The Magnetocardiogram, Tissue Anistropy, and the Cardiac Bidomain

John Wikswo
Franz Baudenbacher
Living State Physics Group
Vanderbilt University
Nashville, TN 37235 USA
The First Clinical VMCG Machine

Vector Magnetocardiography
Stanford
~1974
Questions Regarding the MCG

Information Content?
• Does the MCG contain information not present in the ECG?

The Inverse Problem
• There is no unique solution to the ECG, MCG, or ECG-MCG inverse problem. What role do Silent Sources play?
The uniform double-layer model

- Assumes
  - Uniform thickness
  - Uniform strength
  - Current perpendicular to the wave front

- Dipole moment and potential \( V(r) \) are determined by the solid angle subtended by the double-layer rim
The electric and magnetic heart vectors

- $m = \frac{1}{2} r \times p$ explains relation of electric and magnetic vectors
- Double-layer rim determines both $m$ and $p$
- Little significant new information in the MCG...?

1 millimeter: Cardiac fiber sheets
It’s the anisotropy...
Cardiac fiber orientation is the source of the new information

- Circulating current components are electrically silent
- Only magnetic fields can distinguish between two possible models

The cardiac syncytium: A three-dimensional non-linear anisotropic bidomain

It’s the anisotropy....
2-D Bidomain Equations

- Homogenized
- Coupled $V_m$ & $V_e$
- Nonlinear reaction-diffusion equation
- Boundary value equation

\[
C_m \frac{\partial V_m}{\partial t} = -J_{ion} - \frac{1}{\beta} \nabla \cdot \tilde{g}_e \nabla V_e ,
\]

\[
\nabla \cdot (\tilde{g}_i + \tilde{g}_e) \nabla V_e = -\nabla \cdot \tilde{g}_i \nabla V_m ,
\]

where $\tilde{g}_i$ and $\tilde{g}_e$ are the intracellular and extracellular conductivity tensors; $\beta$ is the ratio of membrane surface area to tissue volume (0.3 $\mu$m$^{-1}$); $C_m$ is the membrane capacitance per unit area (0.01 F/m$^2$); and $J_{ion}$ is the membrane current per unit area.
The Cardiac Bidomain

- Intra- and extracellular spaces have unequal anisotropies in their electrical conductivities. Really?
  - Magnetic fields
  - Virtual electrodes
  - Quatrefoil reentry
  - Defibrillation?
Recording from the Bidomain

- **Extracellular potential**
  - Extracellular electrode arrays (≤1250)
- **Intracellular potential**
  - Intracellular microelectrodes (≤2)
- **Membrane potential**
  - Voltage-sensitive fluorescent dyes (256 – 10,000)
- **Net action currents**
  - Scanning SQUID microscope (1)
Optical Imaging of the Transmembrane Action Potential During Stimulation, Reentry, Fibrillation, and Defibrillation

- Langendorff-perfused rabbit heart
- Voltage-sensitive dye in membrane measures $V_m$
- Laser illumination
- High-speed charge-coupled-device (CCD) camera
Vanderbilt cardiac imaging system

Verdi diode-pumped solid-state laser

Di-4-ANEPPS voltage dye

Light delivered by bundles of optical fibers

Dalsa CCD camera:
- 12 bit
- 64x64 pixels
- 1200 frames/sec

10 x 5 x 7.5 cm³ bath

37 °C Tyrode’s solution
Gus2: MATLAB Data Viewing Program

Four S2 frames indicated by LED

Written by Gustavo Rohde
Injecting -20 mA into Equal-Anisotropy Cardiac Tissue

- Point cathodal stimulation
- Virtual cathode depolarizes (red)
- Wave front propagates from the edge of the virtual cathode (yellow)
Bidomain Anisotropy

There is no single coordinate system in which the tensor conductivity is everywhere diagonal!

\[
\begin{align*}
\sigma_{ix} & = 0.2 \text{ S/m} \\
\sigma_{iy} & = 0.02 \text{ S/m} \\
\sigma_{ex} & = 0.8 \text{ S/m} \\
\sigma_{ey} & = 0.2 \text{ S/m}
\end{align*}
\]

\[
\sigma_{ix} / \sigma_{iy} = 10 \\
\sigma_{ex} / \sigma_{ey} = 4
\]
Virtual electrodes in cardiac tissue

- As a result of unequal electrical anisotropies in intracellular and extracellular spaces:
  - Point cathodal stimulation
  - Virtual cathode depolarizes (red)
  - Virtual anodes hyperpolarize (blue)

Puzzle

Four modes of stimulating cardiac tissue

- **Cathode make** (turn on negative current)
- **Anode make** (turn on positive current)
- **Cathode break** (turn off long negative current)
- **Anode break** (turn off long positive current)

Synchronous Imaging of Point Activation Patterns

--- Virtual Electrodes ---

Cathode Make
-10 mA

Anode Make
+10 mA

Cathode Break
-2 mA

Anode Break
+3 mA

10,000 pixel/frame

Fiber Direction

Depolarized

Hyperpolarized

Optical imaging of quatrefoil reentry

Transmembrane potential distributions from selected frames of a movie for cathodal-break stimulation

Cathodal-Break Isochrones

Anodal-Break Isochrones

Courtesy of Marc Lin

It’s the anisotropy...

Corbin and Scher, 1977
Magnetic Field From a Circular Action LV Free Wall Action Potential:

\[ V_m(x, y) = 52.0 \cdot \tanh \left[ 5.4 \cdot \left( R - \sqrt{x^2 + y^2} \right) \right] - 38 \]
The Apex Will Have a Complicated B Field

SQUID Magnetometers

- Superconducting
- QUantum
- Interference
- Device

- Bandwidth: DC-10 kHz
- Image net action current in x-y plane
- Big, smaller, smallest…
NanoSQUID: Cooled with liquid N\textsubscript{2} and liquid He .......
The SQUID lives in the vacuum space …
Wind a Pickup Coil ....

- Sapphire Bobbin
- 250 – 500 µm
- 25 µm Nb Wire
In Reality ..

- SQUID
- Pickup Coil
- He-Reservoir
- 77K - Radiation Shield
Pickup Coil

5.0 kV x130  231μm

5.0 kV x100  300μm
Image the LV Free Wall ...

- Scanning SQUID microscope
- Isolated rabbit heart
- Point stimulation
- Anisotropy should produce a quatrefoil current pattern
Langendorff-Perfused Isolated Rabbit Heart

15μm Mylar-Foil

Bath
Isolated Rabbit Heart

From Heat Exchanger

Dewar Tail

To Heat Exchanger
MCG From the LV Free Wall

Scan Area

Pixel size 0.16 mm²

Bandwidth = 1 kHz

1 pT ~ B_{earth}/100,000,000
Cathodal Current Injection Followed by Initiation of Action Currents

Stimulus: 5 ms, 1.5 mA

1 ms after Stimulus
Layered Bidomain

Experiment

Total Bidomain Field of 3mm cardiac slice during current injection of 1.5mA z=0.1mm
Propagation of Action Currents

4 ms

10 ms

16 ms
The Magnetic Field From Action Currents in Isolated Cardiac Tissue – The Apex

Stimulus
0.6 mA 5 ms

Near_apex.mpg

Courtesy of Franz Baudenbacher
Forthcoming...

- Measured magnetic field gives current
- Measured $V_m$ gives the voltage
- Model of both requires the bidomain conductivities (Eason and Trayanova)

- Obtain the doubly anisotropic bidomain conductivities by fitting the model to the data
S2- Point Stimulation

Point Electrode

S = 6*Threshold

S2-S1=240 ms

6 ms

12 ms

18 ms
**V_m Isochrones – LV Free Wall**

- **Point Stimulation**
- **Fiber Orientation**

[ventricle_propagation.mpg]
V_m Isochrones - Apex

Point Stimulation

apex_propagation.mpg
Velocities as a function of direction

![Graph showing velocities as a function of direction. The x-axis represents the angle in degrees, ranging from 0 to 350. The y-axis represents the propagation velocity in arbitrary units, ranging from 4 to 24. Two lines are plotted: one for ventricle and one for apex. The ventricle line is shown with a dashed blue line, and the apex line is shown with a solid red line. The graph shows distinct peaks and valleys in the velocity values at different angles.](image_url)
SQUID Senses Spatial $V_m$ Gradients

Repolarization

Injury Currents
Gradients in Repolarization

Magneto Cardio Gram

-0.05 -0.04 -0.03 -0.02 -0.01 0 0.01 0.02 0.03 0.04 0.05

pixel (14,5)

pixel (20,5)

repolarization.mpg
Dipole Signature in ST-segment

71 ms
Information Content of the MCG

• Evidence that electrically silent sources exist.

• Magnetic mapping can provide images of net action current in cardiac tissue.

• Combined electric and magnetic measurements can provide the anisotropic conductivities and the non-linear membrane properties.

• A dimensional biodomain model combined with a realistic fiber architecture may provide a better understanding of the MCG.

• MCG allows probing of gradients in repolarization and resting potentials (injury currents).
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