Imaging of Bioelectromagnetism through EIT and MREIT

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Contents

• Bioelectromagnetism
  • Neuronal Source Current and Magnetic Field
  • Ion Conduction and Conductivity
  • Volume Conduction, Bio-signal, and Voltage Imaging

• Admittivity Imaging
  • Conductivity, Permittivity, and Admittivity
  • Electrical Impedance Tomography (EIT)
  • Trans-Admittance Mammography (TAM)
  • Magnetic Resonance Electrical Impedance Tomography (MREIT)

• Direct Neuroimaging

• Summary
Bioelectromagnetism
Neuronal Source Current

(A) Receptor potential

(B) Synaptic potential

(C) Action potential

Purves et al., 2004

Grimnes and Martinsen, 2008
Magnetic Field by Neuronal Current

Bianciardi, Univ. of Rome, 2004

Xue, Univ. of Iowa, 2008

Luo et al., MRM, 2011
Ion Conduction and Conductivity

\[ \mathbf{J} = c \mu \mathbf{E} = \sigma \mathbf{E} = -\sigma \nabla \mathbf{u} \]

\[ R = \frac{V}{I} = \frac{1}{\sigma} \frac{L}{S} \]

Grimnes and Martinsen, 2008
Bioelectromagnetism (Endogenous)

\[
\begin{align*}
\nabla \cdot (\sigma(r, t) \nabla u(r, t)) &= f(r, t) \text{ in } \Omega \\
-\sigma(r, t) \nabla u(r, t) \cdot \mathbf{n} &= 0 \text{ on } \partial \Omega
\end{align*}
\]

Voltage \quad Source \ Current \ (Endogenous)

\[ J(r, t) = -\sigma(r, t) \nabla u(r, t) \]

Current Density

Conductivity

\[ B(r, t) = \frac{\mu_0}{4\pi} \int_{\Omega} \frac{J(r', t) \times (r - r')}{|r - r'|^3} \, dr' \]

Magnetic Flux Density
Current Flow and Conductivity

**E and J are parallel**

**E and J are not parallel**

- Isotropic Conductivity Anomaly
- Anisotropic Conductivity Anomaly

Grimnes and Martinsen, 2008
Volume Conduction of Source Current

- White lines are current stream lines
- Black lines are equipotential lines

\[
\begin{aligned}
\nabla \cdot (\sigma(r,t)\nabla u(r,t)) &= f(r,t) \text{ in } \Omega \\
-\sigma(r,t)\nabla u(r,t) \cdot n &= 0 \text{ on } \partial \Omega \\
J(r,t) &= -\sigma(r,t)\nabla u(r,t)
\end{aligned}
\]
Bio-electric Signal: ECG (Electrocardiogram)

\[ f(r, t) \]

\[ \nabla \cdot (\sigma(r, t)\nabla u(r, t)) = f(r, t) \]

Medical Instrumentation: Application and Design, 3rd ed., by J. G. Webster
Bio-electric Signal: EEG (Electroencephalogram)

∇ \cdot (\sigma(r, t) \nabla u(r, t)) = f(r, t)
Bio-magnetic Signal: MEG (Magnetoencephalogram)

(Superconducting Quantum Interference Device)

\[ \mathbf{B}(\mathbf{r}, t) = \frac{\mu_0}{4\pi} \int_{\Omega} \frac{\mathbf{J}(\mathbf{r}', t) \times (\mathbf{r} - \mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|^3} d\mathbf{r}' \]

\[ \nabla \cdot (\sigma(\mathbf{r}, t)\nabla u(\mathbf{r}, t)) = f(\mathbf{r}, t) \]

\[ \mathbf{J}(\mathbf{r}, t) = -\sigma(\mathbf{r}, t)\nabla u(\mathbf{r}, t) \]
Voltage Imaging using MEA (Microelectrode Array)

Abdoun et al., Frontiers in Neuroinformatics, 2011
Voltage Imaging using MEA (Microelectrode Array)

Viventi et al., Nature Neuroscience, 2011
Voltage Imaging using Voltage-sensitive Dye

Peterka et al.,
Neuron, 2011
Admittivity Imaging
Conductivity and Resistance

\[ E = -\nabla u \quad F = qE = ma \quad v_d = \mu E \quad J = c v_d \quad J = c \mu E = \sigma E = -\sigma \nabla u \]

\[ E = \frac{V}{L}, \quad J = \sigma E = \sigma \frac{V}{L}, \quad I = JS = \sigma \frac{V}{L} \]

\[ V = \frac{1}{\sigma S} I = \rho \frac{L}{S} I = RI, \quad R = \frac{V}{I} = \frac{1}{\sigma S} \]

Mobile Ions
Permittivity and Capacitance

Immobile Polar Molecules

\[ Q = CV = \varepsilon \frac{S}{L} V \]

\[ v(t) = V \sin(\omega t), \quad i(t) = V \omega C \cos(\omega t) \]

\[ i(t) = \frac{dQ(t)}{dt} = C \frac{dv(t)}{dt} \]

\[ V = V \angle 0, \quad I = V \omega C \angle 90^\circ, \quad Z = \frac{V}{I} = \frac{1}{j\omega C} \]
Cell, Admittivity, and Admittance (or Impedance)

\[
\tau(\mathbf{r}, \omega) = \sigma(\mathbf{r}, \omega) + j\omega\varepsilon(\mathbf{r}, \omega)
\]

\[
Z = R + jX = R_1 + \frac{1}{j\omega C_1} + \frac{1}{j\omega C_2} + R_2
\]

\[
R = Z \cos \theta, \quad X = Z \sin \theta
\]

Cell, Membrane

Extra-cellular Fluid

Intra-cellular Fluid

\[i(t) \sim v(t)\]
Macroscopic Tissue Structure

- Extra-cellular Fluid
- Intra-cellular Fluid
- Cellular Membrane

- Point-wise Admittivity
- Volume-wise Admittivity (or Effective Admittivity)
- Apparent Admittivity
- Isotropic Admittivity
- Anisotropic Admittivity
Admittivity of Liver Tissue

Respiration

Ventilation

Perfusion

Ventilation and Perfusion Ratio (V/Q Ratio)

300 million alveoli
Macroscopic Volume-wise Admittivity

Ventilated Not ventilated

Not perfused Perfused
Tissue Conductivity (1 Hz – 1 MHz)

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Conductivity [S/m]</th>
<th>Anisotropy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>0.05 – 0.6</td>
<td>Local</td>
</tr>
<tr>
<td>Whole blood</td>
<td>0.7</td>
<td>Flow dependent</td>
</tr>
<tr>
<td>Bone</td>
<td>0.005 – 0.06</td>
<td>Strong</td>
</tr>
<tr>
<td>Muscle</td>
<td>0.05 – 0.6</td>
<td>Strong</td>
</tr>
<tr>
<td>Fat</td>
<td>0.02 – 0.05</td>
<td>Small</td>
</tr>
<tr>
<td>Liver</td>
<td>0.2 – 0.3</td>
<td>Unknown</td>
</tr>
<tr>
<td>Saline, 0.9%, 37°C</td>
<td>2</td>
<td>None</td>
</tr>
<tr>
<td>Sea water</td>
<td>5</td>
<td>None</td>
</tr>
</tbody>
</table>

Low- and high-frequency current paths in biological tissue

Grimnes and Martinsen, 2008
Admittivity of Biological Tissue

Structure and Composition

• Molecular composition of cells
• Shape and direction of cells
• Density and structure of cells
• Contents of extra-cellular matrix
• Concentration and mobility of ions
• Concentration and mobility of charge-carrying molecules
• Amounts of intra- and extra-cellular fluids

Function and Pathology

• Neural activity
• Epilepsy
• Tumor
• Ischemic stroke
• Hemorrhage
• Upper airway apnea
• Pulmonary function
• Cardiac function
• Gastric emptying
• Abdominal bleeding
• Temperature
How to probe the passive material property

Injected Current (dc or ac)

\[ I \text{ or } I \sin 2\pi ft \]

Electrode, \( \mathcal{E}^+ \)

\( \mathbb{R}^3 \setminus \Omega \)  
\((\sigma=0, \varepsilon_0, \mu_0)\)

\( \Omega (\sigma, \varepsilon, \mu) \)

\( u, J, E, H \)

Induced Current (ac)

\[ I \sin 2\pi ft \]

Coil, \( C \)

Electrode, \( \mathcal{E}^- \)

\( \mathbb{R}^3 \setminus \Omega \)  
\((\sigma=0, \varepsilon_0, \mu_0)\)

\( \Omega (\sigma, \varepsilon, \mu) \)

\( u, J, E, H \)

\[ \nabla \times \mathbf{H}(\mathbf{r}) = \tau(\mathbf{r})\mathbf{E}(\mathbf{r}) = (\sigma(\mathbf{r}) + j\omega\varepsilon(\mathbf{r}))\mathbf{E}(\mathbf{r}) = \mathbf{J}(\mathbf{r}) \]
Homogeneous and Isotropic

Low Frequency Current

High Frequency Current

Homogeneous Object

Macroscopic Apparent Conductivity Seen by the Current

Homogeneous Object Macroscopic Apparent Conductivity Seen by the Current

Low Frequency Current

High Frequency Current

Homogeneous Object

Macroscopic Apparent Conductivity Seen by the Current

\[ \sigma_0 \]

\[ \sigma_0 \]
Inhomogeneous and isotropic

- Low Frequency Current
  - Solid Anomaly with Conductivity Contrast
  - $\sigma_0$ and $\sigma_1$

- High Frequency Current
  - Macroscopic Apparent Conductivity Seen by the Current
  - $\sigma_0$ and $\sigma_2$
Cell Swelling

Low Frequency Current

High Frequency Current

Hollow Anomaly of Insulating Membrane

Macroscopic Apparent Conductivity Seen by the Current
Membrane Permeability

Low Frequency Current

High Frequency Current

Hollow Anomaly of Insulating Membrane with Hole

Macroscopic Apparent Conductivity Seen by the Current
Anisotropy

Low Frequency Current

High Frequency Current

Hollow Anomaly of Insulating Membrane with Hole

Macroscopic Apparent Conductivity Seen by the Current
Bioelectromagnetism (Endogenous and Exogenous)

\[
\begin{aligned}
\nabla \cdot (\tau(r, t) \nabla u(r, t)) &= f(r, t) \text{ in } \Omega \\
-\tau(r, t) \nabla u(r, t) \cdot n &= g \text{ on } \partial \Omega
\end{aligned}
\]

Voltage \quad Source Current (Endogenous)

Admittivity \quad Injection Current (Exogenous)

\[ J(r, t) = -\tau(r, t) \nabla u(r, t) \]

Current Density

Magnetic Flux Density

\[
B(r, t) = \frac{\mu_0}{4\pi} \int_{\Omega} \frac{J(r', t) \times (r - r')}{|r - r'|^3} \, dr'
\]
Bioelectromagnetism (Exogenous)

\[
\left\{ \begin{align*}
\nabla \cdot (\tau(r,t)\nabla u(r,t)) &= 0 \text{ in } \Omega \\
-\tau(r,t)\nabla u(r,t) \cdot \mathbf{n} &= g \text{ on } \partial\Omega
\end{align*} \right.
\]

Voltage \hspace{1cm} Source Current (Endogenous)

Admittivity \hspace{1cm} Injection Current (Exogenous)

\[
\mathbf{J}(r,t) = -\tau(r,t)\nabla u(r,t)
\]

Current Density

Magnetic Flux Density

\[
\mathbf{B}(r,t) = \frac{\mu_0}{4\pi} \int_{\Omega} \frac{\mathbf{J}(\mathbf{r}',t) \times (\mathbf{r} - \mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|^3} \, d\mathbf{r}'
\]
Volume Conduction of Injection Current
Volume Conduction of Injection Current
Volume Conduction of Injection Current

Conductivity [S/m]  Voltage [V]

Current Density [A/m²]  Magnetic Flux Density [T]
Measurable Quantities

\[ \tau(r, \omega) = \sigma(r, \omega) + j\omega\varepsilon(r, \omega) \]

\[ \nabla \times \mathbf{E}(r) = -j\omega\mu\mathbf{H}(r) \quad \nabla \times \mathbf{H}(r) = \tau(r)\mathbf{E}(r) = \mathbf{J}(r) \]

\[ \nabla \cdot (\tau \nabla u) = j\omega\nabla \tau \cdot \mathbf{A} \]

or

\[ -\nabla^2 \mathbf{H} = \nabla \ln \tau \times (\nabla \times \mathbf{H}) - j\omega\mu\tau \mathbf{H} \]

Measurable quantities

- Voltage, \( u \) with \( -\nabla u = \mathbf{E} \)
- Magnetic field, \( \mathbf{H} \)
Admittivity Imaging Methods

- **EIT (≤ 1 MHz)**: boundary voltage using electrodes
- **MIT (≈ 10 MHz)**: external magnetic field using coils
- **MREIT (≤ 1 kHz)**: internal magnetic field using MRI
- **MREPT (128 MHz at 3T)**: internal magnetic field using MRI
Electrical Impedance Tomography (EIT)
Frontal Plane Impedance Camera (1978)

EIT (Electrical Impedance Tomography)

\[ I_p = I_m \angle 0 \quad \text{: Injection Current} \]
\[ Z_{pq} = Z_{pq} \angle \theta \quad \text{: Transfer Impedance} \]
\[ V_q = Z_{pq} I_m \angle \theta \quad \text{: Measured Voltage} \]

Transfer impedance \( Z_{pq} \) depends on
- electrode configuration
- conductivity distribution
- geometry (boundary shape and size)

\[ \begin{align*}
\nabla \cdot \left( \tau (\mathbf{r}, t) \nabla u(\mathbf{r}, t) \right) &= 0 \text{ in } \Omega \\
- \tau (\mathbf{r}, t) \nabla u(\mathbf{r}, t) \cdot \mathbf{n} &= g \text{ on } \partial \Omega
\end{align*} \]
Tomographic Imaging of Thorax (1990s)


Tomographic Imaging of Head (2000s)

Lessons from 30 Years of EIT Research

• Must attach many (8 to 64 or more) electrodes
• Current flows (spreads) in the entire 3D region
• Current pathway depends nonlinearly on all pixels
• Voltage depends nonlinearly on all pixels
• Voltage on an electrode is sensitive to the region nearby
• Voltage depends strongly on geometry

• Do not try static structural imaging
• Try real-time functional imaging
• Maximize hardware performance
• Choose proper application
Boundary Current-Voltage Data (Neumann-to-Dirichlet Map)

\[ \sigma + j \omega \varepsilon \text{ in } \Omega \]

\[ \nabla \cdot (\tau(r) \nabla u(r)) = 0 \text{ in } \Omega \]
\[ -\tau(r) \nabla u(r) \cdot n = g \text{ on } \partial \Omega \]
\[ J(r) = -\tau(r) \nabla u(r) \]

Electrode Number

<table>
<thead>
<tr>
<th>Electrode</th>
<th>Boundary Current</th>
<th>Boundary Voltage</th>
</tr>
</thead>
<tbody>
<tr>
<td>E1</td>
<td>(10^-3-10^-4 A)</td>
<td>(10^-4-10^-6 V)</td>
</tr>
<tr>
<td>E2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E3</td>
<td></td>
<td></td>
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<tr>
<td>E4</td>
<td></td>
<td></td>
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<tr>
<td>E5</td>
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<td>E6</td>
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<td>E7</td>
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<td>E8</td>
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<td>E9</td>
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<td>E10</td>
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<td>E11</td>
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</tr>
<tr>
<td>E15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E16</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IIRC, Kyung Hee Univ. May, 2014
Current and Voltage on Boundary
Phase-sensitive Demodulation

\[ i(t) = I \sin(\omega t) \]

\[ Z = R + jX = Z \angle \theta \]

\[ R = Z \cos \theta, \quad X = Z \sin \theta \]

\[ v(t) = ZI \sin(\omega t + \theta) = ZI \cos \theta \sin(\omega t) + ZI \sin \theta \cos(\omega t) \]

Real Part (In-phase Component)

Imaginary Part (Quadrature Component)
KHU Mark 1 EIT System

16-channel System

32-channel System
KHU Mark 1 and Mark 2 EIT Systems

64-channel KHU Mark 1

Expandable 16-channel KHU Mark 2
KHU Mark 2.5 EIT System

- Number of voltmeters: 8 - 64
- Number of current sources: 8 - 64
- Frequency range: 50Hz - 500kHz
- Flexible electrode configuration
- Maximum 100 frame/sec
- Automatic self-calibration
- Cascaded mode
- Event trigger mode
KHU Mark 2 EIT System Software

Measurement protocol & method

Image display

Image format
-Magnitude
-Phase
-Real
-Imaginary

Electrode contact status

Boundary voltage pattern

Voltage overflow

Control window
Image display window
Contact check window
Overflow check window

Reciprocity error
PVDF Nanofiber Web Electrode

Ag-plated PVDF Nanofiber Web Electrode

Electrode Belt

Inner Band

Outer Band

Sponge
Smart Electrode and Belt

http://www.bmedical.com  http://www.alphatrace.at

http://www.alphatrace.at
Static Imaging in EIT

- Image of absolute admittivity \((\sigma + j\omega\varepsilon)\) values
- Must overcome the following problems
  - Three-dimensional geometry is unknown and varying
  - Electrode positions are unknown and varying
  - Very accurate three-dimensional forward model is needed
  - Higher degree of measurement accuracy is needed
Difference Imaging in EIT

• Image of change in admittivity ($\sigma + j\omega\varepsilon$) with respect to time and/or frequency

• Common systematic errors can be cancelled out
  • Unknown boundary geometry
  • Uncertainty in electrode position
  • Systematic artifacts
EIT (Electrical Impedance Tomography)

\[ \begin{align*}
\n\n\n\end{align*} \]
Boundary Current-Voltage Data (Neumann-to-Dirichlet Map)

\[
F_{t,\omega} = \begin{bmatrix}
V_{t,\omega}^{1,1} & V_{t,\omega}^{1,2} & \cdots & \cdots & V_{t,\omega}^{1,E} \\
V_{t,\omega}^{2,1} & V_{t,\omega}^{2,2} & \cdots & \cdots & V_{t,\omega}^{2,E} \\
\vdots & \vdots & \ddots & \cdots & \vdots \\
V_{t,\omega}^{E,1} & V_{t,\omega}^{E,2} & \cdots & \cdots & V_{t,\omega}^{E,E}
\end{bmatrix}
\]

\[
F_{t,\omega} = \begin{bmatrix}
V_{t,\omega}^{1,1} & \cdots & V_{t,\omega}^{1,E} & V_{t,\omega}^{2,1} & \cdots & V_{t,\omega}^{2,E} & \ldots & \ldots & V_{t,\omega}^{E,1} & \cdots & V_{t,\omega}^{E,E}
\end{bmatrix}^T
\]

- How to invert NtD map to recover $\tau$?
Image Reconstruction Problem

- **Governing Equation**
  \[
  \begin{align*}
  \nabla \cdot (\tau(r, t) \nabla u(r, t)) &= 0 \text{ in } \Omega \\
  -\tau(r, t) \nabla u(r, t) \cdot n &= g \text{ on } \partial \Omega
  \end{align*}
  \]

- **Sensitivity using Reciprocity Theorem**
  \[
  I^{}(f_{t,\omega} - f_{0,\omega}) \cdot e_p = \int_{\Omega} \left( \frac{1}{\gamma_{t,\omega}} - \frac{1}{\gamma_{0,\omega}} \right) \nabla u^k \cdot \nabla u^j \, dr \\
  \approx \frac{1}{\hat{\gamma}_{0,\omega} \hat{\gamma}_{t,\omega}} \int_{\Omega} (\gamma_{0,\omega} - \gamma_{t,\omega}) \nabla u^k \cdot \nabla u^j \, dr \\
  = \frac{\hat{\gamma}_{0,\omega}^2 \alpha_{0,\omega} \alpha_{t,\omega}}{\hat{\gamma}_{0,\omega} \hat{\gamma}_{t,\omega}} \int_{\Omega} (\gamma_{0,\omega} - \gamma_{t,\omega}) \nabla u^k \cdot \nabla u^j \, dr
  \]

- **Linearized Forward Relation**
  \[
  f_{t,\omega} - f_{0,\omega} = \frac{1}{I^{} \hat{\gamma}_{0,\omega}^2 \alpha_{0,\omega} \alpha_{t,\omega}} \mathcal{S}(h_{0,\omega} - h_{t,\omega})
  \]

- **Inverse Solution**
  \[
  g_{t,\omega} = h_{t,\omega} - h_{0,\omega} = -I^{} \hat{\gamma}_{0,\omega}^2 \alpha_{0,\omega} \alpha_{t,\omega} \mathcal{A}(f_{t,\omega} - f_{0,\omega})
  \]
\[ \tau = \sigma + j \omega \epsilon = 1 \]

\[ \mathbf{f}_0 = \begin{bmatrix} f_{0,0}^{1,1} \\ \vdots \\ f_{0,0}^{1,E} \\ f_{0,0}^{2,1} \\ \vdots \\ f_{0,0}^{2,E} \\ \vdots \\ f_{0,0}^{E,1} \\ \vdots \\ f_{0,0}^{E,E} \end{bmatrix} \]

\[ \tau_q = 1 + 1 = 2 \text{ in } \Lambda_q \]

\[ \mathbf{f}_{0,q} = \begin{bmatrix} f_{0,q}^{1,1} \\ \vdots \\ f_{0,q}^{1,E} \\ f_{0,q}^{2,1} \\ \vdots \\ f_{0,q}^{2,E} \\ \vdots \\ f_{0,q}^{E,1} \\ \vdots \\ f_{0,q}^{E,E} \end{bmatrix} \]

\[ S_{0,q}^f = \mathbf{s}_{0,q} = \mathbf{f}_{0,q} - \mathbf{f}_{0,0} = \begin{bmatrix} f_{0,q}^{1,1} - f_{0,0}^{1,1} \\ \vdots \\ f_{0,q}^{1,E} - f_{0,0}^{1,E} \\ f_{0,q}^{2,1} - f_{0,0}^{2,1} \\ \vdots \\ f_{0,q}^{2,E} - f_{0,0}^{2,E} \\ \vdots \\ f_{0,q}^{E,1} - f_{0,0}^{E,1} \\ \vdots \\ f_{0,q}^{E,E} - f_{0,0}^{E,E} \end{bmatrix} = \begin{bmatrix} s_{1,q} \\ \vdots \\ s_{E,q} \\ s_{E+1,q} \\ \vdots \\ s_{2E,q} \\ \vdots \\ s_{E(E-1)+1,q} \\ \vdots \\ s_{E^2,q} \end{bmatrix} \]
Sensitivity and Linearization

\[
S_{0,q}^{f_0} = s_{0,q} = f_{0,q} - f_{0,0} =
\begin{bmatrix}
    f_{0,0}^{1,1} - f_{0,0}^{1,0} \\
    \vdots \\
    f_{0,q}^{1,E} - f_{0,0}^{1,0} \\
    f_{0,0}^{2,1} - f_{0,0}^{2,0} \\
    \vdots \\
    f_{0,q}^{2,E} - f_{0,0}^{2,0} \\
    \vdots \\
    f_{0,q}^{E,1} - f_{0,0}^{E,0} \\
    \vdots \\
    f_{0,q}^{E,E} - f_{0,0}^{E,E}
\end{bmatrix}
= 
\begin{bmatrix}
    s_{1,q} \\
    \vdots \\
    s_{E,q} \\
    s_{E+1,q} \\
    \vdots \\
    s_{2E,q} \\
    \vdots \\
    s_{E(E-1)+1,q} \\
    \vdots \\
    s_{E^2,q}
\end{bmatrix}
\]

\[
f_{0,(x,y)} - f_{0,0} = \Delta_x
\]

\[
\begin{bmatrix}
    s_{1,x} \\
    \vdots \\
    s_{E,x} \\
    s_{E+1,x} \\
    \vdots \\
    s_{2E,x} \\
    \vdots \\
    s_{E(E-1)+1,x} \\
    \vdots \\
    s_{E^2,x}
\end{bmatrix}
+ \begin{bmatrix}
    s_{1,y} \\
    \vdots \\
    s_{E,y} \\
    s_{E+1,y} \\
    \vdots \\
    s_{2E,y} \\
    \vdots \\
    s_{E(E-1)+1,y} \\
    \vdots \\
    s_{E^2,y}
\end{bmatrix}
\]
Sensitivity Matrix and Linearization

Among $E^2$ measurements, $E(E-1)/1$ are independent.

\[
\begin{bmatrix}
  s_{1,1} \\
  \vdots \\
  s_{E,1} \\
  s_{E+1,1} \\
  \vdots \\
  s_{2E,1} \\
  \vdots \\
  s_{E(E-1)+1,1} \\
  \vdots \\
  s_{E^2,1}
\end{bmatrix} + \cdots + \Delta_Q
\begin{bmatrix}
  s_{1,Q} \\
  \vdots \\
  s_{E,Q} \\
  s_{E+1,Q} \\
  \vdots \\
  s_{2E,Q} \\
  \vdots \\
  s_{E(E-1)+1,Q} \\
  \vdots \\
  s_{E^2,Q}
\end{bmatrix} =
\begin{bmatrix}
  s_{1,1} & s_{1,2} & \cdots & s_{1,Q} \\
  \vdots & \vdots & \ddots & \vdots \\
  s_{E,1} & s_{E,2} & \cdots & s_{E,Q} \\
  \vdots & \vdots & \ddots & \vdots \\
  s_{E+1,1} & s_{E+1,2} & \cdots & s_{E+1,Q} \\
  \vdots & \vdots & \ddots & \vdots \\
  s_{2E,1} & s_{2E,2} & \cdots & s_{2E,Q} \\
  \vdots & \vdots & \ddots & \vdots \\
  s_{E(E-1)+1,1} & s_{E(E-1)+1,2} & \cdots & s_{E(E-1)+1,Q} \\
  \vdots & \vdots & \ddots & \vdots \\
  s_{E^2,1} & s_{E^2,2} & \cdots & s_{E^2,Q}
\end{bmatrix}
\begin{bmatrix}
  \Delta_1 \\
  \Delta_2 \\
  \vdots \\
  \Delta_Q
\end{bmatrix} = S \Delta \tau
\]

\[
[f - f_0]_{E^2 \times 1} = S_{E^2 \times Q} \Delta \tau_{Q \times 1}
\]
Sensitivity Matrix and TSVD

- Sensitivity matrix $S$
  - Real matrix computed with $\tau = 1$
  - Contains information on the geometry and electrode configuration
- Reconstruction matrix $R$
  - TSVD of $S$
  - Rank of $S$ determines effective spatial resolution

$$\tau = \overline{\tau}$$

$$f_m^l - f_m^R = \frac{1}{I\overline{\tau}_m^l\overline{\tau}_m^R} S\tau_m^l$$

$$\tau_m^l = I\overline{\tau}_m^l\overline{\tau}_m^R R(f_m^l - f_m^R)$$
Ill-posedness

- Low Sensitivity
- Nonlinearity

Difference imaging with
- Low spatial resolution
- High temporal resolution
**Time-difference Imaging**

Time-difference images of two cylindrical anomalies of TX151 (0.27 S/m) and carrot in the background 0.2 S/m saline

<table>
<thead>
<tr>
<th>Frequency (Hz)</th>
<th>TX151</th>
<th>Carrot</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>![Image of TX151 at 10Hz]</td>
<td>![Image of Carrot at 10Hz]</td>
</tr>
<tr>
<td>100</td>
<td>![Image of TX151 at 100Hz]</td>
<td>![Image of Carrot at 100Hz]</td>
</tr>
<tr>
<td>1k</td>
<td>![Image of TX151 at 1kHz]</td>
<td>![Image of Carrot at 1kHz]</td>
</tr>
<tr>
<td>10k</td>
<td>![Image of TX151 at 10kHz]</td>
<td>![Image of Carrot at 10kHz]</td>
</tr>
<tr>
<td>50k</td>
<td>![Image of TX151 at 50kHz]</td>
<td>![Image of Carrot at 50kHz]</td>
</tr>
<tr>
<td>100k</td>
<td>![Image of TX151 at 100kHz]</td>
<td>![Image of Carrot at 100kHz]</td>
</tr>
<tr>
<td>500k</td>
<td>![Image of TX151 at 500kHz]</td>
<td>![Image of Carrot at 500kHz]</td>
</tr>
</tbody>
</table>

**Graph:**

- **Conductivity (S/m):**
  - **Carrot:** Blue line
  - **0.1% Saline:** Red line
  - **0.1% TX151:** Green line

**X-axis:** Frequency (Hz)

**Y-axis:** Conductivity (S/m)
Frequency-difference Imaging

Reference frequency: 1kHz
Clinical Applications

• Time-difference imaging
  • Pulmonary function
  • Cardiac function
  • Bleeding
  • Gastric emptying
  • Epilepsy imaging
  • Neural activity imaging
  • Upper airway apnea
  • Temperature imaging

• Frequency-difference imaging
  • Tumor imaging
  • Stoke imaging
How much current can we inject for EIT

- **Patient auxiliary current (IEC 601-1)**: current flowing in a patient in normal use between any patient connection and all other patient connections and not intended to produce a physiological effect
  - 0 Hz – 0.1 Hz : $0.01 \text{ mA}_{\text{rms}}$
  - 0.1 Hz – 1 kHz : $0.1 \text{ mA}_{\text{rms}}$
  - 1 kHz – 100 kHz : $0.1 \times f \text{ (in kHz)} \text{ mA}_{\text{rms}}$
  - Above 100 kHz : $10 \text{ mA}_{\text{rms}}$
Lung Ventilation Imaging

EIT system: KHU Mark 2

Protocol
- 16 electrodes
- Adjacent injection and measurement
- 9 frames/s scan speed

Ventilation: 15 breaths/min

MR Image

EIT Image

Normalized DZ in Lungs
Lung Ventilation
Tidal Volume Ventilation Imaging

Time-series EIT Images

Average Tidal Image

http://eidors3d.sourceforge.net
3D Image Reconstruction

http://www.timpel.com.br

http://eidors3d.sourceforge.net
PEEP Maneuver

Acute Lung Injury

Surfactant Treatment

http://eidors3d.sourceforge.net
Cardiac Function Imaging

(a) ECG signal [mV]

(b) Relative conductivity @ Pixel x

(c) Images with annotations

http://eidors3d.sourceforge.net
Ventilation and Perfusion (Neonate)

http://eidors3d.sourceforge.net
Perfusion Imaging

EIT of Ventilation and Perfusion Combined

Contrast Enhanced EIT using Bolus Injection of Hypertonic Saline

http://www.timpel.com.br
Stomach Motility

Filling

0s 20s (Intake) 35s 45s 56s 1m 3s 1m 33s 1m 48s 1m 54s

Emptying

15m 20m 22m 29s 25m 32m 30s 35m 50m 52m 29s
Abdominal Bleeding

- Inject blood between channel 1 and 16
- Injection speed: 180 ml/hour
- Injection volume: 30 ml
- EIT belt around the abdomen
- Operating frequency: 10 kHz
- Average: 16

Detection of conductivity changes after injecting 0.75ml (15 seconds)
Upper Airway Apnea

Open
Closed

Open
Closed

Open
Closed
Open
Trans-Admittance Mammography
(TAM)
TAS (Trans-admittance Scanner)

- Apply voltage at hand-held electrode
- Measure exit currents through array of electrodes in the planar scan probe
- Display trans-admittance map
- Estimate location and size of anomalies
TAS System and Probe
Time-difference TAS Images

Size = 6mm$^3$

- Depth : 5mm
- Depth : 10mm
- Depth : 15mm
- Depth : 20mm

Depth = 10mm

- Size : 4mm$^3$
- Size : 6mm$^3$
- Size : 8mm$^3$
- Size : 10mm$^3$
Frequency-difference TAS Images

Depth : 10mm, Size : 523.6mm³ Ball

Real Part

Imaginary Part

50kHz – 10kHz 100kHz – 10kHz 200kHz – 50kHz 200kHz – 100kHz
TAM (Trans-Admittance Mammography)
TAM (Trans-Admittance Mammography)

500Hz, Real

50kHz, Real

500kHz, Real

500Hz, Imaginary

50kHz, Imaginary

500kHz, Imaginary

Tissue A

Tissue B

Max

Min

Max

Min
Micro-EIT in Biology
and Tissue Engineering
Micro-EIT for Tissue Culture

Voltage Maps on Three Surfaces

Projection and Reconstruction Image
Electric Cell-substrate Impedance Sensing

- **ECIS**
  - Real-time, label-free, non-invasive monitoring for live cell
  - Functional and morphological change detection using impedance for the activities of cells

- **Cultureware**
  - Gold electrodes with insulating film
  - Several electrodes at the base in the well
  - Oxygen plasma process to improve the adhesion of cells

- Diameter of electrode: 15 – 500 μm
- Electrodes per well: 1 – 40
- Well volume: 100 – 600 μL

Wegener, Keese, and Giaever, Cell Research, 2000
http://www.biophysics.com
Bio-impedance Cell Sensors

• Impedance spectroscopy for cellular bio-sensing
• Observation and measurement of physiological properties of cells
• Non-invasive, real time, and label-free

Heileman et al., Biosens. & Bioelectron., 2011
Sarro et al., Biosens. & Bioelectron., 2011
Reitinger et al., Biosens. & Bioelectron., 2012
EIT for Industrial Applications
Non-destructive Testing using EIT

Crack Identification in Concrete

8th. World Congress on Computational Mechanics (WCCM8)
5th. European Congress on Computational Methods in Applied Sciences and Engineering (ECCOMAS 2008)
June 30 – July 5, 2008 Venice, Italy
Pressure Imaging using EIT
Magnetic Resonance Electrical Impedance Tomography (MREIT)
Volume Conduction of Injection Current

Conductivity: $\sigma_{11}$, $\sigma_{22}$, $\sigma_{33}$

Conductivity: $\sigma_{12}$, $\sigma_{13}$, $\sigma_{23}$

Voltage [V], Current Density [A/m$^2$], Magnetic Flux Density [nT]
MRI (Magnetic Resonance Imaging)

3T (KHU)  

9.4T (YU)  

3T (KHUH)
Magnetic Field Imaging using MRI

\[ S^\pm(m,n) = \int_{-\infty}^\infty \int_{-\infty}^\infty M(x,y) e^{j\delta(x,y)} e^{\pm j\gamma B_z(x,y)T_c} e^{j(xm\Delta_k_x + yn\Delta_k_y)} dx dy \]

Magnetic Field Imaging using MRI

MRI Parameters:
- TR/TE = 1400/60ms
- FOV = 200mm
- Matrix size = 128 × 128
- Slice thickness/Gap = 3/0mm
- Number of slices = 8
- Average = 2
- Current amplitude = 27mA
- Current pulse width = 24ms
- Voxel size = 1.5625×1.5625×3mm³

Phantom:
- Solution: 2S/m (NaCl=12.5g/l, CuSO₄=2g/l)
- Object (agar): 0.5S/m (NaCl=2g/l, CuSO₄=2g/l, Agar=15g/l)
Magnetic Field Imaging using MRI

MR Magnitude Image

Wrapped Phase Image
Magnetic Flux Density Image

Horizontal Injection Current

\[ \nabla^2 B_z = 0 \]

\[ \mu_0 J = \nabla \times B \]

\[ J = -\sigma \nabla u \]

\[ \nabla^2 B = -\mu_0 \nabla u \times \nabla \sigma \]

Vertical Injection Current

\[ \nabla^2 B_z \neq 0 \]

\[ \nabla^2 B_z \neq 0 \]
Conductivity vs. Magnetic Flux Density

\[ \sigma(r) = c(r) \mu(r) \]

\[ \mu_0 J = \nabla \times B \quad J(r) = -\sigma(r) \nabla u(r) \]

\[ \nabla^2 B = -\mu_0 \nabla \times \nabla \sigma \]

\[ \nabla^2 B_z = \mu_0 \left( \frac{\partial \sigma}{\partial x}, \frac{\partial \sigma}{\partial y}, \frac{\partial u}{\partial y} - \frac{\partial u}{\partial x} \right) \]
MREIT (Magnetic Resonance Electrical Impedance Tomography)

\[ \mu_0 \mathbf{J} = \nabla \times \mathbf{B} \]
\[ \mathbf{J}(\mathbf{r}) = -\sigma(\mathbf{r}) \nabla u(\mathbf{r}) \]
\[ \nabla^2 \mathbf{B} = -\mu_0 \nabla \times \nabla \sigma \]
\[ \nabla^2 B_z = \mu_0 \left( \frac{\partial \sigma}{\partial x}, \frac{\partial \sigma}{\partial y} \right) \left( \frac{\partial u}{\partial y}, -\frac{\partial u}{\partial x} \right) \]

Image
\[ \begin{bmatrix} \frac{\partial \ln \sigma}{\partial x}(\mathbf{r}) \\ \frac{\partial \ln \sigma}{\partial y}(\mathbf{r}) \end{bmatrix} = \frac{1}{\mu_0} \left( \mathbb{A}[\sigma_0](\mathbf{r}) \right)^{-1} \begin{bmatrix} \nabla^2 B_{z,1}(\mathbf{r}) \\ \nabla^2 B_{z,2}(\mathbf{r}) \end{bmatrix} \]

Model (from Data)

where
\[ \begin{cases} \mathbf{\nabla} \cdot (\sigma_0 \mathbf{\nabla} u_j[\sigma_0]) = 0 & \text{in } \Omega \\ I = \int_{\varepsilon^+} \sigma_0 \frac{\partial u_j[\sigma_0]}{\partial \mathbf{n}} \, ds = - \int_{\varepsilon^-} \sigma_0 \frac{\partial u_j[\sigma_0]}{\partial \mathbf{n}} \, ds \\ \mathbf{\nabla} u_j[\sigma_0] \times \mathbf{n}_{\varepsilon^+ \cup \varepsilon^-} = 0, \\ \sigma_0 \frac{\partial u_j[\sigma_0]}{\partial \mathbf{n}} = 0 & \text{on } \partial \Omega \setminus \varepsilon^+ \cup \varepsilon^- \end{cases} \]

and
\[ \mathbb{A}[\sigma_0](\mathbf{r}) = \begin{bmatrix} \sigma_0 \frac{\partial u_1[\sigma_0]}{\partial y}(\mathbf{r}) & -\sigma_0 \frac{\partial u_1[\sigma_0]}{\partial x}(\mathbf{r}) \\ \sigma_0 \frac{\partial u_2[\sigma_0]}{\partial y}(\mathbf{r}) & -\sigma_0 \frac{\partial u_2[\sigma_0]}{\partial x}(\mathbf{r}) \end{bmatrix} \]
CoReHA (Conductivity Reconstructor using Harmonic Algorithms)

http://iirc.khu.ac.kr
CoReHA (Conductivity Reconstructor using Harmonic Algorithms)

Segmentation  Electrode Modeling  Meshing and Modeling

Harmonic Inpainting
Validation

Agar (1 S/m)
Chicken Breast (0.17 S/m)
Chicken Breast (0.2 S/m)
TX151 (2 S/m)

\[
\begin{array}{c}
\sigma_{11} \\
\sigma_{12} \\
\sigma_{13} \\
\sigma_{22} \\
\sigma_{23} \\
\sigma_{33}
\end{array}
\]

\[
\begin{array}{c}
B_2^1 \\
B_2^2
\end{array}
\]
How much current can we inject for MREIT

- Threshold to stimulate a nerve with 20 μm diameter
  - 1 A/m² below 1 kHz
  - 2.5 mA through 5×5 cm² uniform current density electrode

Conventional Electrode

Uniform Current Density Electrode

(σ = 0.17 S/m)
MREIT Image

2002 - 2005

$B_z$

> 10 nT

2006 - 2009

$\sim 10$ nT

2010 - 2012

$\sim 1$ nT

Conductivity
MREIT Image

Canine Head

Canine Chest

Canine Abdomen

Canine Pelvis

Human Leg

Human Knee

Canine Head
MRI vs. Conductivity Image

Heart

- Left atrioventricular valve
- Left ventricle
- Right ventricle
- Ventricular septum
- Right atrioventricular valve

Kidney

- Cortex
- Medulla
- Renal pelvis
- Ureter

Prostate

- Urethral crest
- Central zone
- Fibrous connective tissue
- Peripheral zone
MRI vs. Conductivity Image (Canine Pelvis)
Animal Disease Model (Brain Abscess)

Before
Normal

6 hours
Edema

12 hours
Ring-shaped Membrane

18 hours

24 hours
Necrosis
Diffusion Tensor MRI

\[ D = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix} = S_D A_D S_D^T \]

T2-weighted Image  
FA  
Color-coded FA

Tractographic Images

From H. J. Kim
DT-MREIT of Canine Brain  \[ \mathbf{c} = \begin{pmatrix} \sigma_{xx} & \sigma_{xy} & \sigma_{xz} \\ \sigma_{xy} & \sigma_{yy} & \sigma_{yz} \\ \sigma_{xz} & \sigma_{yz} & \sigma_{zz} \end{pmatrix} = \eta \mathbf{D} \]
DT-MREIT of Human Leg

- Water Diffusion Tensor

- Conductivity Tensor
CDI during DBS (Deep Brain Stimulation)

DBS Electrode

MR Magnitude Image

Electrode

Mono-polar Excitation

Bi-polar Excitation

Current Density Image
CDI during tDCS (Transcranial Direct Current Stimulation)

ηD = C
Temperature Imaging during RF Ablation

RF power of 50 W and exposure time of 3 minutes
Direct Neuroimaging
Brain Mapping Project

• Human Brain Project (HBP)
  • European Union
  • US$ 1.3 Billion
  • Computational model of the brain

• Brain Research through Advancing Innovative Neurotechnologies (BRAIN)
  • United States
  • US$ 1 Billion
  • Experimental tools for imaging and control of the brain
Scale and Complexity

$10^7$ Neurons/cm$^2$  $10^4$ Synapses/Neuron  $10^{10}$ Neurons

Blue Brain Project
Functional Connectomics

From Anatomy to Connectivity Graph (Brain’s Wiring Diagram)

Cell, Tissue, Animal

Human

Bock et al., Nature, 2011

Park and Friston, Science, 2013
Optical Imaging of Cell and Tissue

Dye Loading

A. Single cell loading
- Sharp electrode
- Whole-cell patch clamp
- Single cell electroporation

B. ‘Acute’ network loading
- AM loading
- Dextran-conjugate loading
- Bulk electroporation

C. GECI expression
- Viral transduction
- In utero electroporation
- Transgenic mice

Imaging

A. Photodiode array
- Light source
- Dichroic mirror
- Specimen

B. CCD-based camera
- Light source
- Dichroic mirror
- Specimen

C. Confocal microscope
- CW Laser
- Dichroic mirror
- Pinhole
- PMT
- Specimen

D. Two-photon microscope
- Scanner
- Pulsed Laser
- Dichroic mirror
- PMT
- Specimen

E. Endoscope
- Micro-optical probe
- Specimen

F. Portable microscope
- Head-fixed microscope

Grienberger and Konnerth, Neuron, 2012
Optical Voltage Imaging of Neurons

Grienberger and Konnerth, Neuron, 2012
EEG and MEG Source Imaging

http://www.egi.com

http://www.elekta.com
Functional MRI

From Hyung Joong Kim
Neuronal Source Current

(A) Receptor potential

(B) Synaptic potential

(C) Action potential

\[
t_1, t_2, t_3
\]

Purves et al., 2004

Grimnes and Martinsen, 2008
Magnetic Field by Neuronal Current

Bianciardi, Univ. of Rome, 2004

Xue, Univ. of Iowa, 2008

Luo et al., MRM, 2011
Conductivity Change during Neural Activity

Action Potential (AP)

Compound AP

Impedance

Δσ

Crab Nerve

Current Source

Action Potential
Direct Neuroimaging through Bioelectromagnetism

- Requirements
  - Direct
  - Fast
  - Multi-scale
  - Non-invasive

\[
\begin{align*}
\nabla \cdot (\sigma(r, t) \nabla u(r, t)) &= f(r, t) \text{ in } \Omega \\
-\sigma(r, t) \nabla u(r, t) \cdot \mathbf{n} &= g \text{ on } \partial \Omega \\
J(r, t) &= -\sigma(r, t) \nabla u(r, t) \\
B(r, t) &= \frac{\mu_0}{4\pi} \int_{\Omega} \frac{J(r', t) \times (r - r')}{|r - r'|^3} dr'
\end{align*}
\]

- Simultaneous and separate measurements of bioelectromagnetic parameters
  - (Surface) Voltage
    - (Endogenous) Volume conduction voltage induced by neuronal current: \(< (10 \ \mu V, 1 \ mm, 1 \ ms)\)
    - (Exogenous) Volume conduction voltage induced by injection current: \(< (1 \ mV, 0.1\%, 1 \ mm, 1 \ ms)\)
  - (Internal) Magnetic flux density
    - (Endogenous) Magnetic flux density induced by neuronal current: \(< (0.1 \ nT, 5 \ mm, 1 \ s)\)
    - (Exogenous) Magnetic flux density induced by injection current: \(< (10 \ nT, 3\%, 1 \ mm, 1 \ s)\)
  - (Internal) Conductivity
    - (Passive) Tissue conductivity: \(< (2 \ S/m, 5 \ mm, 0.1 \ s)\)
    - (Active) Conductivity change during neural activity: \(< (5\%, 5 \ mm, 1 \ ms)\)
How far from direct neuroimaging
How far from direct neuroimaging

Imaging Time

- 30 min
- 8 sec

Neural Activity Imaging
- 0.1 nT, 1 sec, 500μA

2009
- 10 nT, 30 min, 9 mA

2013
- 1 nT, 8 sec, 1 mA

Multi-channel RF coil
- Fast MREIT pulse sequence
- Phase optimization
- Constant current source

2013
- Ultra fast pulse sequence
- Extra B0 shimming
- k-space sampling
- Contrast agent

Imaging Current
- 1 mA
- 9 mA
How to overcome limitations

• Measurement
  • Measurements of directly influenced parameters
  • Surface voltage (endo- and exo-), internal magnetic flux density (endo- and exo-), conductivity
  • SNR (signal, noise, sensitivity, specificity)

• Processing
  • Multi-scale models of neuron, bi-domain, and volume conduction
  • *A priori information* (physiology, structure, other images and signals)

• Use of time
  • Repeated recordings (real-time, time-division recordings)
  • Retrospective and model-based data synthesis
Summary
From Physiology to Pixel

- Physiology and pathology
- Clinical specialty
- Bioelectromagnetism (conduction, polarization, dispersion, etc)
- Composition and molecular structure
- Ion concentration and mobility
- Extra- and intra-cellular fluids
- Cell membrane, shape and density
- Tissue structure
- Maxwell's equations
- Partial differential equation
- Volume conduction
- Point-wise admittivity
- Volume-wise or effective admittivity

- Human interface and electrode contact
- Electrode configuration
- Probing current (amplitude and frequency)
- Data collection protocol
- Apparent admittivity and calibration
- Electronics, SNR, CMRR, RE, stability
- Numerical method and programming
- Modeling error in 3D
- Sensitivity and nonlinearity
- Linearization
- Reconstruction algorithm
- Post-processing method
Research Directions

• Micro-EIT
  • Tissue Culture (Non-invasive, Long-term, Label-free)
  • Cell Function (Non-invasive, Long-term, Label-free)

• EIT
  • Upper Air Way Apnea (for Surgery Plan)
  • Regional Ventilation (with Ventilator)
  • Cardiac Function (with Patient Monitor)
  • Acute Stroke Type (Ischemia or Hemorrhage)
  • Non-destructive Testing (such as Process Tomography and Pressure Imaging)

• TAM
  • Breast Tumor (Adjunct Use with X-ray Mammography)

• MREIT
  • Tumor (Early Stage)
  • Electromagnetic Therapy Planning and Monitoring (Ablation, DBS, tDCS, Electroporation)
  • Neural Activity (Direct Functional Neuroimaging)
International Collaborations

- Soleimani Manuchehr
  EIT, fEIT
  Univ. of Bath
  UCL
  Univ. of Stuttgart
  Ecole Polytech.
  Univ. of Ljubljana

- Damijan Miklavcic
  Electroporation
  Univ. of Ljubljana

- David Holder
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  Univ. of Minnesota
  Florida State Univ.
  Arizona State Univ.

- Zijun Liu
  Image reconstruction
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  MUST
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For more information

**Nonlinear Inverse Problems in Imaging**
Authors: J K Seo and E J Woo  
Year: 2013  
ISBN: 978-0-470-66942-6  
Publisher: [WILEY](#)

**Electro-Magnetic Tissue Properties MRI**
Authors: J K Seo, E J Woo, U Katcher and Y Wang  
Year: 2014  
ISBN: 978-1-78326-339-4  
Publisher: [Imperial College Press](#)
Acknowledgements

• Researchers at Impedance Imaging Research Center (IIRC)
  • Mathematicians
  • Engineers
  • Biologists and clinicians

• International Collaborators

• National Research Foundation (NRF) of Korea
  • Impedance Imaging Research Center (IIRC)
  • Ion Conduction Imaging Group

• Kyung Hee University
EOD