Modeling Neural Tissue and Membrane Behavior During Far-field Current Injection

Rosalind Sadleir
J. Crayton Pruitt Family Department of Biomedical Engineering
University of Florida

Atul Minhas, Eung Je Woo
Department of Biomedical Engineering
Kyung Hee University
MREIT: From Magnetic Flux Density to conductivity

Material Property:
\[ \sigma : \text{conductivity}, \quad \rho = \frac{1}{\sigma} : \text{resistivity} \]

Neumann Boundary Value Problem:
\[ \nabla \cdot \left[ \sigma(r) \nabla V(r) \right] = 0 \quad -\sigma \frac{\partial V}{\partial n} = J_n \quad \text{on } \partial \Omega \]

Value Problem:
\[ J(r) = -\sigma(r) \nabla V(r) \quad \nabla \cdot J(r) = 0 \]

\[ \nabla \cdot B = 0 \Rightarrow \nabla \times J = -\frac{1}{\mu_o} \nabla^2 B \]

\[ -\frac{1}{\mu_o} \nabla^2 B_z = \frac{\partial \sigma}{\partial y} \frac{\partial V}{\partial x} - \frac{\partial \sigma}{\partial x} \frac{\partial V}{\partial y} \]
Pulse Sequence (Spin Echo)

RF

Slice selection

Phase encoding

Reading

Positive current, $I^+$

Negative current, $I^-$

$90^\circ$  $180^\circ$

$T_c/2$  $T_c/2$
Tissue phantom trials

Conductivities in S/m

11 T MR magnitude image

Turkey: \( \sigma = 0.531 \)

Pork: \( \sigma = 0.485 \)

Agar: \( \sigma = 1.3 \)
$B_z$ data

S.E. 20mA
G.E. 20mA
S.E. 10mA
G.E. 10mA
Methods for detecting neural activity

- MEG
- EEG

In MRI
- BOLD contrast (Ogawa and Lee 1990)
- $B_0$ perturbation
  - RF (3T and above) (Bodurka et al. 1999)
  - Low frequency ($\mu$Hz) (Kraus et al 2008)
- Lorentz effect imaging (Truong et al. 2008)
- Membrane Conductivity Changes (Sadleir et al. 2010)
Membrane Conductance variation

$\Delta V_m$ vs. $V_m$ [mV]

$V_r - V_{Na} = -115$ mV

$V_m = 0$

Threshold potential

$G_m = G_K + G_{Na}$

$G_Na$

$G_K$

$V_r - V_{K} = +12$ mV

Time [ms]

$G$ [mS/cm$^2$]

Malmivuo and Plonsey 1995
Aplysia Model
Bidomain conductivity modelling

after Roth (2000)
Bidomain Model

\[ \nabla \cdot J_i = - \nabla \cdot J_e = i_m \]

\[ V_m = \phi_i - \phi_e \]

\[ J_i = - D_i \nabla \phi_i \]

\[ J_e = - D_e \nabla \phi_e \]

3 application modes
Vo (bath), Ve and Vi (tissue)

At boundaries: \[ \frac{\partial \phi_i}{\partial n} = 0 \] i.e. insulation
\[ V_e = V_o \]

Table 1. Bidomain Parameters and Constants

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Units</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \sigma_i )</td>
<td>3.63</td>
<td>S/m</td>
<td>intracellular conductivity</td>
</tr>
<tr>
<td>( \sigma_e )</td>
<td>5.07</td>
<td>S/m</td>
<td>extracellular conductivity</td>
</tr>
<tr>
<td>( \sigma_o )</td>
<td>5.07</td>
<td>S/m</td>
<td>bath conductivity</td>
</tr>
<tr>
<td>( \sigma_p )</td>
<td>1</td>
<td>S/m</td>
<td>port conductivity</td>
</tr>
<tr>
<td>( f_i )</td>
<td>0.7</td>
<td>-</td>
<td>intracellular filling fraction</td>
</tr>
<tr>
<td>( \beta )</td>
<td>20 000</td>
<td>m(^{-1})</td>
<td>surface to volume ratio</td>
</tr>
<tr>
<td>( G_{m,rest} )</td>
<td>6.7</td>
<td>S/m(^2)</td>
<td>membrane conductivity, rest</td>
</tr>
<tr>
<td>( G_{m,active} )</td>
<td>320</td>
<td>S/m(^2)</td>
<td>membrane conductivity, active</td>
</tr>
</tbody>
</table>
Measurement with MREIT

- Detection of changes in $B_z$ (current flow) data as a result of changes in membrane conductance
- Signal size depends on observing membrane conductivity change during application of imaging current
Current Limits

90 μA applied
Max scale at 1.2 A/m²
\[ \Delta x = \Delta y = 281 \ \mu m \]
\[ \Delta z = 1 \ mm \]

**B_z and \( \Delta B_z \) data**

Y current direction

X current direction

\( B_z \)

\( \Delta B_z \)
Percentage Changes

$\Delta x = \Delta y = 281 \mu m$

$\Delta x = \Delta y = 562 \mu m$

$\Delta x = \Delta y = 1120 \mu m$

$\Delta z = 1 \text{ mm}$
SNR at 17.6 T

\[ sd(B_z) = \frac{1}{\sqrt{2\gamma T_c Y_M}} \]

**Table 2.** Expected \( B_z \) Noise Levels (T) at different SNR levels in a 17.6 T main field

<table>
<thead>
<tr>
<th>Resolution</th>
<th>Pixel Size</th>
<th>( \Delta z )</th>
<th>Predicted Noise (T) NEX=2</th>
<th>Predicted Noise (T) NEX=1</th>
</tr>
</thead>
<tbody>
<tr>
<td>128 x 128 x 16</td>
<td>140 ( \mu m )</td>
<td>0.5 ( mm )</td>
<td>( 8.0 \times 10^{-9} )</td>
<td>( 1.2 \times 10^{-8} )</td>
</tr>
<tr>
<td>64 x 64 x 8</td>
<td>281 ( \mu m )</td>
<td>1 ( mm )</td>
<td>( 2.8 \times 10^{-9} )</td>
<td>( 4.4 \times 10^{-9} )</td>
</tr>
<tr>
<td>32 x 32 x 8</td>
<td>562 ( \mu m )</td>
<td>1 ( mm )</td>
<td>( 1.4 \times 10^{-9} )</td>
<td>( 2.2 \times 10^{-9} )</td>
</tr>
<tr>
<td>16 x 16 x 8</td>
<td>1120 ( \mu m )</td>
<td>1 ( mm )</td>
<td>( 7.0 \times 10^{-10} )</td>
<td>( 1.1 \times 10^{-9} )</td>
</tr>
</tbody>
</table>
$\Delta B_z$ distributions

Vertical

Horizontal

$\Delta x = \Delta y = 140 \, \mu m$
$\Delta z = 500 \, \mu m$

$\Delta x = \Delta y = 281 \, \mu m$
$\Delta z = 1000 \, \mu m$

$\Delta x = \Delta y = 562 \, \mu m$
$\Delta z = 1000 \, \mu m$

$\Delta x = \Delta y = 1120 \, \mu m$
$\Delta z = 1000 \, \mu m$
Active-Rest reconstruction
Active Behavior?

• Replace passive membrane with ODE model (e.g. Hodgkin Huxley)
• Helps with dynamic behavior prediction and current pattern design
Bidomain Model

\[ V_m = \phi_i - \phi_e \]

\[ \nabla \cdot J_i = -\nabla \cdot J_e = i_m \]

\[ i_m = \beta G_m V_m \]

\[ i_m = \beta(C_m \frac{dV_m}{dt} + (V_m - V_{Na})G_{Na} + (V_m - V_K)G_K + (V_m - V_L)G_L) \]

\[ J_i = -D_i \nabla \phi_i \]

\[ J_e = -D_e \nabla \phi_e \]

3 application modes
Vo (bath), Ve and Vi (tissue)

At boundaries: \[ \frac{\partial \phi_i}{\partial n} = 0 \] i.e. insulation

\[ V_e = V_o \]

Table 1. Bidomain Parameters and Constants

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Units</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \sigma_i )</td>
<td>3.63</td>
<td>S/m</td>
<td>intracellular conductivity</td>
</tr>
<tr>
<td>( \sigma_e )</td>
<td>5.07</td>
<td>S/m</td>
<td>extracellular conductivity</td>
</tr>
<tr>
<td>( \sigma_o )</td>
<td>5.07</td>
<td>S/m</td>
<td>bath conductivity</td>
</tr>
<tr>
<td>( \sigma_p )</td>
<td>1</td>
<td>S/m</td>
<td>port conductivity</td>
</tr>
<tr>
<td>( f_i )</td>
<td>0.7</td>
<td>-</td>
<td>intracellular filling fraction</td>
</tr>
<tr>
<td>( \beta )</td>
<td>20,000</td>
<td>m(^{-1})</td>
<td>surface to volume ratio</td>
</tr>
<tr>
<td>( G_{m,rest} )</td>
<td>6.7</td>
<td>S/m(^2)</td>
<td>membrane conductivity, rest</td>
</tr>
<tr>
<td>( G_{m,active} )</td>
<td>320</td>
<td>S/m(^2)</td>
<td>membrane conductivity, active</td>
</tr>
</tbody>
</table>
\[ i_m = \beta (C_m \frac{dV_m}{dt} + (V_m - V_{Na})G_{Na} + (V_m - V_K)G_K + (V_m - V_L)G_L ) \]

\[ G_{Na} = G_{Na \text{ max}} m^3 h \]

\[ G_{K} = G_{K \text{ max}} n^4 \]

\[ G_L = \text{constant} \]

\[ \frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m \]

\[ \frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h \]

\[ \frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n \]

**TRANSFER RATE COEFFICIENTS**

\[ \alpha_m = \frac{0.1 \cdot (25 - V)}{e^{(25-V)/10}} \frac{1}{-1 \text{ m s}} \]

\[ \alpha_h = \frac{0.07}{e^{V/20}} \frac{1}{\text{ m s}} \]

\[ \alpha_n = \frac{0.01(10 - V)}{e^{(10-V)/10}} \frac{1}{-1 \text{ m s}} \]

\[ \beta_m = \frac{4}{e^{(V'/18)}} \frac{1}{\text{ m s}} \]

\[ \beta_h = \frac{1}{e^{(30 - V')/10}} \frac{1}{+1 \text{ m s}} \]

\[ \beta_n = \frac{0.125}{e^{V'/80}} \frac{1}{\text{ m s}} \]

**CONSTANTS**

\[ V_r - V_{Na} = -115 \]

\[ V_r - V_K = +12 \]

\[ V_r - V_L = -10.613 \text{ mV} \]

\[ C_m = 1 \mu F/cm^2 \]

\[ G_{Na \text{ max}} = 120 \text{ ms/cm}^2 \]

\[ G_{K \text{ max}} = 36 \text{ ms/cm}^2 \]

\[ G_L = 0.3 \text{ ms/cm}^2 \]
Reduced HH model
(Kepler, Abott and Marder 1992)

• 2 application modes in HH model (n follows h)

\[
\frac{dm}{dt} = k_m \left[ m(V_m) - m \right]
\]

\[
\frac{dh}{dt} = k_m \left[ h(V_m) - h \right]
\]
Basic Behavior

• Central cylinder only: 3 App modes (h, m, V_m)
• External constant current $i_e = 0.05 \text{ A/m}^3$

\[ \nabla \cdot J_m = i_m + i_e \]
Model 2

- Central cylinder only: 4 App modes (h, m, V_i, V_e)
- Externally Injected Source on opposite sides
- Coupling parameter $\beta = 1$ (should be 30000)
Model 2 dynamic view
Model 3

- Central cylinder + Bath : 5 App modes (h, m, V_i, V_e, V_o)
- Current injected into ports of bath
- Coupling parameter $\beta = 1$ (should be 30000)
Conclusions

• Bidomain model is a good way of estimating volume averaged activity
• Results plausibly consistent with others’ estimations
• Moderate scale/high field essential to proving concept
• Can be used to explore excitability and/or imaging
• Tweaking of final model is required
  – Solver settings
  – Adding anisotropy
Future Work

- Modelling
  - Active Membrane Model
  - Retinal Ganglion Model
  - Cortical Experiments and Models?
- MREIT Technology (increased SNR)
  - Pulse Sequences ->
    - reduced current and/or increased injection time/TR
  - Noise reduction
    - In data acquisition
    - In postprocessing
  - Anisotropic Reconstructions
- Technical Considerations
  - Pharmacological manipulation of thresholds