U}{\partial t} &= -M^{-1}KU + f_1(U, V) \\
\frac{\partial V}{\partial t} &= f_2(U, V)
\end{align*}
\]

- \( u \): excitation variable: TMP
- \( v \): recovery variable: current
- \( D \): diffusion tensor

![Graph showing time series of u and v](graph.png)
System observation: TMP-to-BSP mapping

- Quasi-static electromagnetism
- Poisson’s equation
- Mixed meshfree and boundary element methods

**Governing equation**

\[ \sigma \nabla^2 \phi(r) = \nabla \cdot (D(r) \nabla u(r)) \]

**Direct solution method**

\[
\begin{align*}
&c(\xi) \phi(\xi) + \int_{\Gamma_i} \phi(r) q^*(\xi, r) d\Gamma_i - \int_{\Gamma_i} \frac{\partial \phi(r)}{\partial n} \phi^*(\xi, r) d\Gamma_i \\
&= \frac{1}{4\pi\sigma} \left( \int_{\Gamma_i} \frac{D_i(r)}{|\xi - r|} \frac{\partial u(r)}{\partial n} d\Gamma_i - \int_{\Omega_i} \nabla \frac{1}{|\xi - r|} \cdot (D_i(r) \nabla u(r)) d\Omega_i \right)
\end{align*}
\]

**Surface integral: BEM**

**Volume integral: meshfree**
State space system representation

\[
\begin{align*}
\frac{\partial U}{\partial t} &= -M^{-1}KU + f_1(U, V, \theta) \\
\frac{\partial V}{\partial t} &= f_2(U, V, \theta)
\end{align*}
\]

TMP activity:
\[
\Phi = HU
\]

TMP-to-BSP mapping:
- Nonlinear dynamic model
  - Local linearization
  - Temporal discretization
- Large-scale & high-dimensional system
  - U, V is of dimension 2000-3000

Uncertainty:
\[\omega, \mu\]

Monte Carlo integration

Prediction
Correction

Nonlinear Transformation

Parameter:

Uncertainty:
\[\omega, \mu\]
Sequential data assimilation

- Combination of unscented transform (UT) and Kalman filter: unscented Kalman filter

**Prediction: UT**
- (MC integration + deterministic sampling)
- Preserve intact model nonlinearity
- Black-box discretization

**Correction: KF update**
- Computational feasibility
**TMP estimator: reconstructing TMP from BSP**

\[
\hat{U}_k = U_k - K_k u (Y_k - H U_k) \\
\hat{P}_{uk} = (I - K_k u H) P_{uk}
\]

\[
K_k u = P_{uk} H^T (HP_{uk} H^T + R_{v_k})^{-1}
\]

\[
\hat{\xi}_k = \sum_{i=0}^n W_i^m \xi_{k|k-1,i} \pm \sqrt{(n/2 + \lambda) \hat{P}_{uk-1}}
\]

**Ensemble generation (unscented transform)**

\[
S_k^n = \begin{pmatrix} \hat{U}_{k-1} & \hat{U}_{k-1} + \sqrt{(n/2 + \lambda) \hat{P}_{uk-1}} \\ \hat{U}_{k-1} - \sqrt{(n/2 + \lambda) \hat{P}_{uk-1}} \end{pmatrix}
\]

**Prediction (MC integration)**

\[
\begin{align*}
\bar{U}_k &= \sum_{i=0}^n W_i^m \xi_{k|k-1,i} \\
\bar{V}_k &= \sum_{i=0}^n W_i^m \xi_{k|k-1,i} \\
P_{uk} &= \sum_{i=0}^n W_i^c (\xi_{k|k-1,i} - \bar{U}_k)(\xi_{k|k-1,i} - \bar{U}_k)^T + Q_{\omega_k}^u
\end{align*}
\]
Parameter estimator: reconstructing model parameters

**Initialization**
\[
\begin{pmatrix} \hat{\Theta}_0 \\ \hat{P}_{\Theta_0} \end{pmatrix}
\]

**Ensemble generation** (unscented transform)
\[
\{\varphi_{k-1,i}\}_{i=0}^{2n} = \begin{pmatrix} \hat{\Theta}_{k-1} \\ \hat{\Theta}_{k-1} \pm \sqrt{n+\lambda}\hat{P}_{\Theta_{k-1}} \end{pmatrix}
\]

**Prediction (MC integration)**
\[
\begin{align*}
\zeta_{k|k-1,i}^{(\Theta)} &= \tilde{F}_d(\hat{U}_{k-1}, \varphi_{k-1,i}) \\
\Psi_{k|k-1,i}^{(\Theta)} &= \tilde{H}\zeta_{k|k-1,i}^{(\Theta)} \\
\hat{P}_{\Theta_k} &= \hat{P}_{\Theta_{k-1}} + Q_{\omega_{\Theta_k}} \\
\overline{Y}_{k}^{(\Theta)} &= \sum_{i=0}^{2n} W_i^m \Psi_{k|k-1,i} \\
P_{y_k} &= \sum_{i=0}^{2n} W_i^c (\Psi_{k|k-1,i}^{(\Theta)} - \overline{Y}_{k}^{(\Theta)}) (\Psi_{k|k-1,i}^{(\Theta)} - \overline{Y}_{k}^{(\Theta)})^T + R_{\nu_k} \\
P_{\Theta_{k|y_k}} &= \sum_{i=0}^{2n} W_i^c (\varphi_{k-1,i} - \hat{\Theta}_{k-1}) (\Psi_{k|k-1,i}^{(\Theta)} - \overline{Y}_{k}^{(\Theta)})^T
\end{align*}
\]

**Correction (KF update)**
\[
\begin{align*}
\hat{\Theta}_k &= \hat{\Theta}_{k-1} + K_k^{(\Theta)} (Y_k - \overline{Y}_{k}^{(\Theta)}) \\
\hat{P}_{\Theta_k} &= P_{\Theta_k} - K_k^{(\Theta)} P_{y_k} K_k^{(\Theta)T}
\end{align*}
\]

**Filter Gain**
\[
K_k^{(\Theta)} = P_{\Theta_k y_k} P_{y_k}^{-1}
\]

**Nonlinear measurement model**
Experiments (PhysioNet.org): electrocardiographic imaging of myocardial infarction

- Four post-MI patients
  - MRI → personalized heart-torso structures
  - BSP
  - Gd-enhanced MRI → gold standard

Cardiac: 1.33×1.33×8mm
Whole-body: 1.56×1.56×5mm

123 electrodes, QRST @ 2KHz sampling
Goals and procedures

- Quantitative reconstruction of tissue property and electrical functioning
  - Tissue excitability
  - TMP dynamics

Procedures
- Initialization – TMP estimation with general normal model
- Simultaneous estimation of TMP and excitability
- Identify arrhythmogenic substrates (imaging + quantitative evaluation)
- Localize abnormality in TMP and excitability
- Investigate the correlation of local abnormality between TMP and excitability
Result: case II

- Infarct location: septal-inferior basal-middle LV
Result: case II

- Black contour: abnormal TMP dynamics
- Color: recovered tissue excitability

- Location, extent, and 3D complex shape of infarct tissues
- Correlation of abnormality between electrical functions and tissue property
  - Abnormal electrical functioning occurs within infarct zone
  - Border zone exhibits normal electrical functioning
Delay enhanced MRI registered with epicardial electrical signals

Delayed activation: 4-9
Infarct: 3-14

Result: case I

- Infarct: septal-anterior basal LV, septal middle LV
Result: case III

- Infarct: inferior basal-middle LV, lateral middle-apical LV
Result: case V

- Infarct: anterior basal LV, septal middle-apical LV
Quantitative validation

<table>
<thead>
<tr>
<th></th>
<th>case 1</th>
<th>case 2</th>
<th>case 3</th>
<th>case 4</th>
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<tr>
<td></td>
<td>Reference</td>
<td>Results</td>
<td>Reference</td>
<td>Results</td>
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<tr>
<td>EP</td>
<td>31%</td>
<td>17%</td>
<td>30%</td>
<td>20%</td>
</tr>
<tr>
<td>CE</td>
<td>8</td>
<td>9</td>
<td>3/4/9/10</td>
<td>9</td>
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<tr>
<td>SO</td>
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<td>97%</td>
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<td>segments</td>
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<td>1-3,8-9</td>
<td>3,4,9,10</td>
<td>3,4,9,10</td>
</tr>
</tbody>
</table>

- EP: Percentage of infarct in ventricular mass
- CE: Center of infarct, labeled by segment
- Segments: A set of segments which contain infarct
- SO: Percentage of correct identification compared to gold standard
Comparison with existent results

<table>
<thead>
<tr>
<th></th>
<th>Our results</th>
<th>Mneimneh</th>
<th>Dawoud</th>
<th>Farina</th>
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<tbody>
<tr>
<td></td>
<td>case 3</td>
<td>case 4</td>
<td>case 3</td>
<td>case 4</td>
</tr>
<tr>
<td><strong>EPD</strong></td>
<td>18%</td>
<td>4%</td>
<td>25%</td>
<td>2%</td>
</tr>
<tr>
<td><strong>CED</strong></td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
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<tr>
<td><strong>SO</strong></td>
<td>100%</td>
<td>100%</td>
<td>90%</td>
<td>25%</td>
</tr>
</tbody>
</table>

- EPD: difference of EP from gold standard
- CED: difference of CE from gold standard

- *Dawoud et al*: epicardial potential imaging
- *Farina et al*: optimization of infarct model
- *Mneimneh et al*: pure ECG analysis
Conclusion

- Personalized noninvasive imaging of volumetric cardiac electrophysiology

Noninvasive observations → Personalized volumetric cardiac electrophysiology → Latent substrates