The Magnetocardiogram, Tissue Anistropy, and the Cardiac Bidomain

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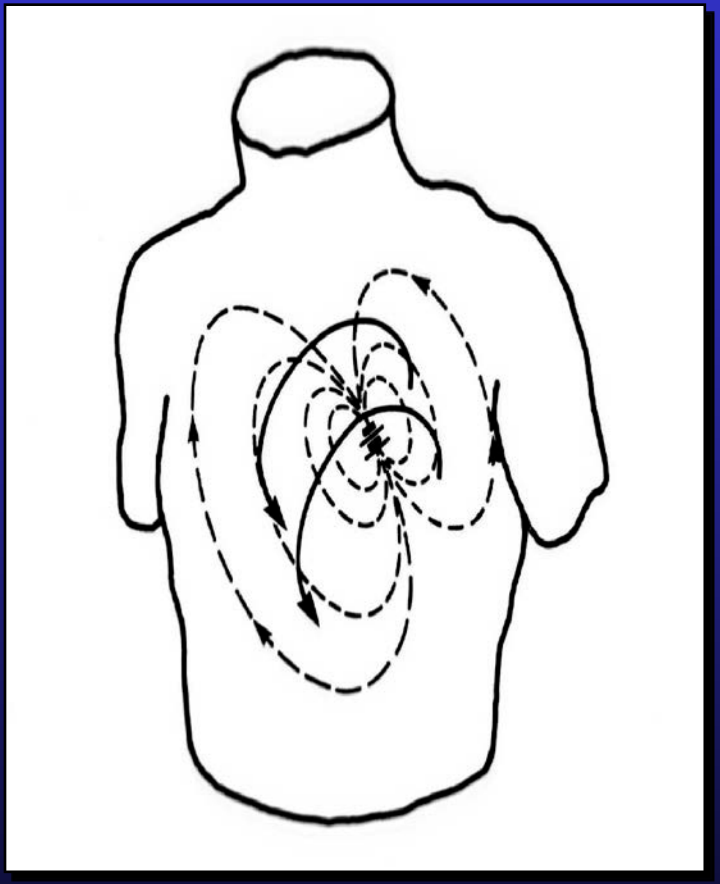
1 meter

The First Clinical VMCG Machine

Vector Magnetocardiography
Stanford
~1974

Questions Regarding the MCG



Information Content?

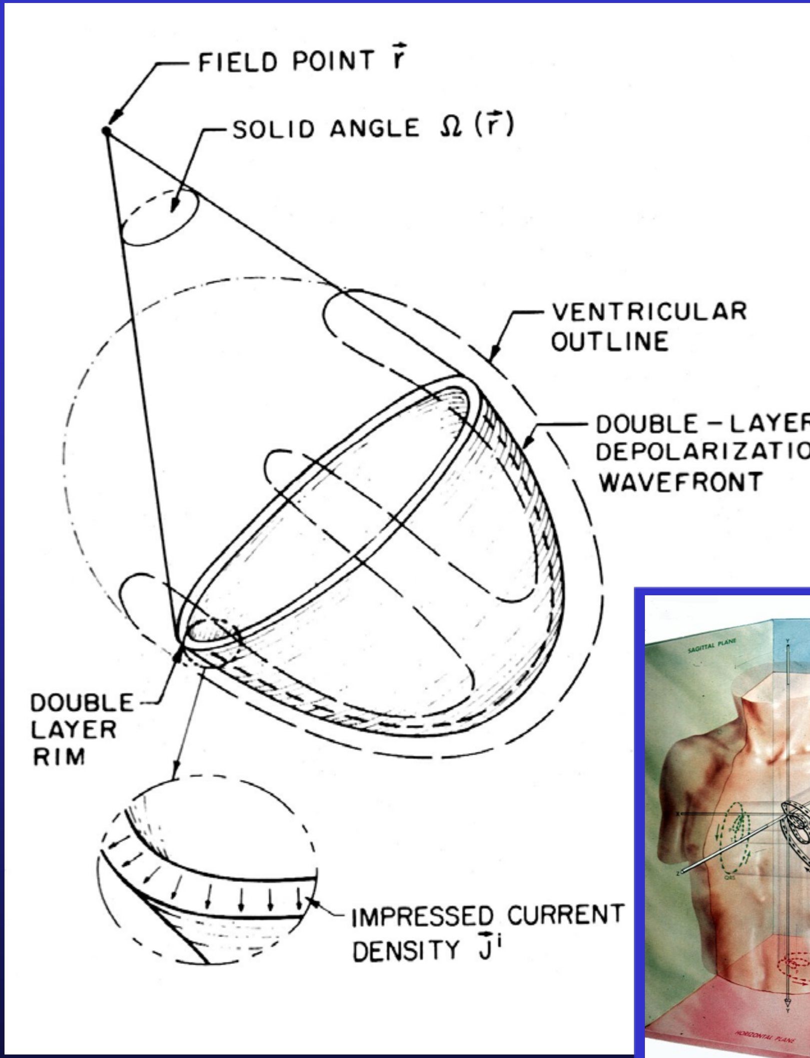
- Does the MCG contain information not present in the ECG?

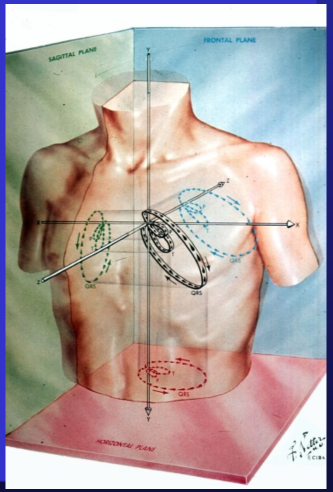
The Inverse Problem

- 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





Heart vector or dipole moment versus time

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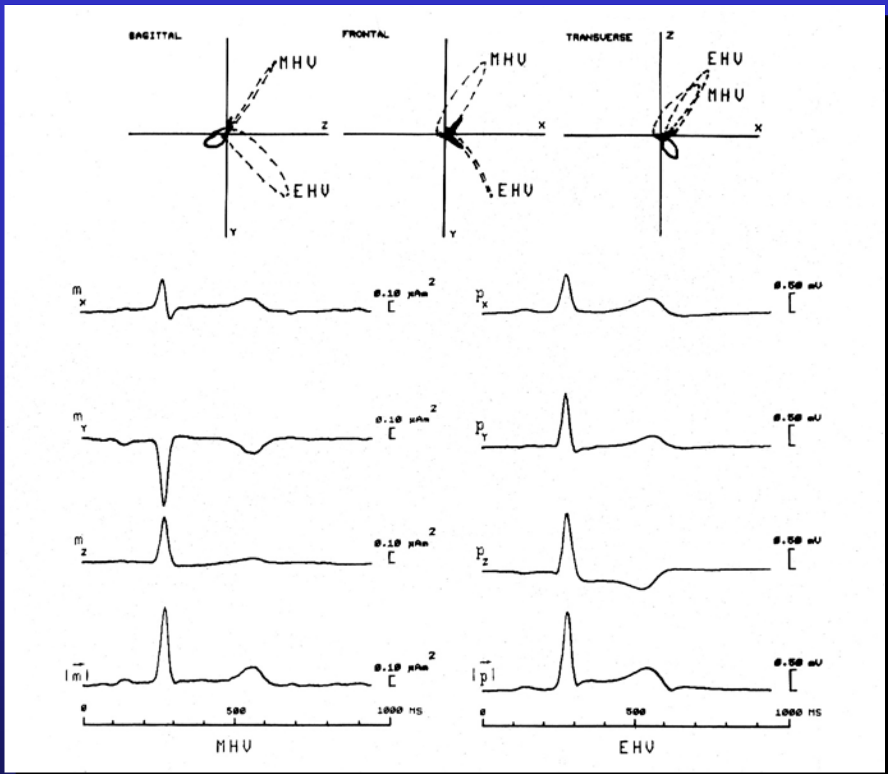
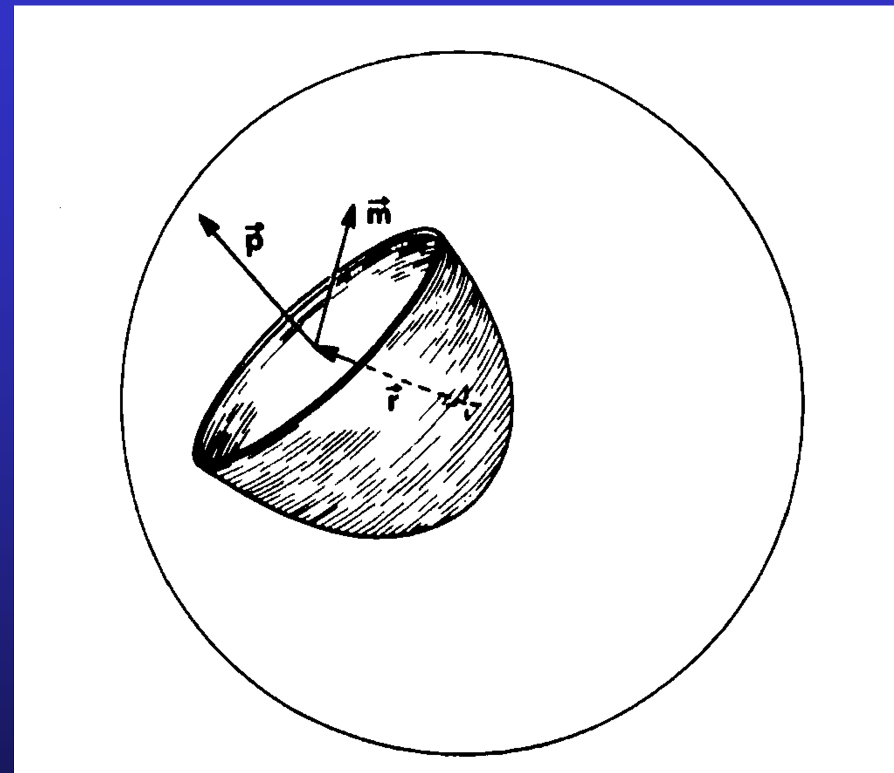
10 centimeters

The electric and magnetic heart vectors



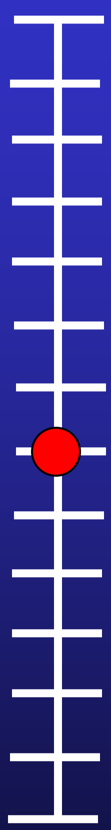


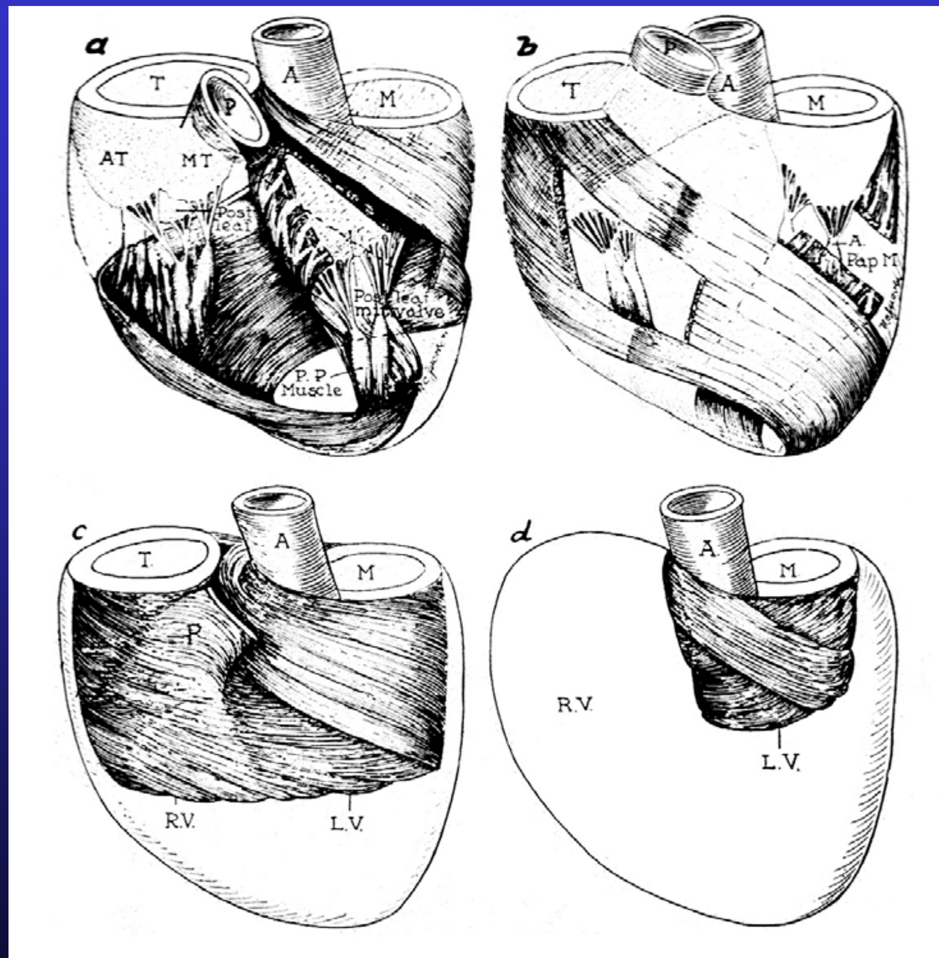
- m = ½ $r \times p$ explains relation of electric and magnetic vectors
- Double-layer rim determines both *m* and *p*
- Little significant new information in the MCG…?

W.H. Barry, et al., Science, 198: 1159-1162 (1977);; Cardiovascular Physics, Karger, Basil, 1979, pp. 1-67.

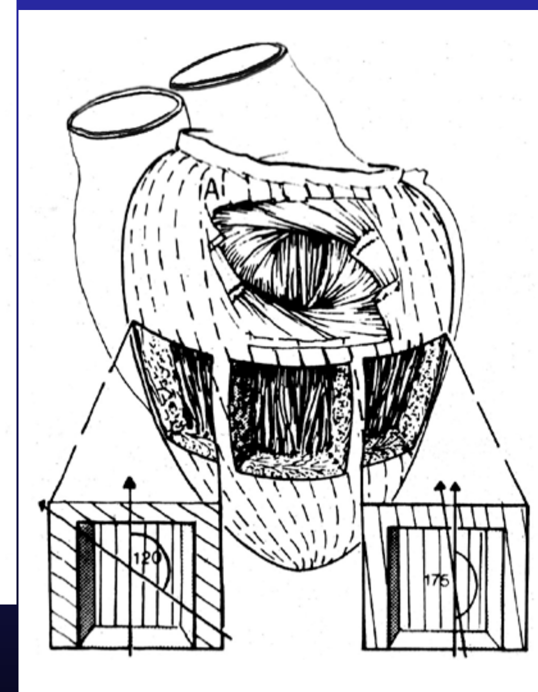
s0338 s0159

1 millimeter: Cardiac fiber sheets





s00397



S00703

s02734

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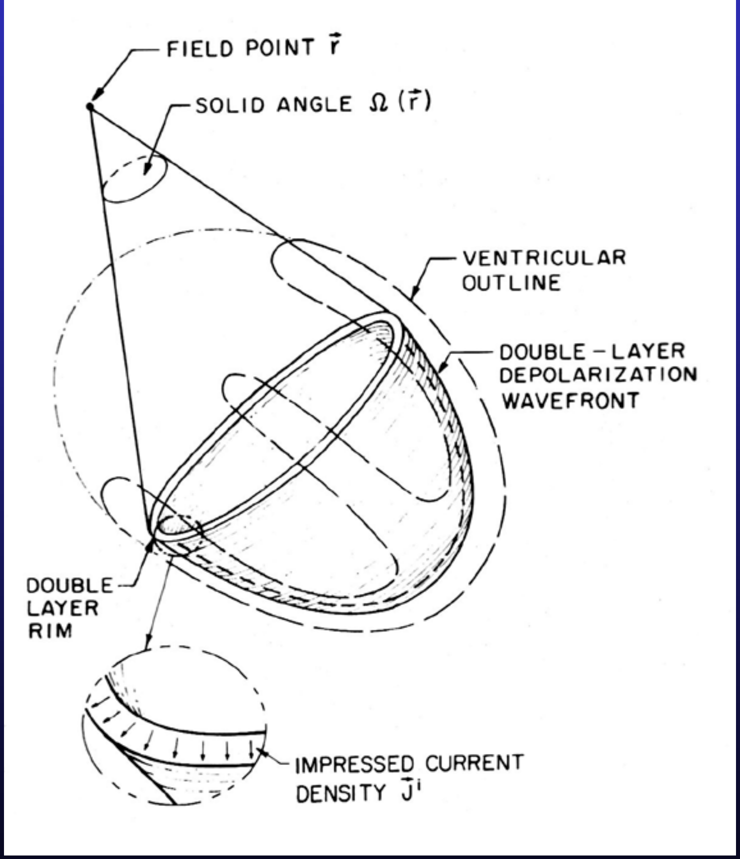
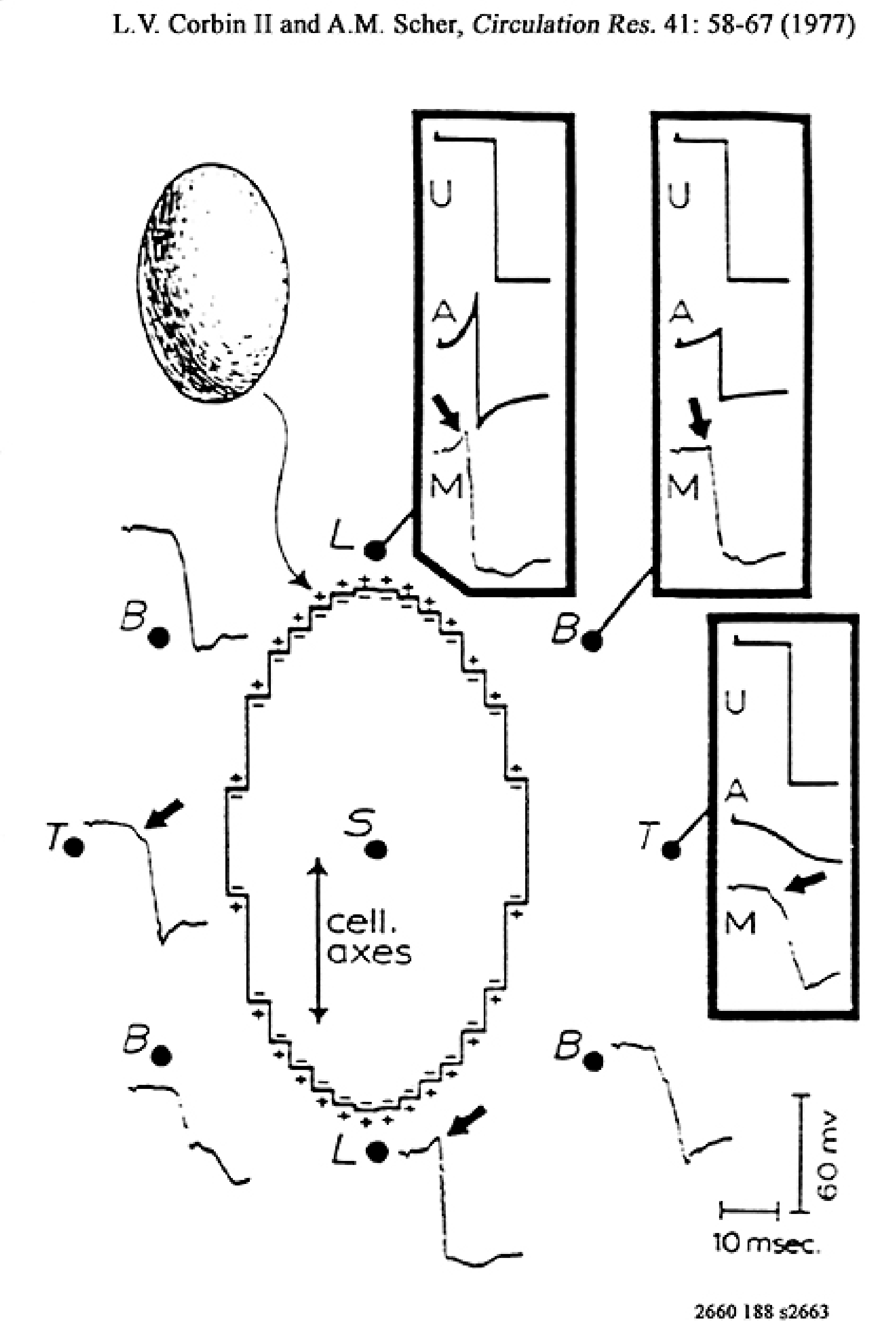
It's the anisotropy…

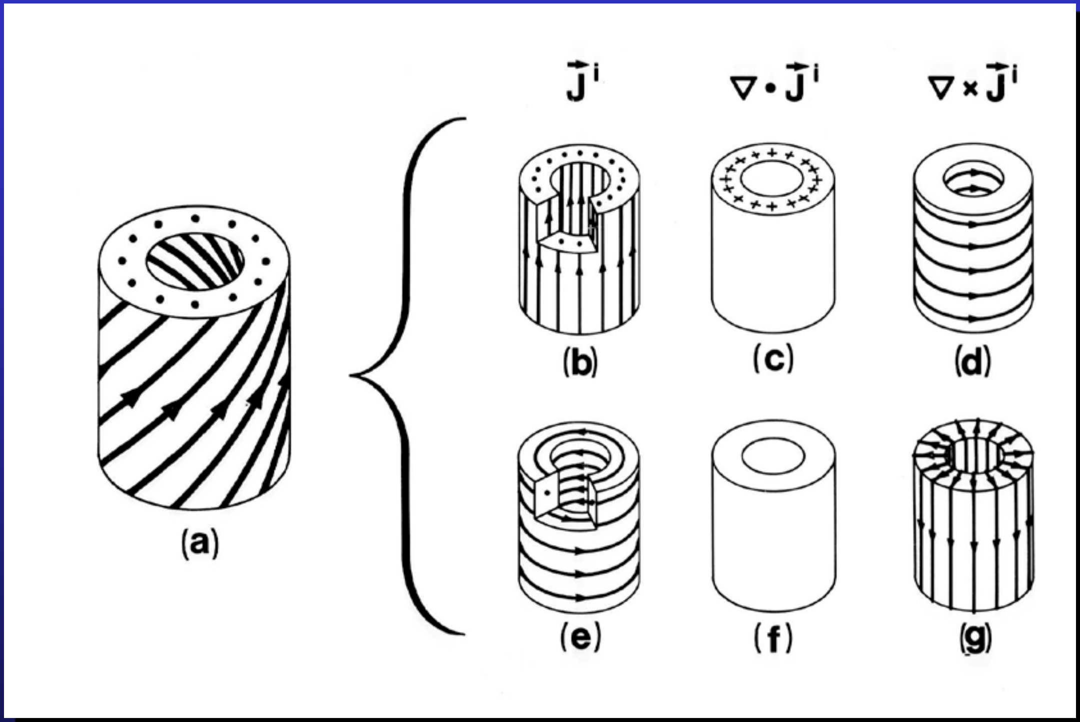


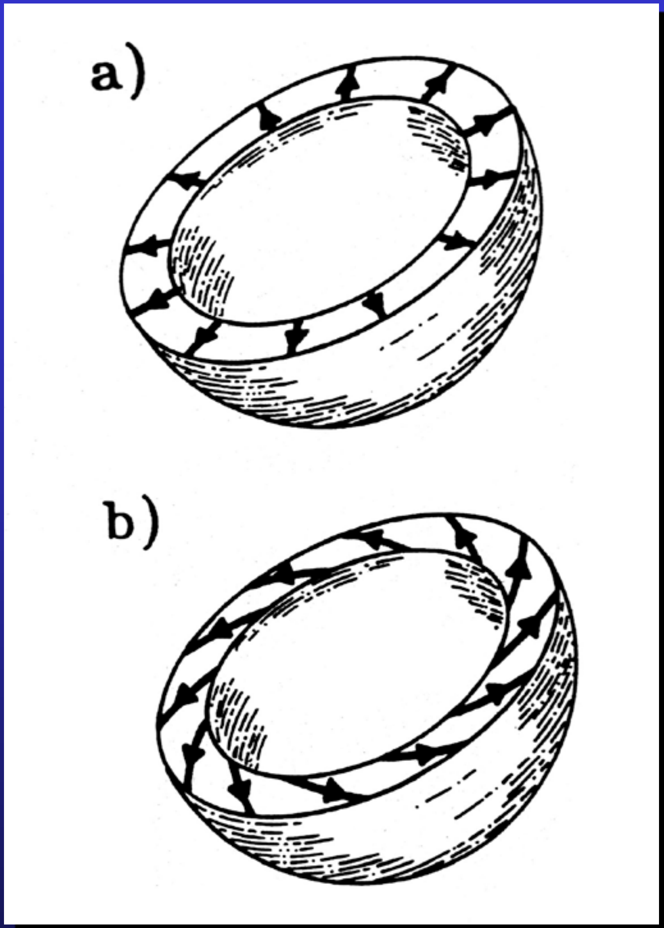


Corbin and Scher, 1977

10 centimeters

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

Wikswo and Barach, J. Theoretical Biol., 95: 721-729 (1982)

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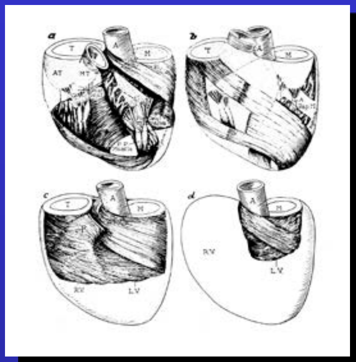
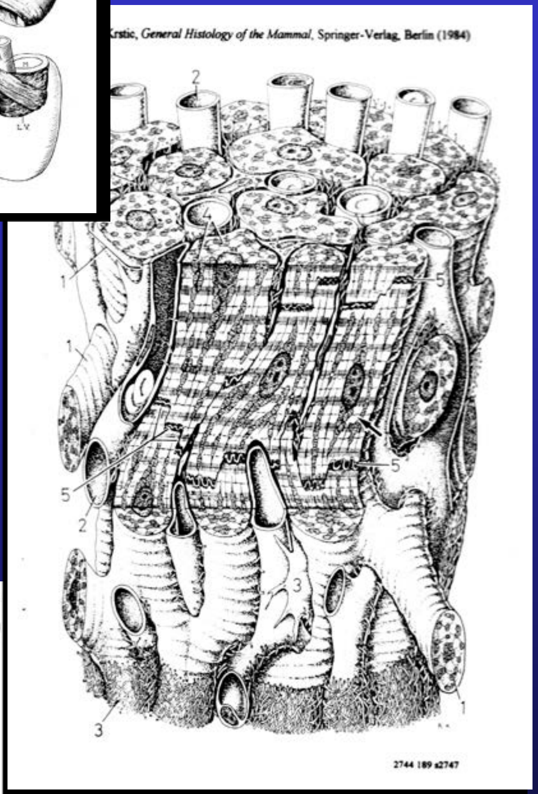
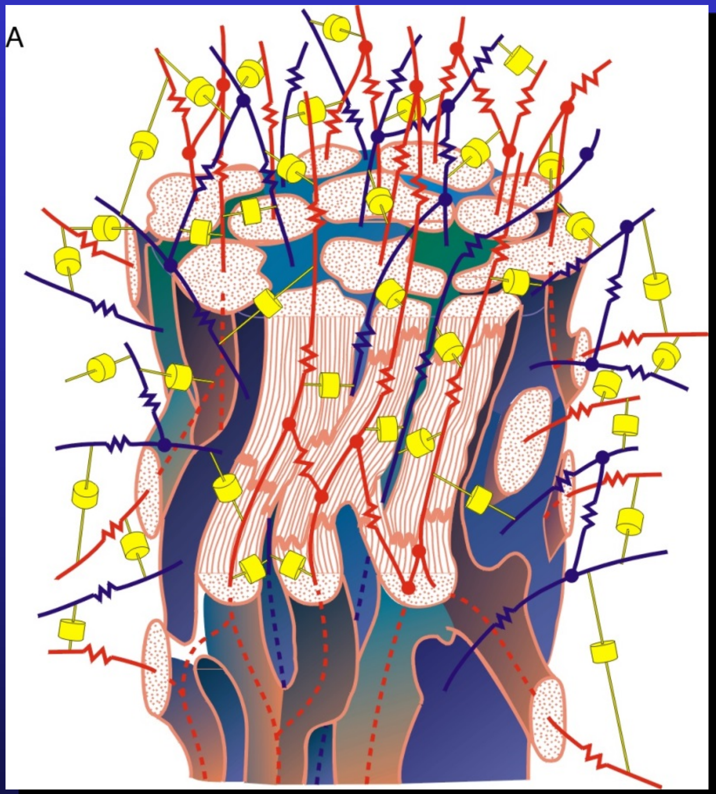
1 millimeter

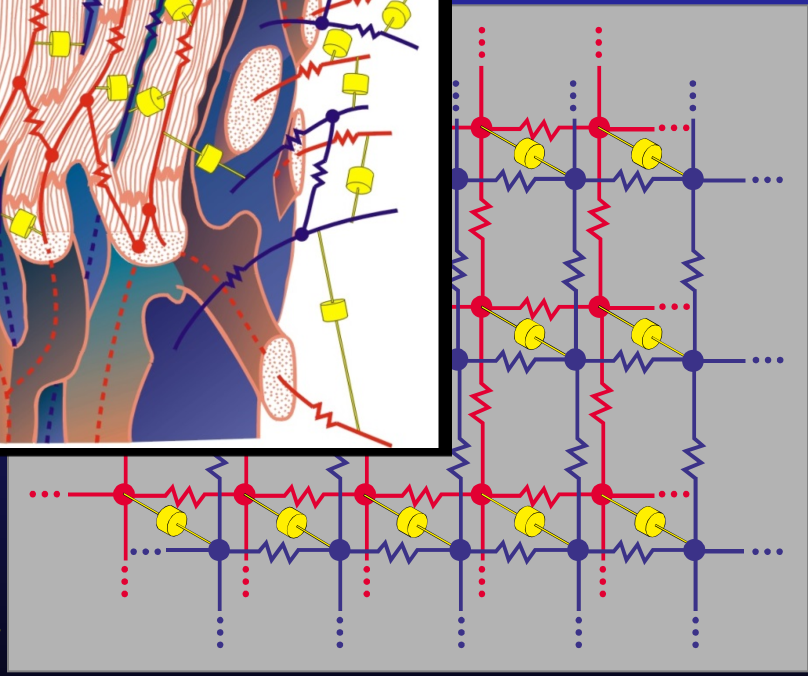
The cardiac syncytium: A three-dimensional non-linear anisotropic bidomain

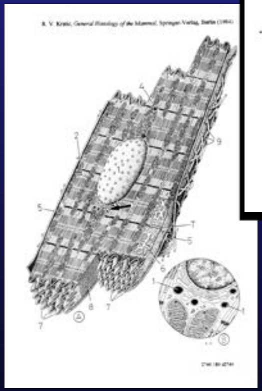






3-D
vs.
2-D





It's the anisotropy….

2-D Bidomain Equations

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

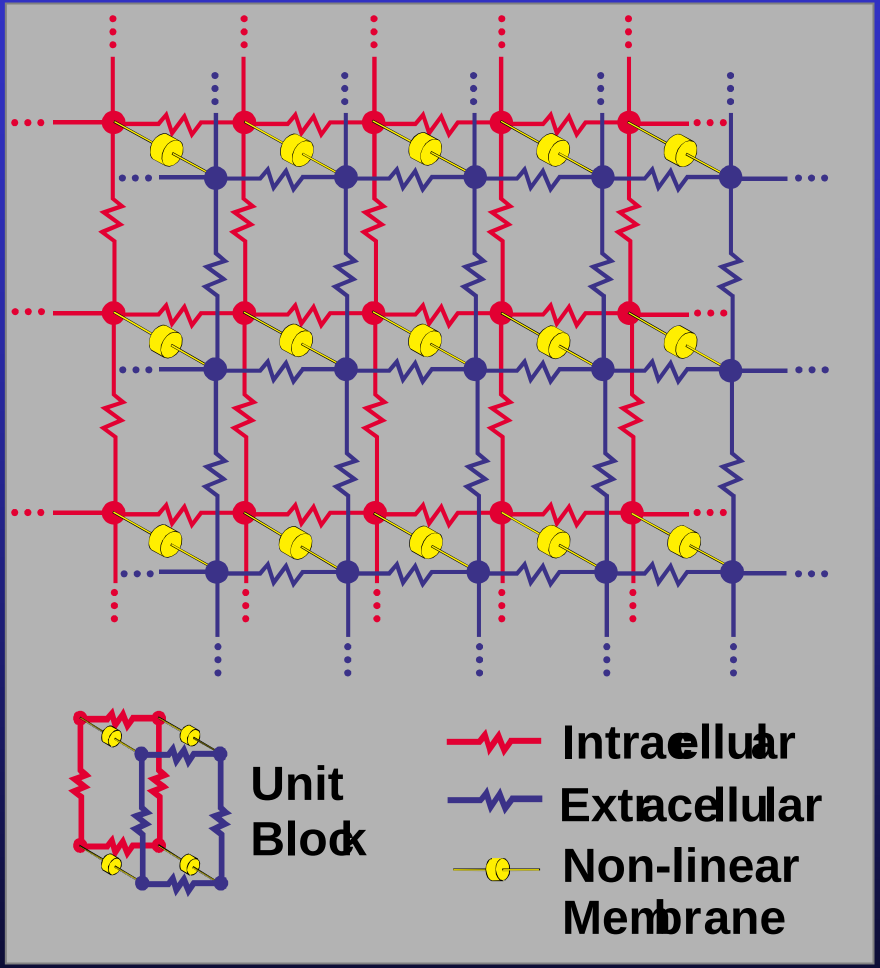
$$C_m \frac{\partial V_m}{\partial t} = -J_{ion} - \frac{1}{\beta} \nabla \bullet \tilde{g}_e \nabla V_e \quad ,$$

$$\nabla \bullet \left(\tilde{g}_i + \tilde{g}_e \right) \nabla V_e = -\nabla \bullet \tilde{g}_i \nabla V_m \, ,$$

where $\tilde{g}_i$ and $\tilde{g}_e$ are the intracellular and extracellular conductivity tensors; β 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?

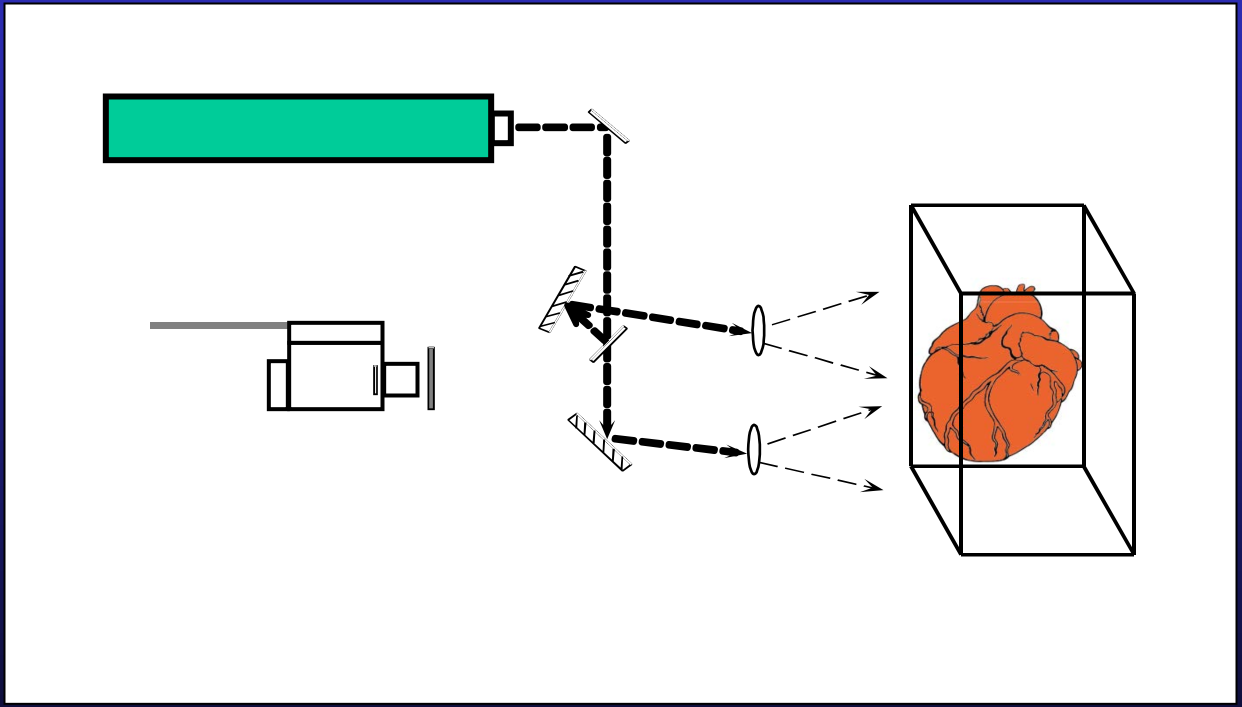


Recording from the Bidomain

- Extracellular potential
  - Extracellular electrode arrays ($\leq$1250)
- Intracellular potential
  - Intracellular microelectrodes ($\leq$ 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



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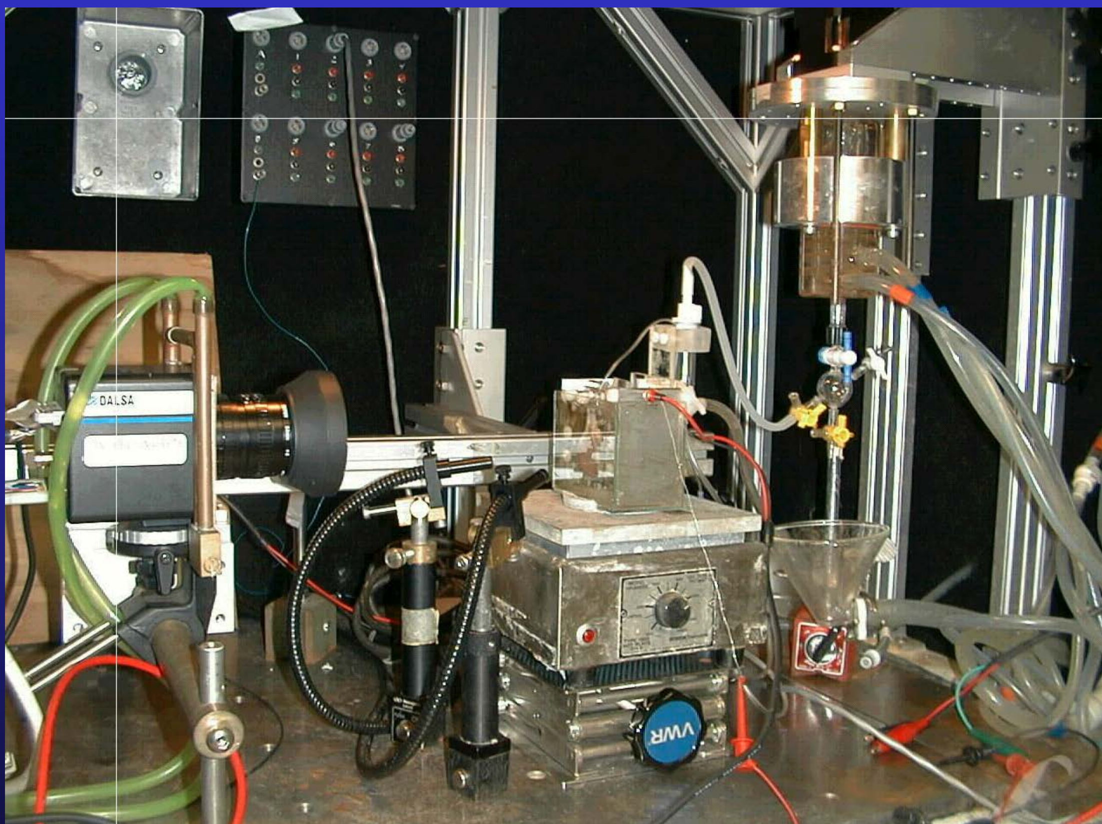
Vanderbilt cardiac imaging system



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 cm^3 bath

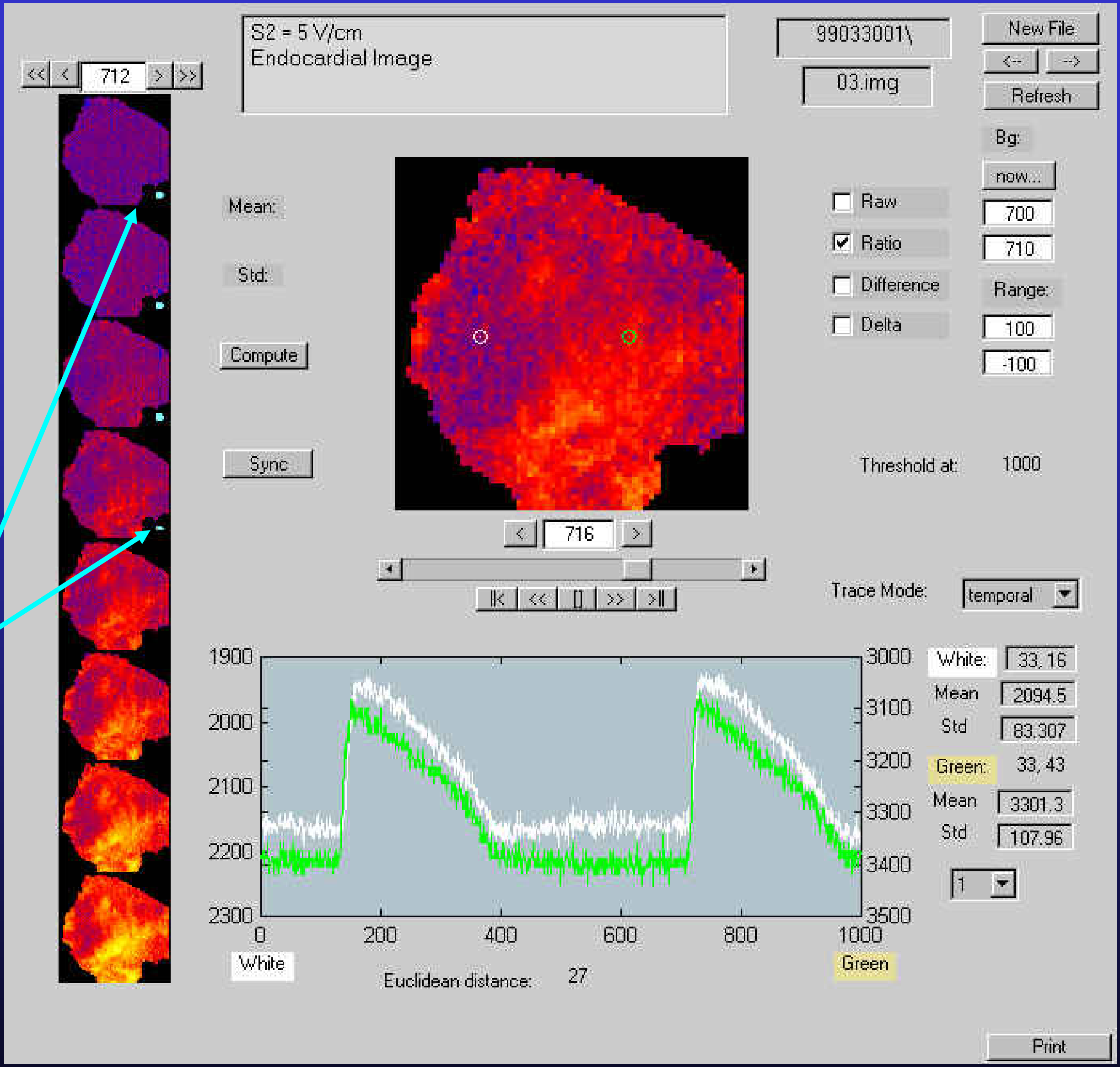
37 ^{o}C Tyrode's solution

Gus2:

MATLAB
Data Viewing
Program

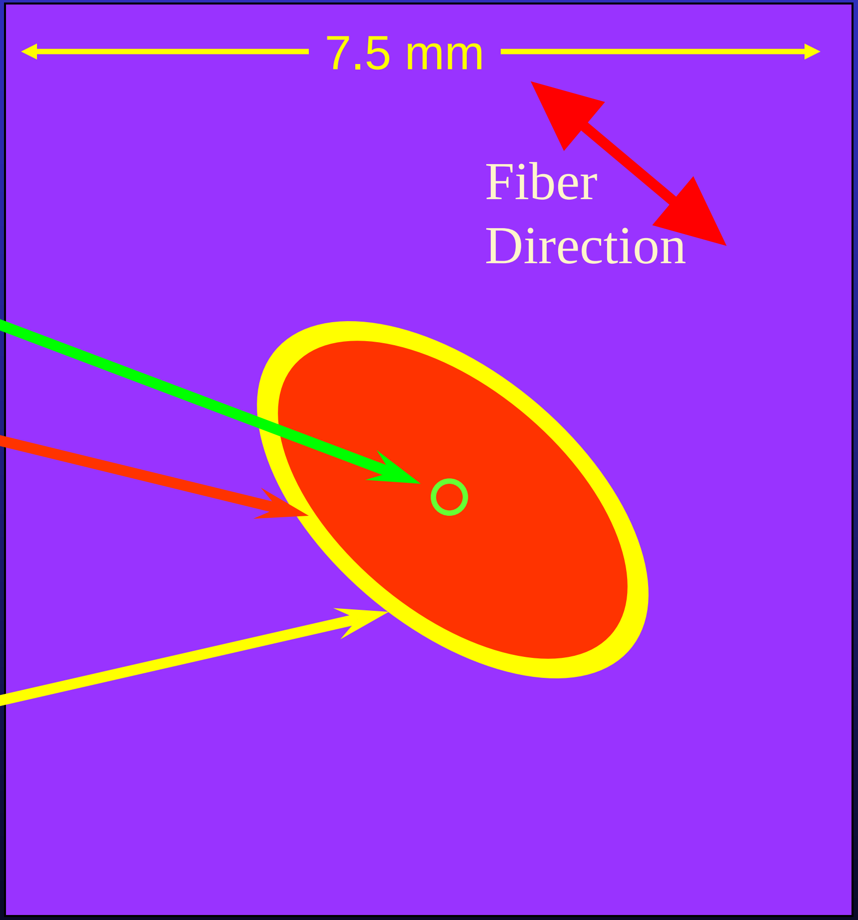
Four S2 frames indicated by LED

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)



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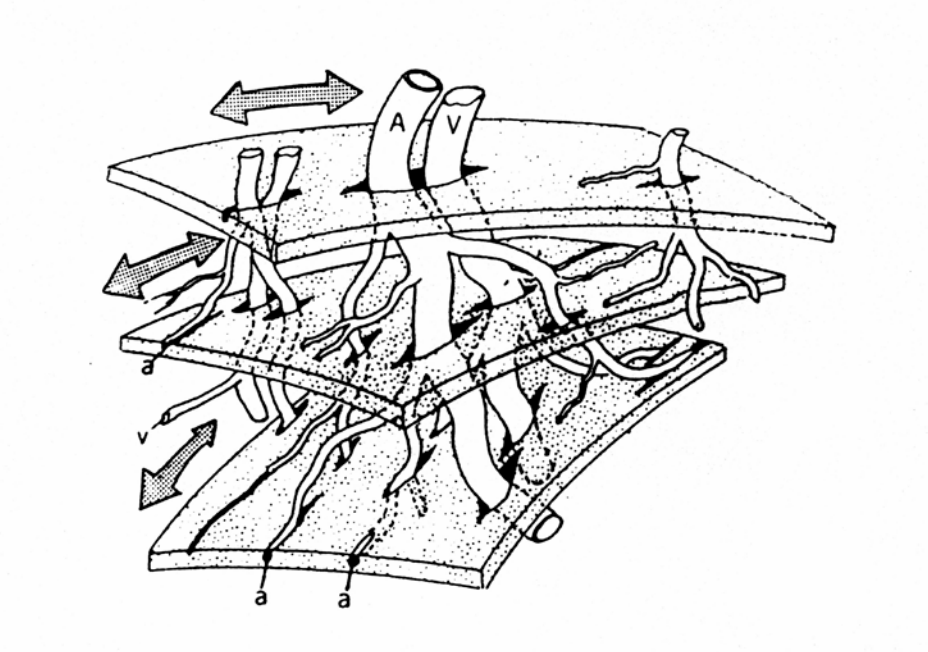
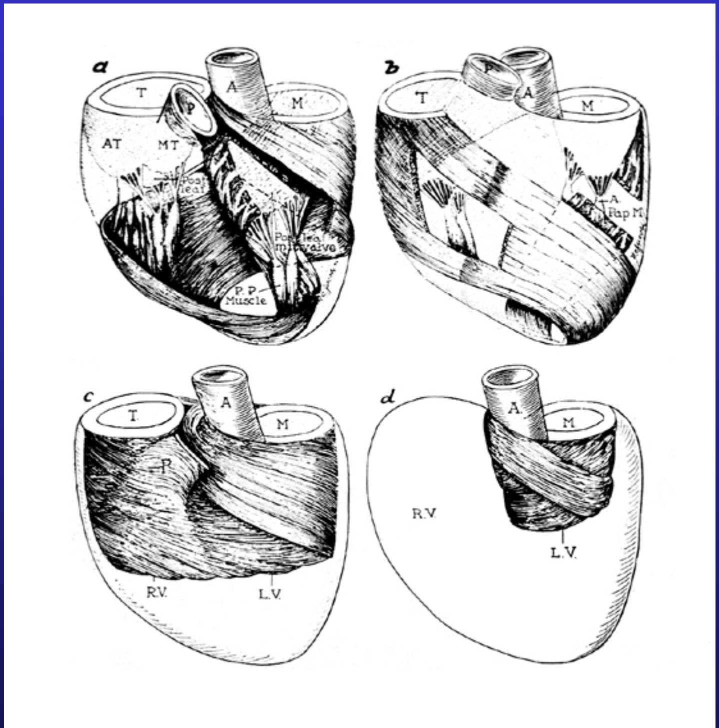
Bidomain Anisotropy





σ_{ix} 0.2 S/m

σ_{iy} 0.02 S/m

σ_{ex} 0.8 S/m

σ_{ey} 0.2 S/m

$\sigma_{ix} / \sigma_{iy} = 10$

$\sigma_{ex} / \sigma_{ey} = 4$

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

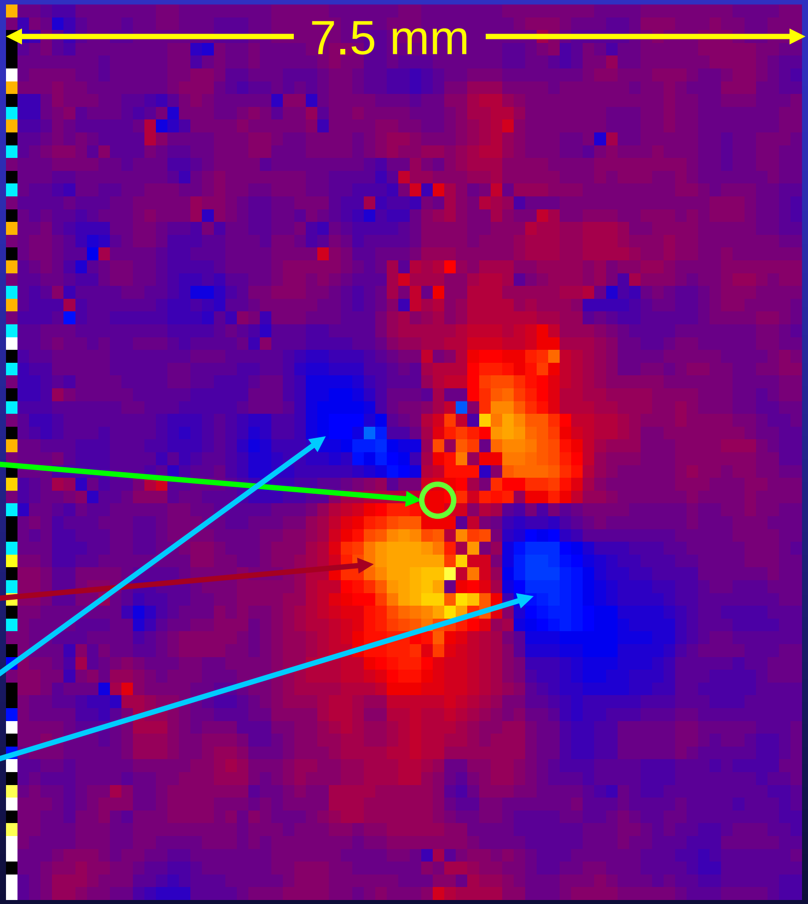
s0704

s1325

1 millimeter

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)



Wikswo, Lin and Abbas. *Biophys. J.* 69 :2195-2210, 1995

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)

Dekker, E. "Direct current make and break thresholds for pacemaker electrodes on the canine ventricle." Circ Res, 27:811, 1970

1 millimeter

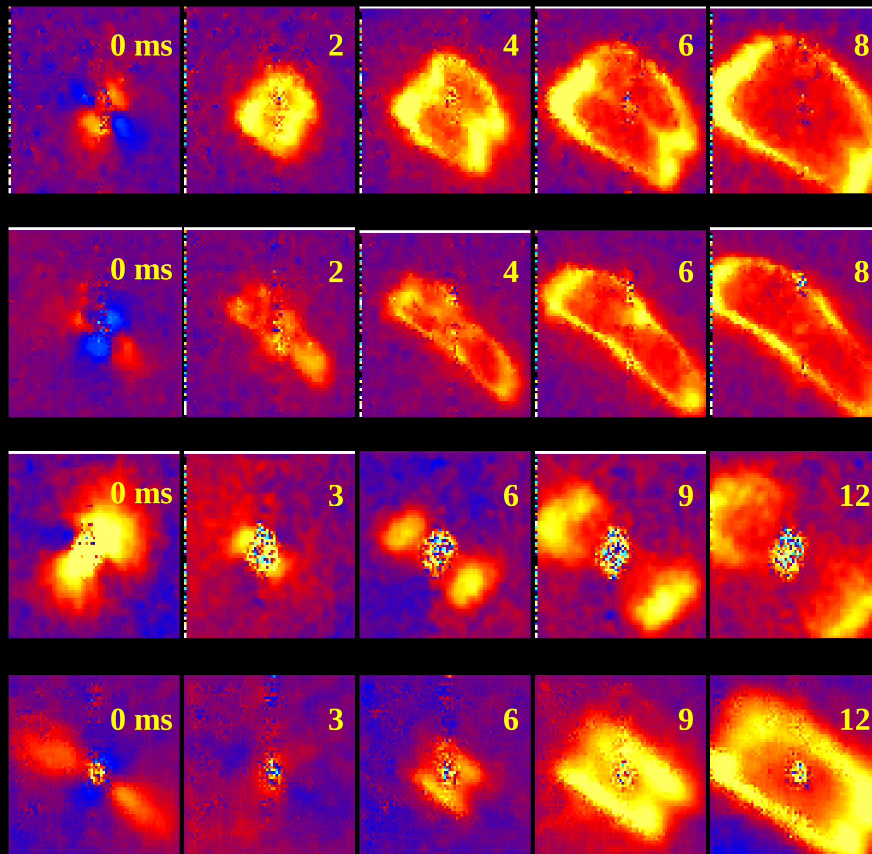
Synchronous Imaging of Point Activation Patterns
--- Virtual Electrodes ---

Cathode Make -10 mA

Anode Make +10 mA

Cathode Break -2 mA

Anode Break +3mA

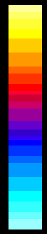


1 mm

10,000 pixel/frame

Fiber Direction

Depolarized



Hyperpolarized

Wikswo, Lin and Abbas. *Biophys. J.* 69 :2195-2210, 1995

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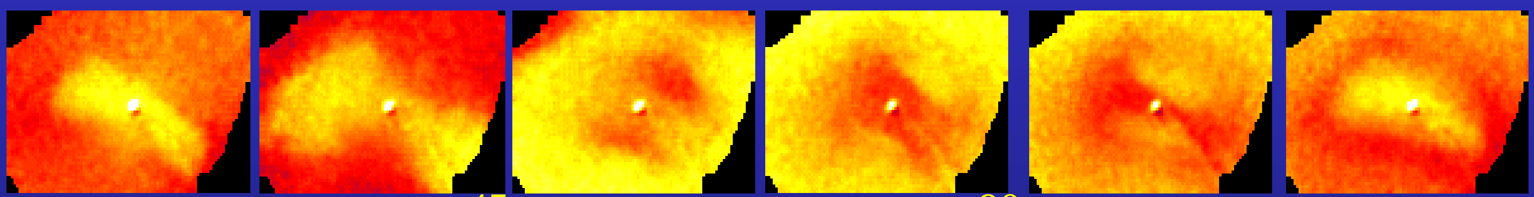
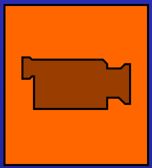
1 millimeter

Optical imaging of quatrefoil reentry

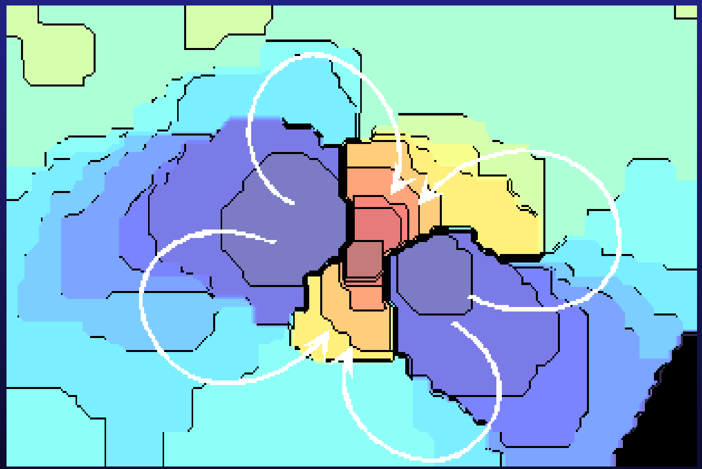
Transmembrane potential distributions from selected frames of a movie for cathodal-break stimulation

Vm_expt.mpg

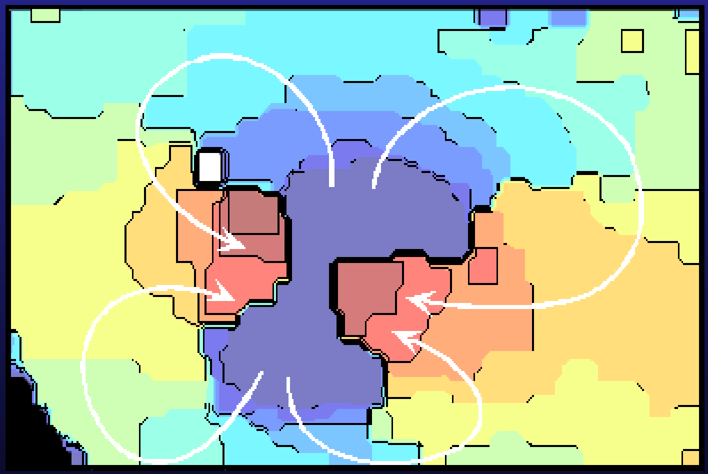




Cathodal-Break Isochrones



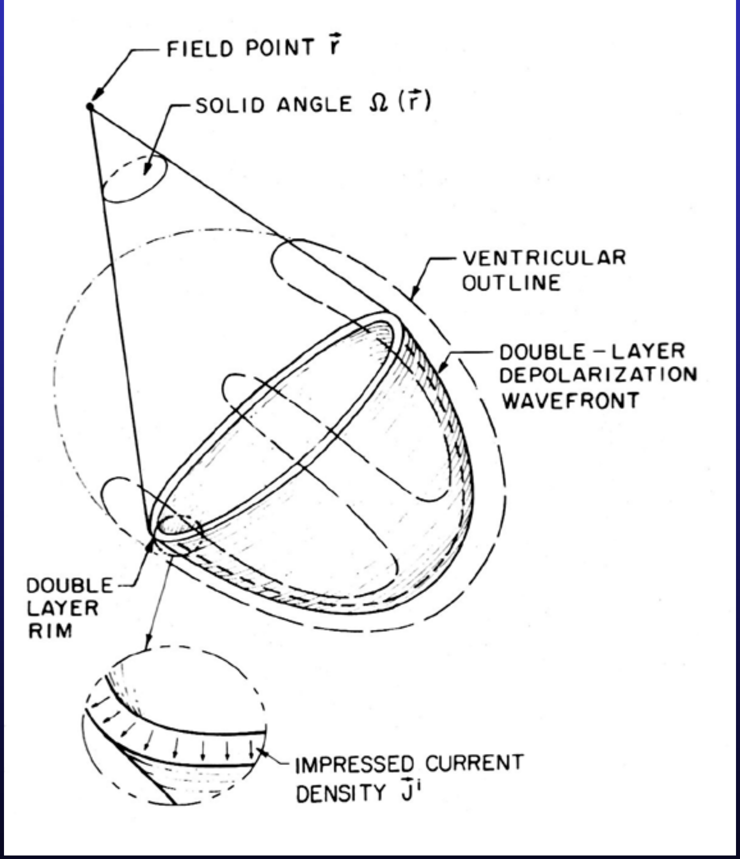
Anodal-Break Isochrones



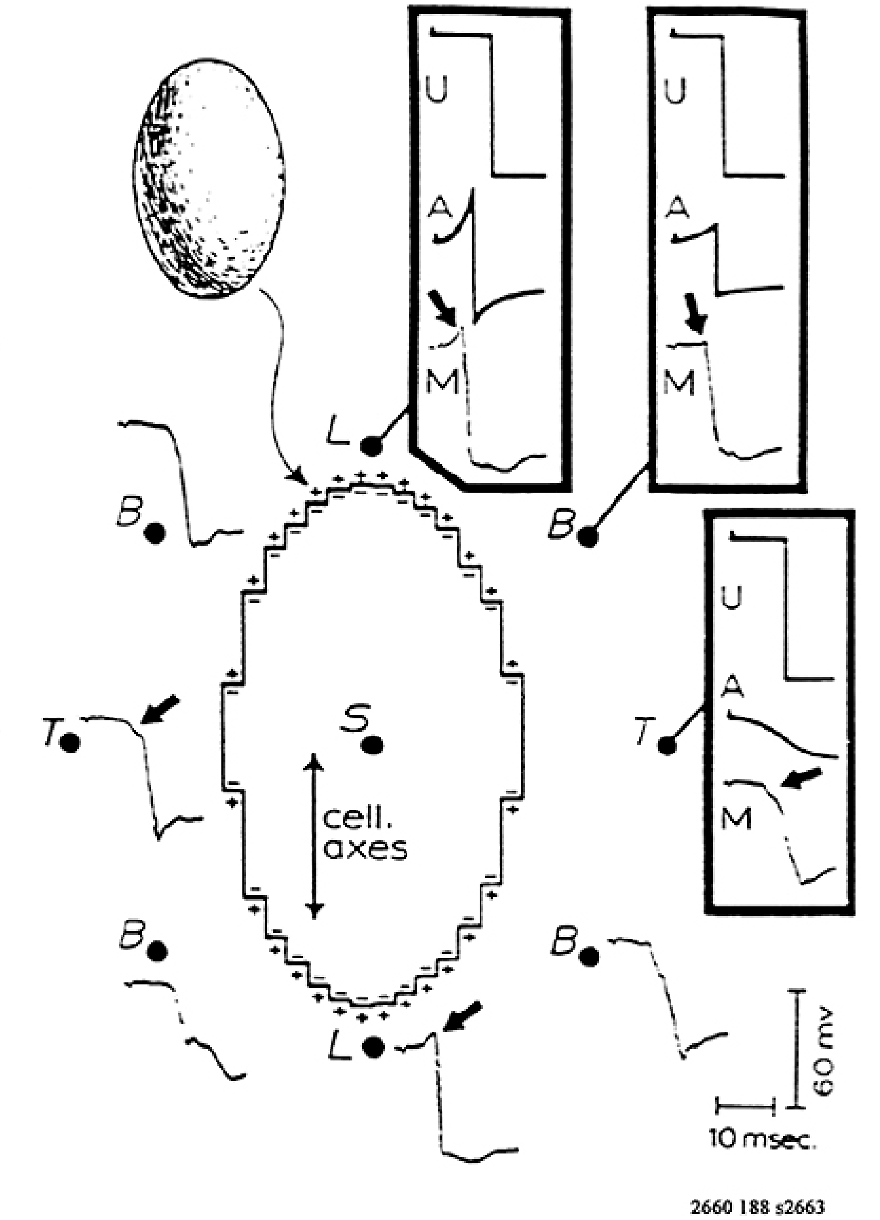
Courtesy of Marc Lin

Lin, Roth, and Wikswo, J. Cardiovasc. Electrophysiol., 10: 574-586 (1999)

It’s the anisotropy…



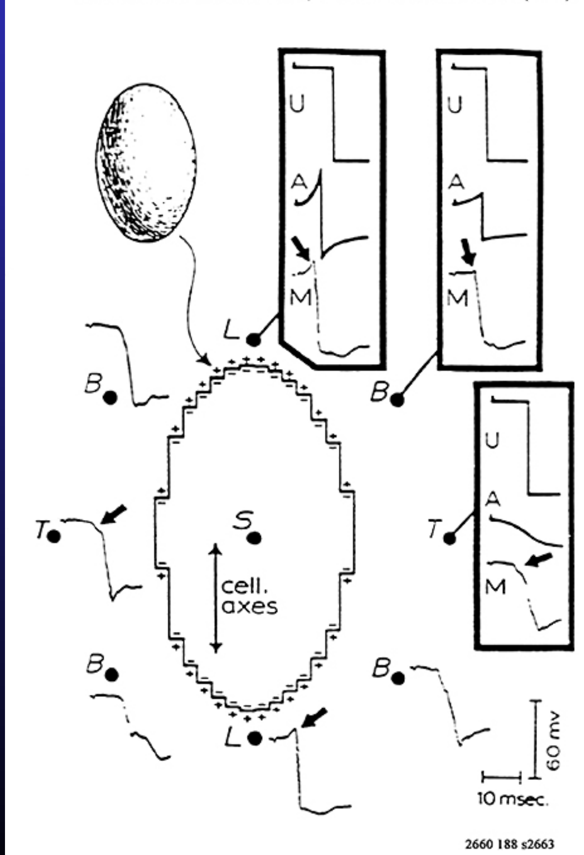
L.V. Corbin II and A.M. Scher, *Circulation Res.* 41: 58-67 (1977)

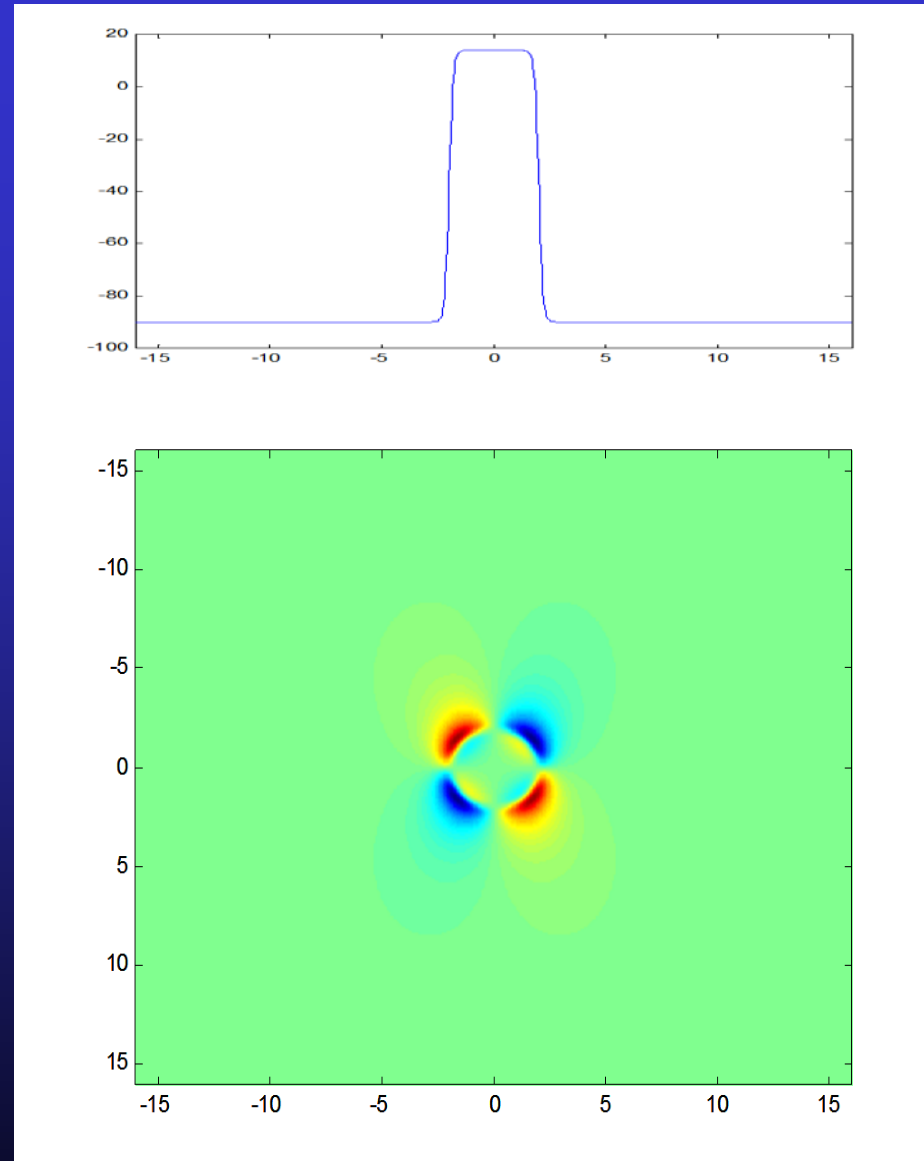


Corbin and Scher, 1977

Magnetic Field From a Circular Action LV Free Wall Action Potential:

L.V. Corbin II and A.M. Scher, *Circulation Res.* 41: 58-67 (1977)





$$V_m(x,y) = 52.0 \cdot \tanh\left[5.4 \cdot \left(R - \sqrt{x^2 + y^2}\right)\right] - 38$$

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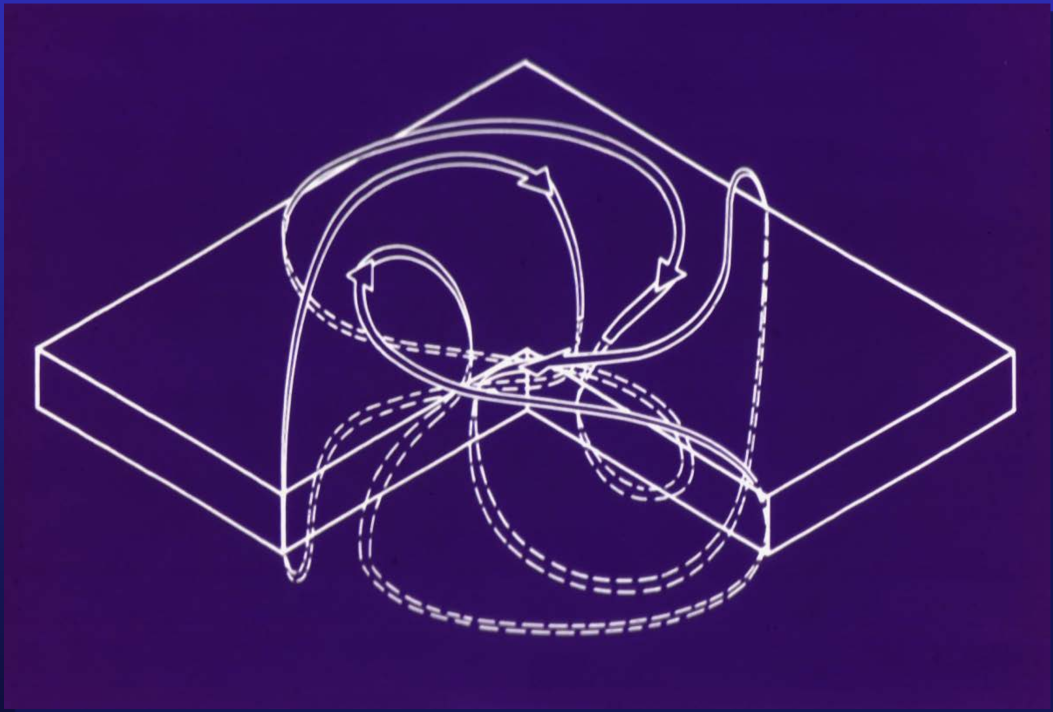
10 centimeters

The Apex Will Have a Complicated B Field



Roth and Wikswo, Biophys. J., 50: 739-745 (1986)

s1157

s1151

SQUID Magnetometers

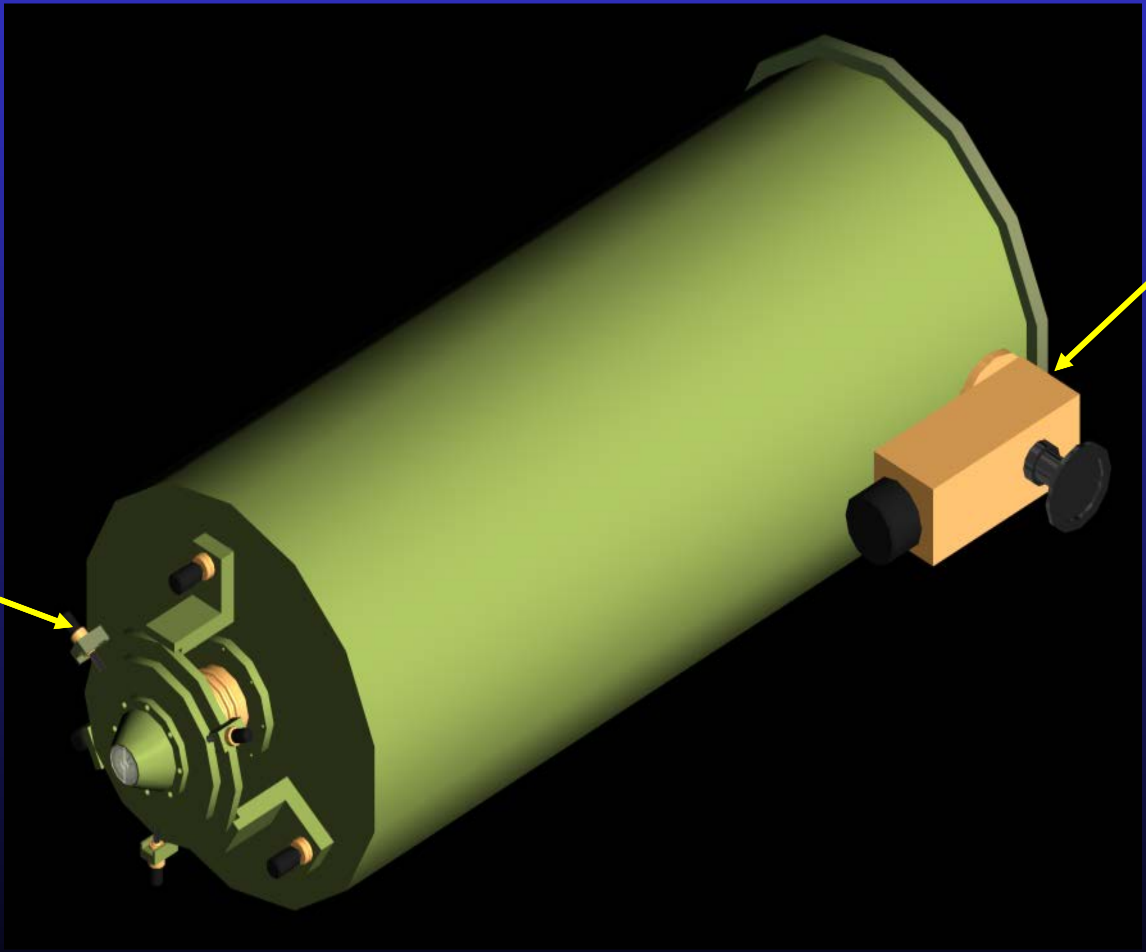
- Superconducting
- QUantum
- Interference
- Device

- Bandwidth: DC-10 kHz
- Image net action current in x-y plane
- Big, smaller, smallest…

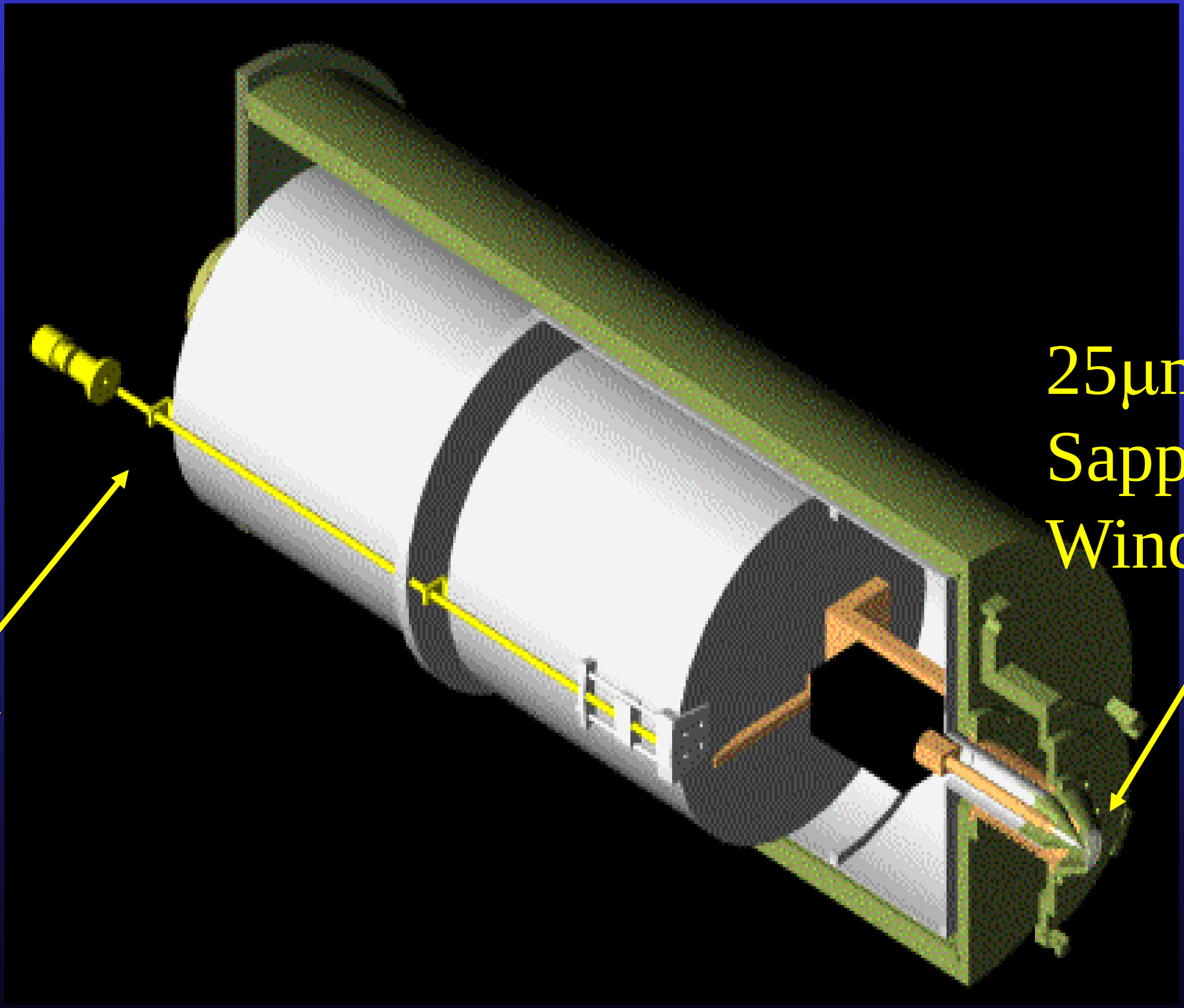
NanoSQUID: Cooled with liquid N_2 and liquid He ……

Vacuum Port

Bellows Mechanism



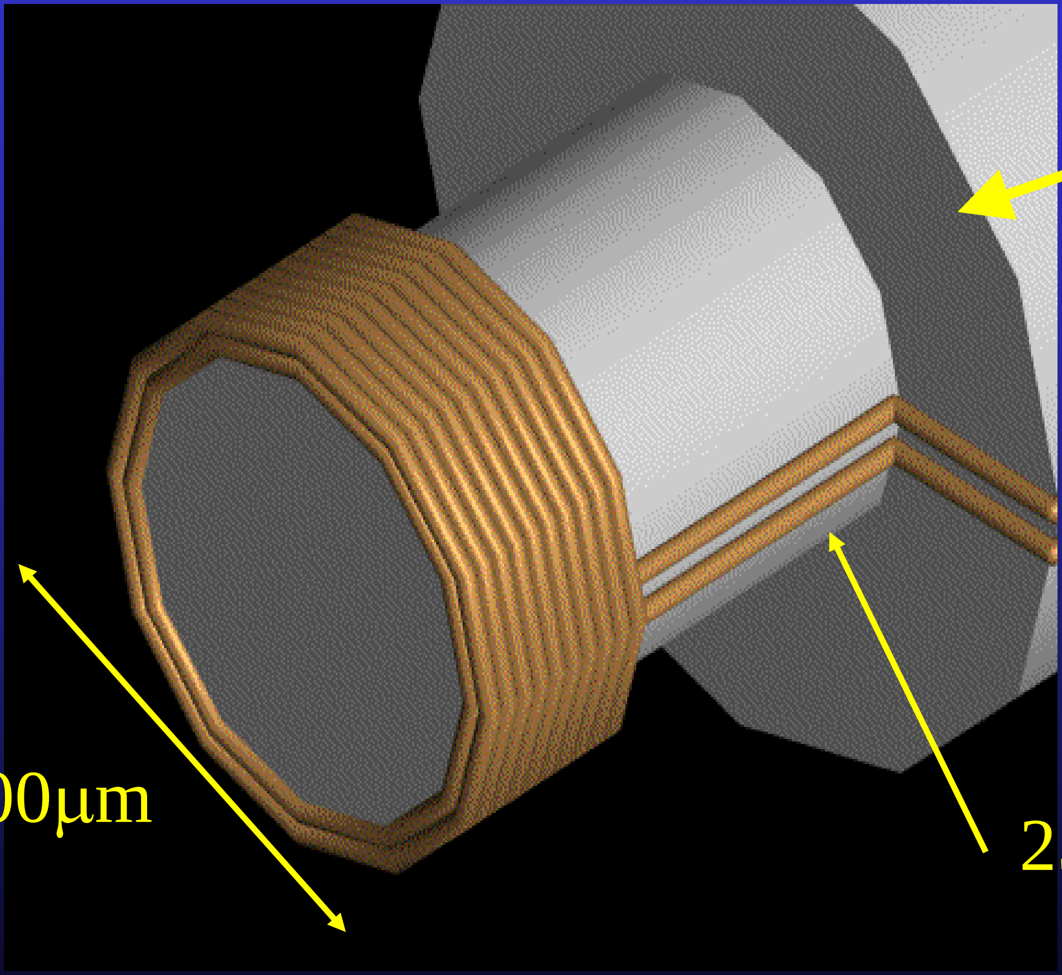
The SQUID lives in the vacuum space …



Lever Mechanism

25μm Sapphire Window

Wind a Pickup Coil ….



Sapphire Bobbin

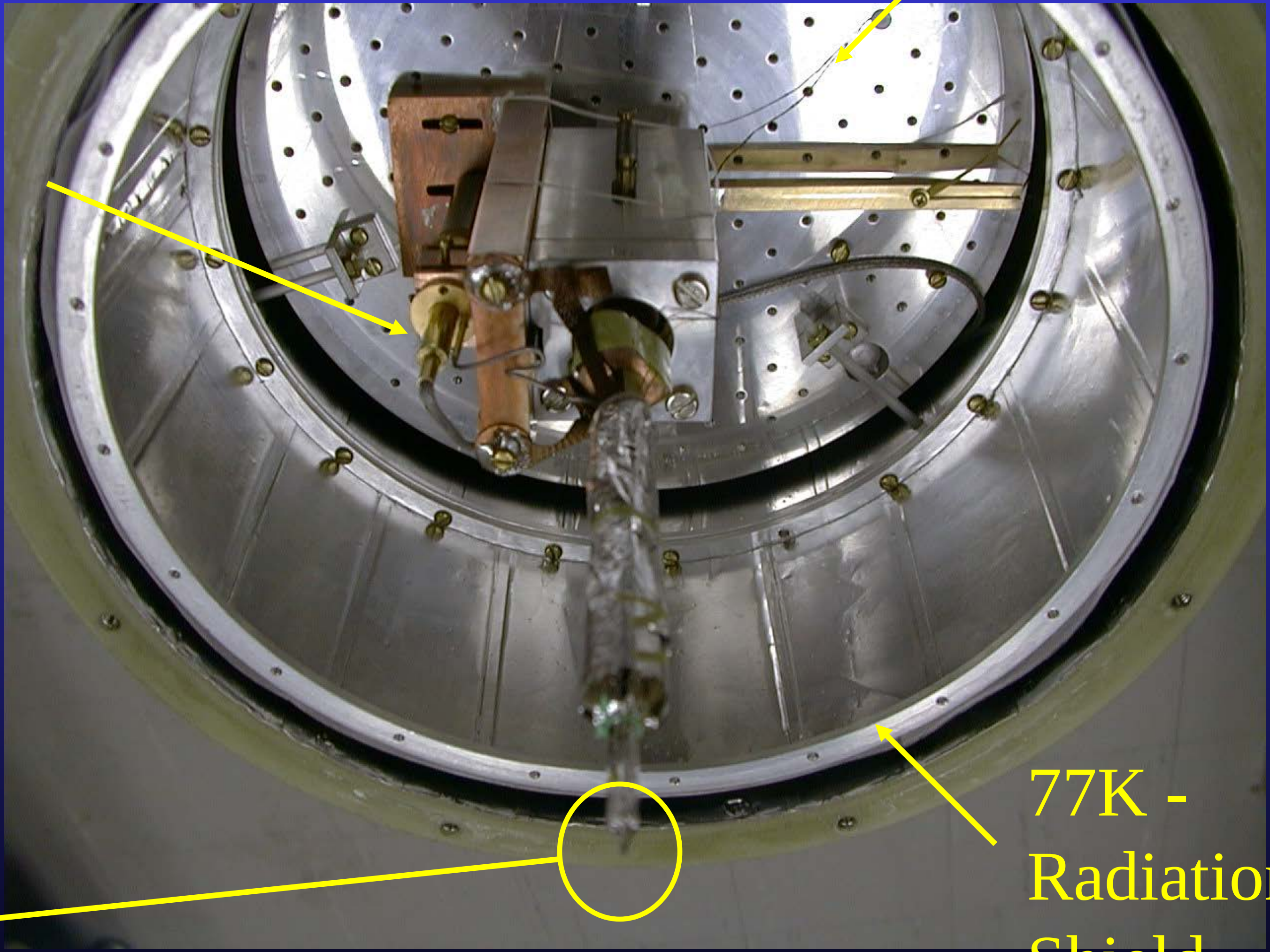
250 – 500μm

25μm Nb Wire

In Reality ..

He-
Reservoir

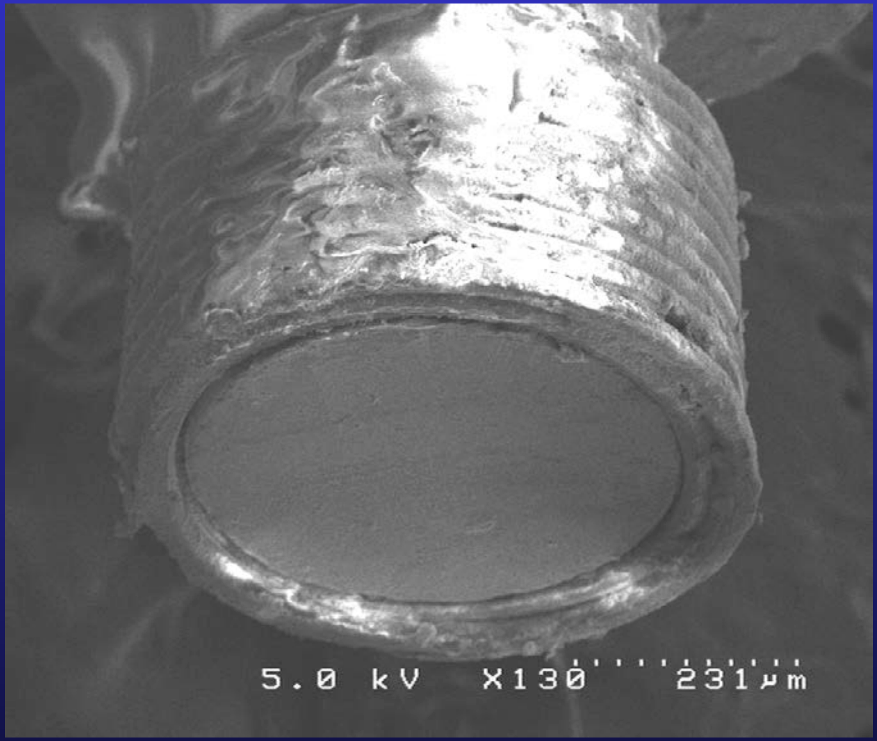
SQUID



Pickup
Coil

77K -
Radiation
Shield

Pickup Coil



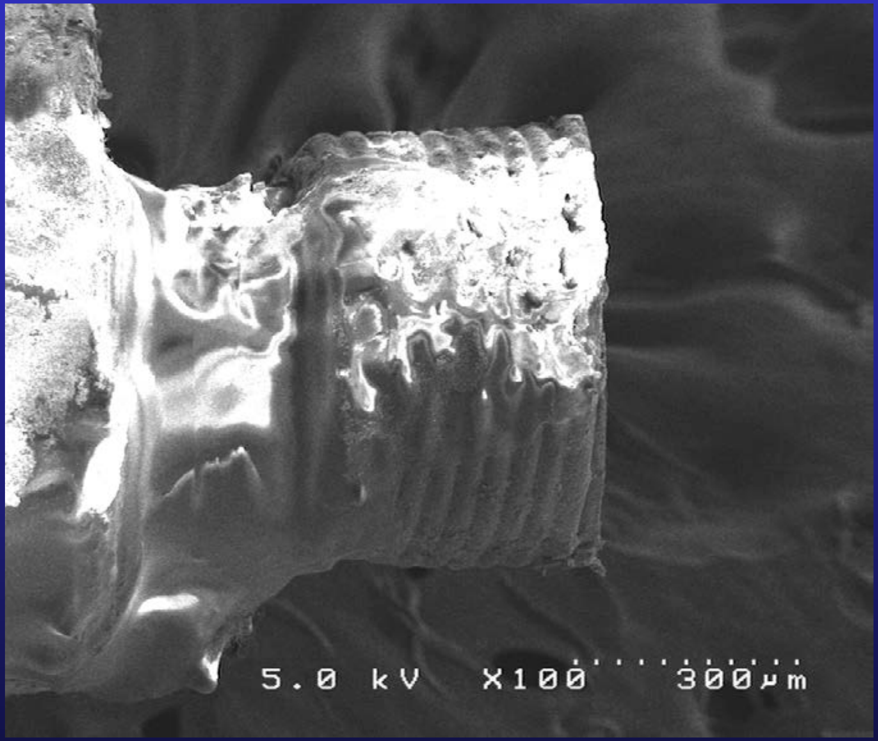
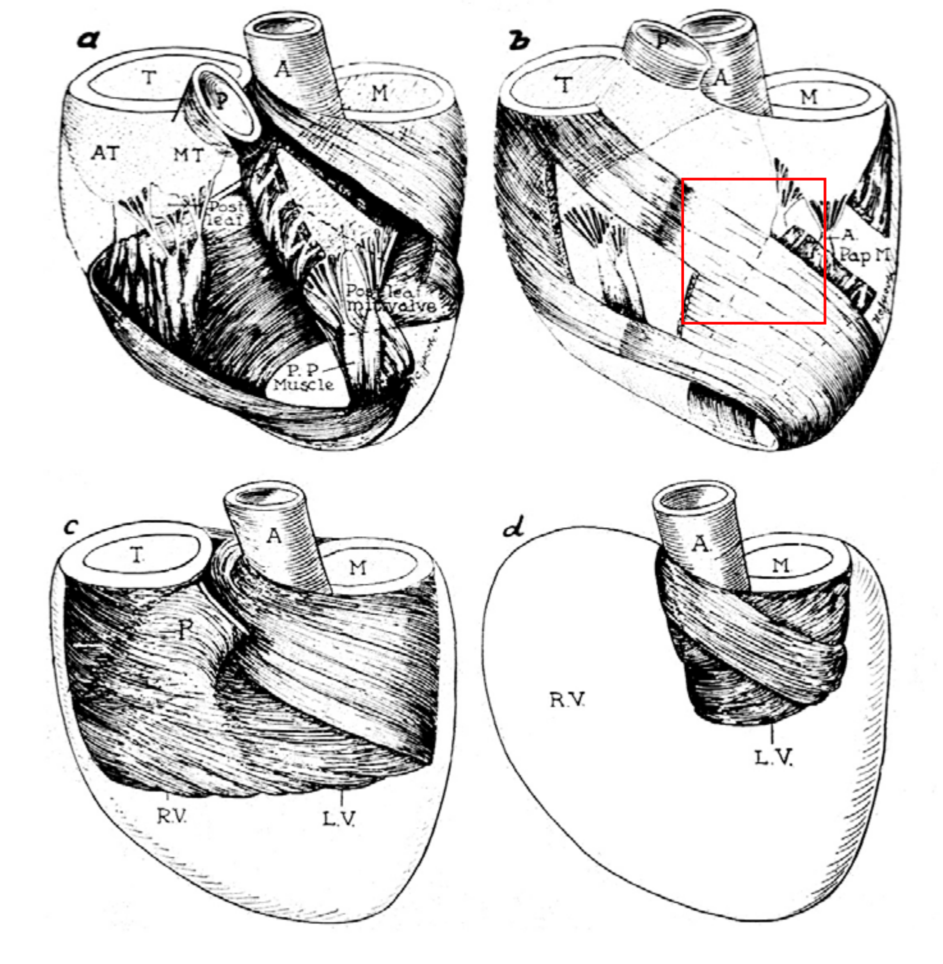


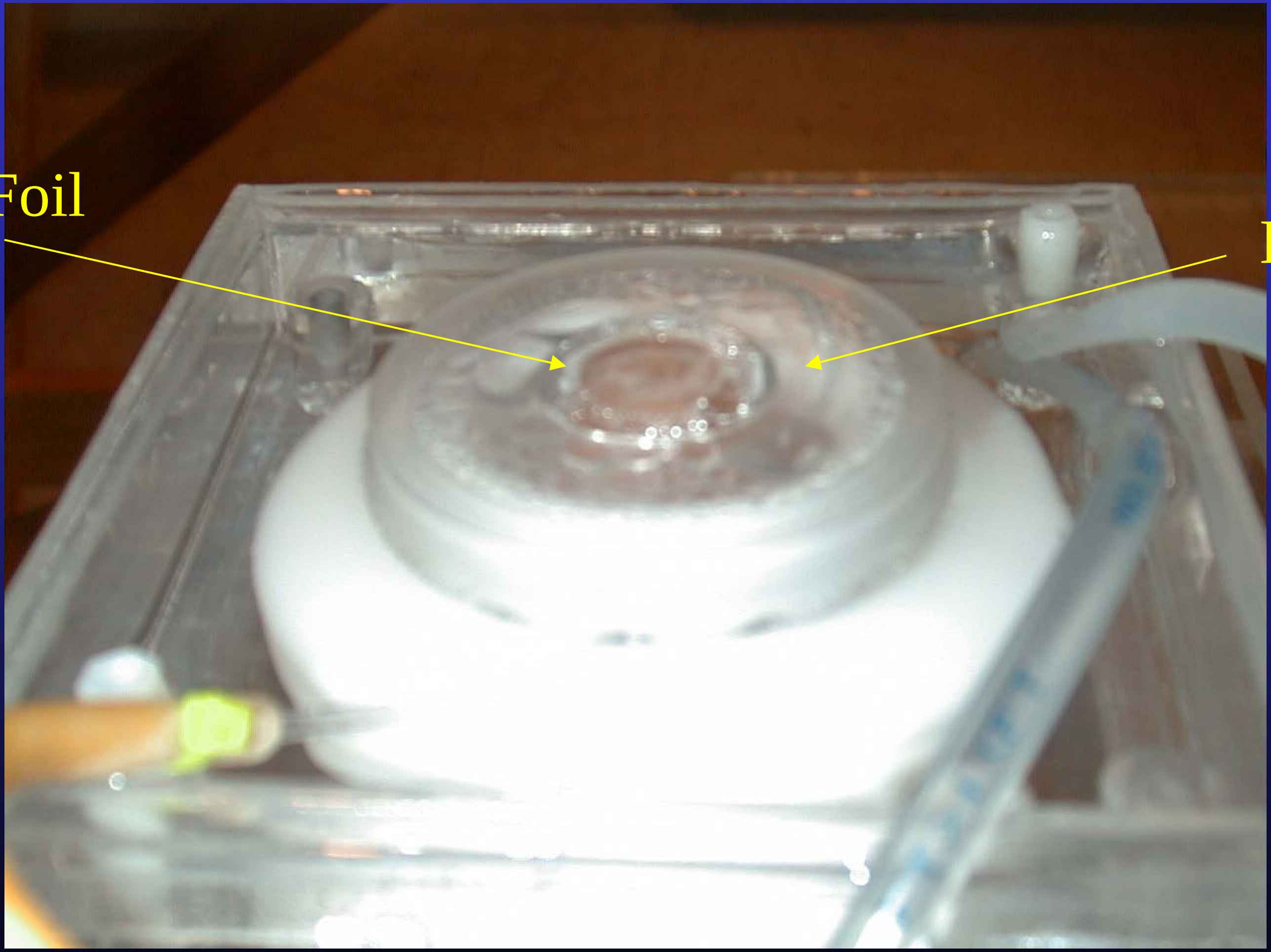
Image the LV Free Wall ...



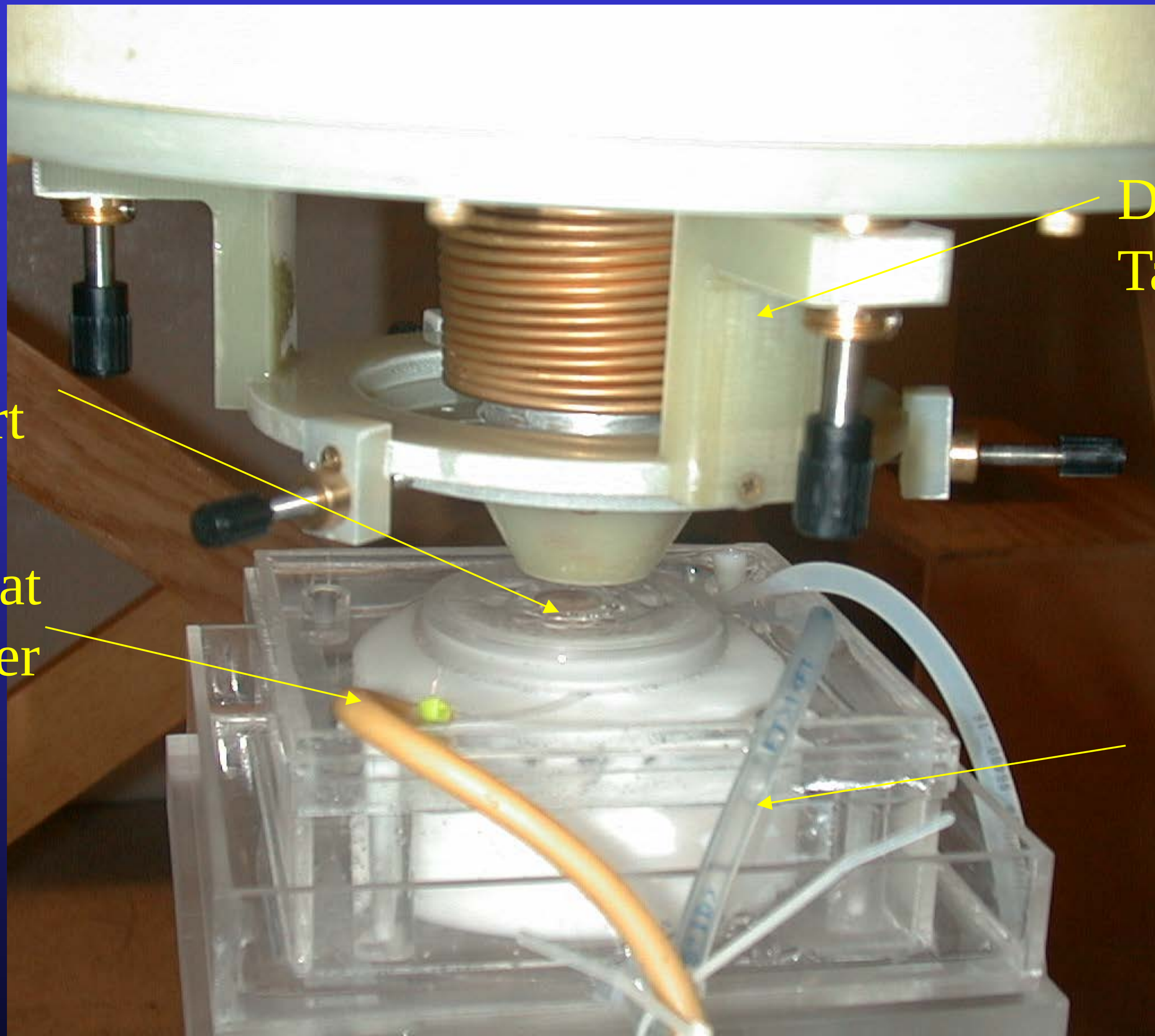
- Scanning SQUID microscope
- Isolated rabbit heart
- Point stimulation
- Anisotropy should produce a quatrefoil current pattern

Langendorff-Perfused Isolated Rabbit Heart

15µm Mylar-Foil



Bath


Dewar Tail
Isolated Rabbit Heart
From Heat Exchanger
To Heat Exchanger

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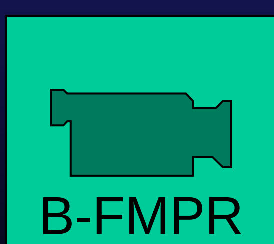
MCG From the LV Free Wall

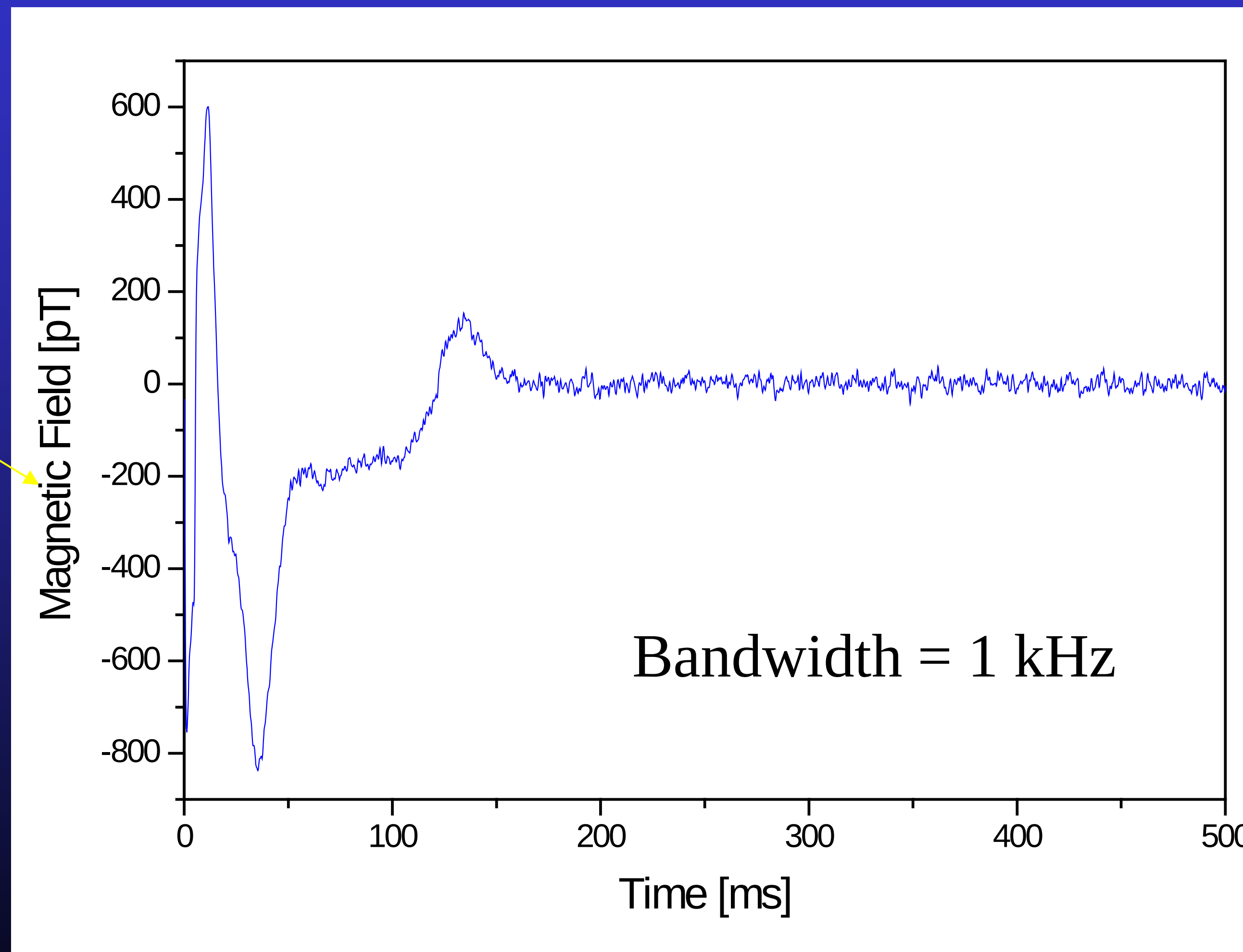
Scan Area

16 mm

16 mm

Pixel size 0.16 mm^2





1 pT ~ B_{earth}/100,000,000

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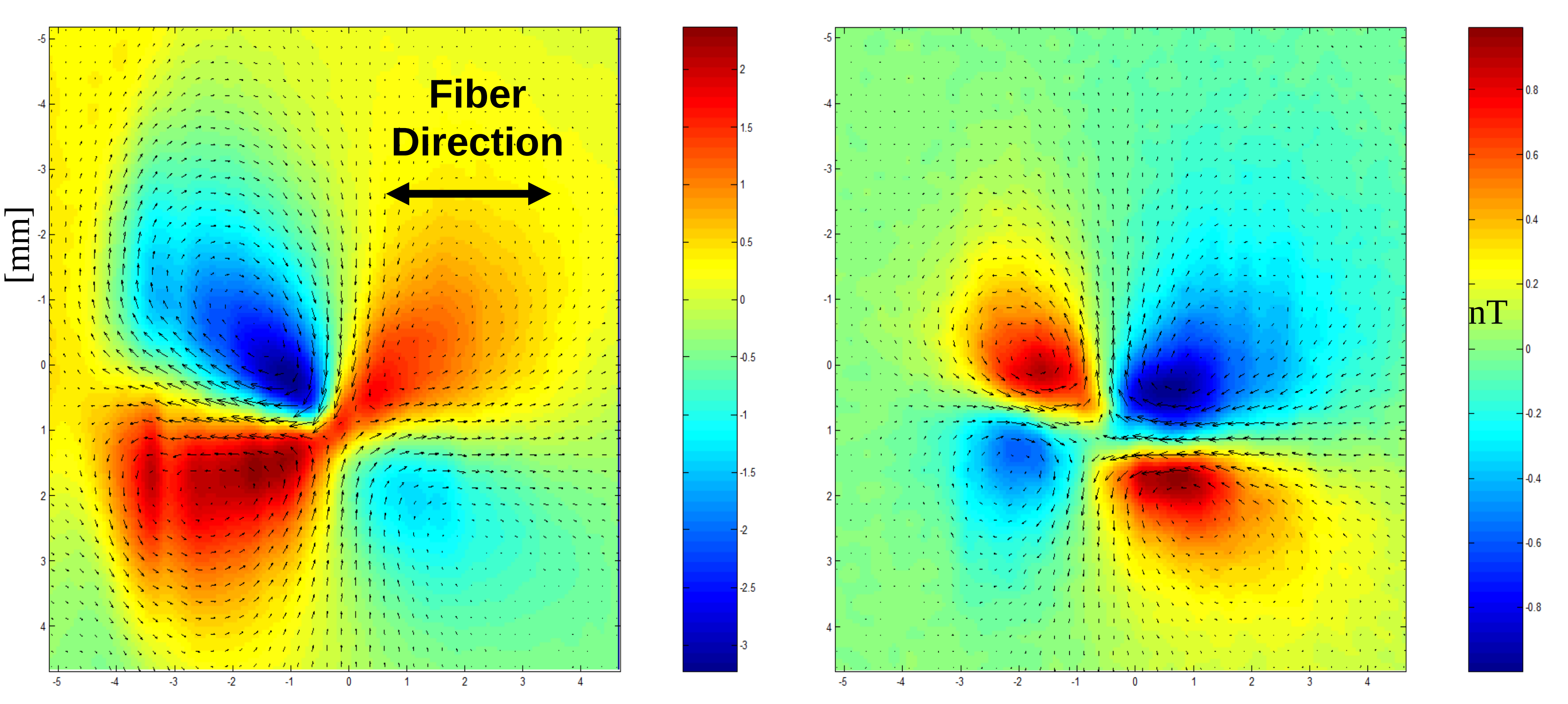
Cathodal Current Injection Followed by Initiation of Action Currents

Stimulus: 5 ms, 1.5 mA

1 ms after Stimulus



1 cm

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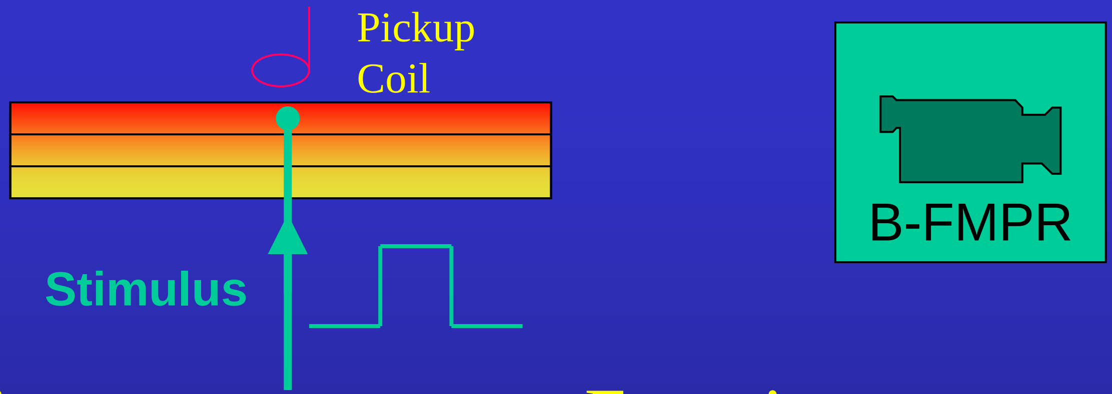
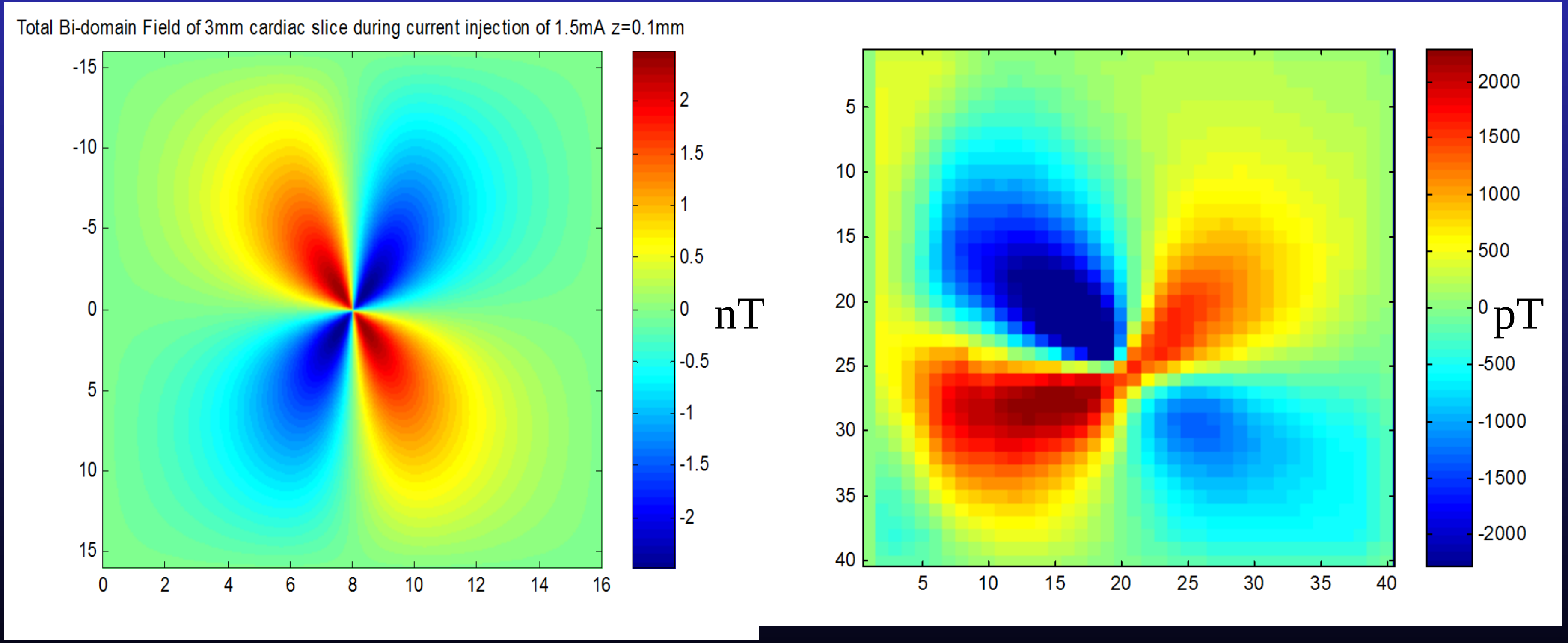
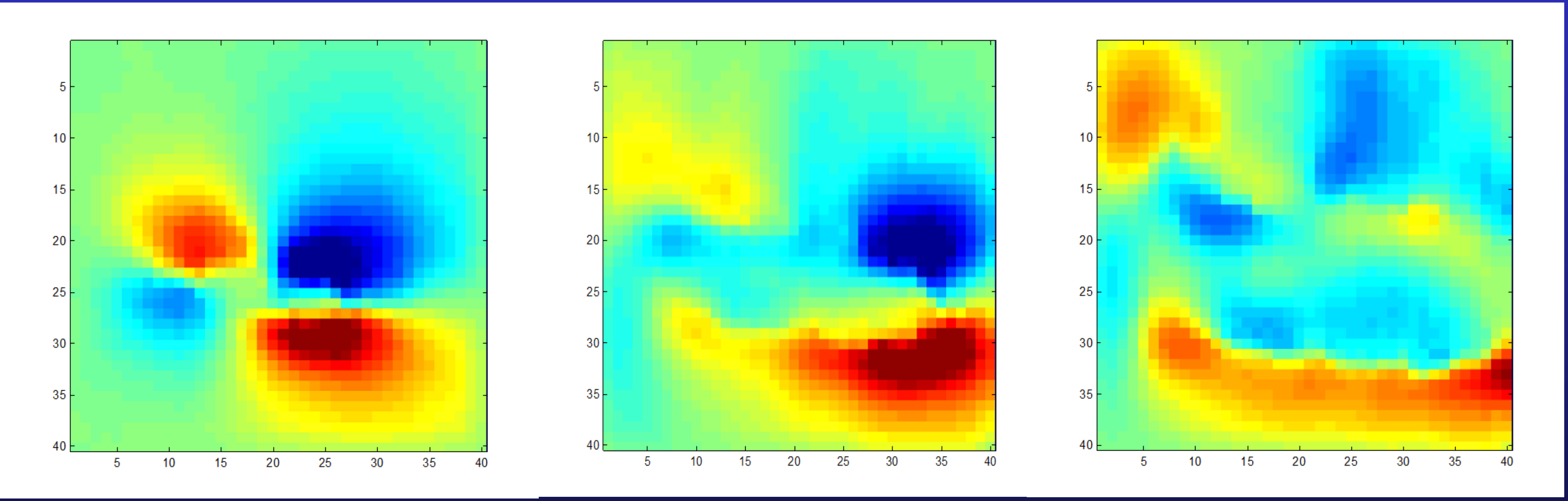


Layered Bidomain

Experiment



Propagation of Action Currents



4 ms 10 ms 16 ms

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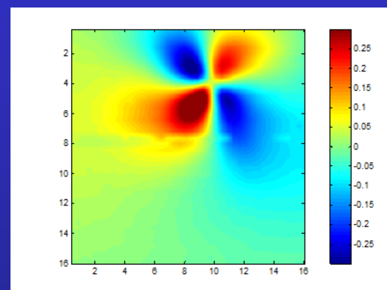
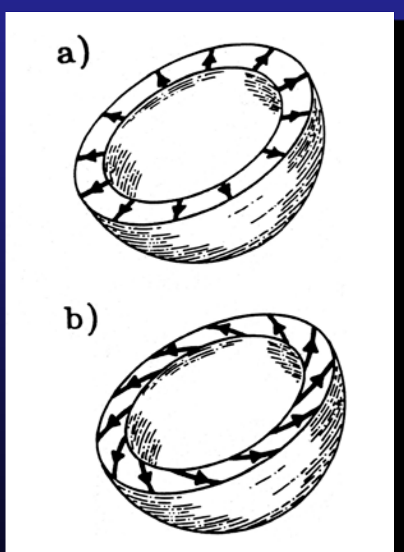
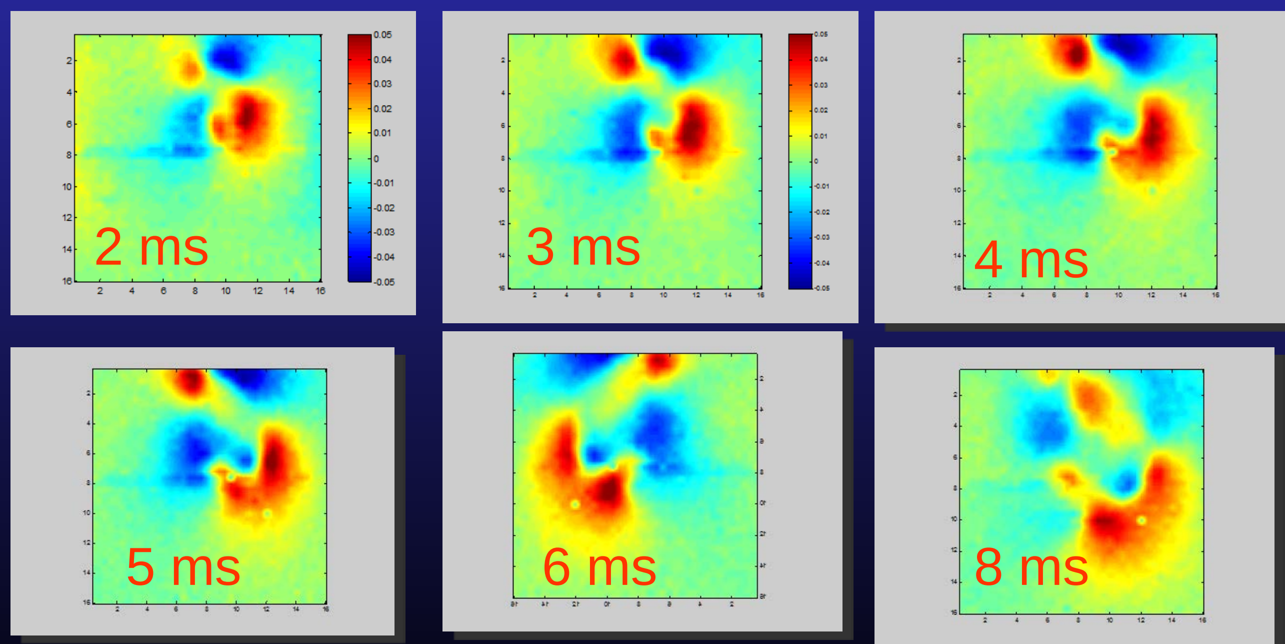
The Magnetic Field From Action Currents in Isolated Cardiac Tissue – The Apex



Stimulus
0.6 mA 5 ms

Near_apex.mpg





S00835A

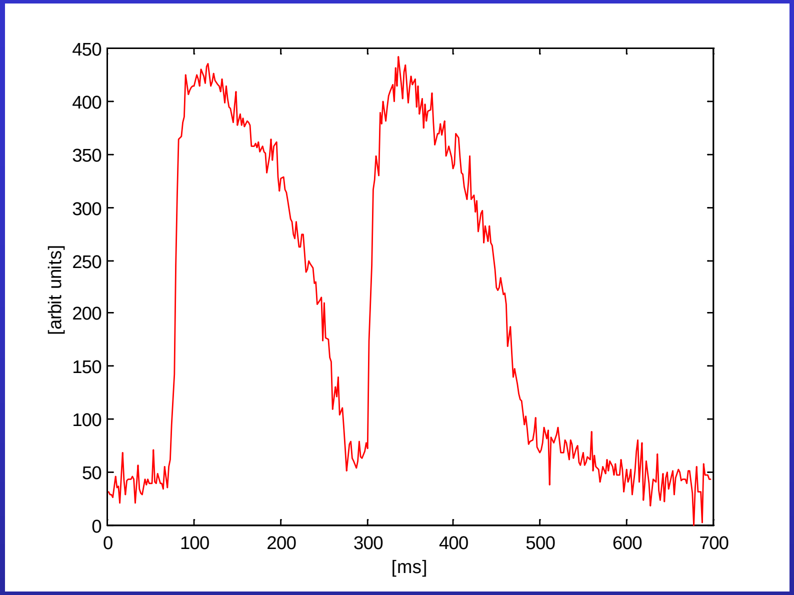
Courtesy of Franz Baudenbacher

Forthcoming…

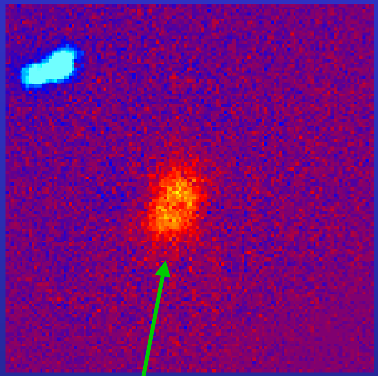
- Measured magnetic field gives current
- Measured V_m gives the voltage
- Model of both requires the bidomain conductivities (Eason and Trayanova)

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

S2- Point Stimulation

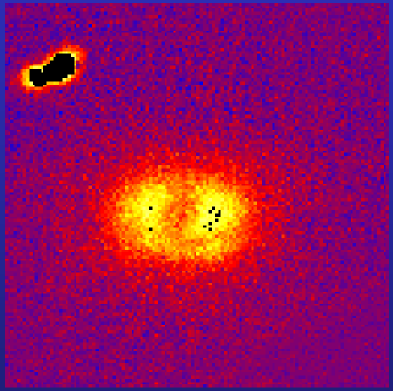


S2-S1=240 ms

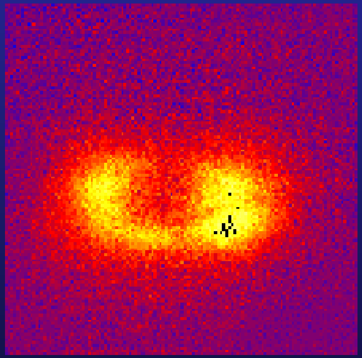


Point Electrode

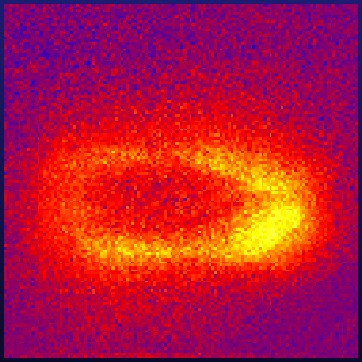
S = 6*Threshold



6 ms

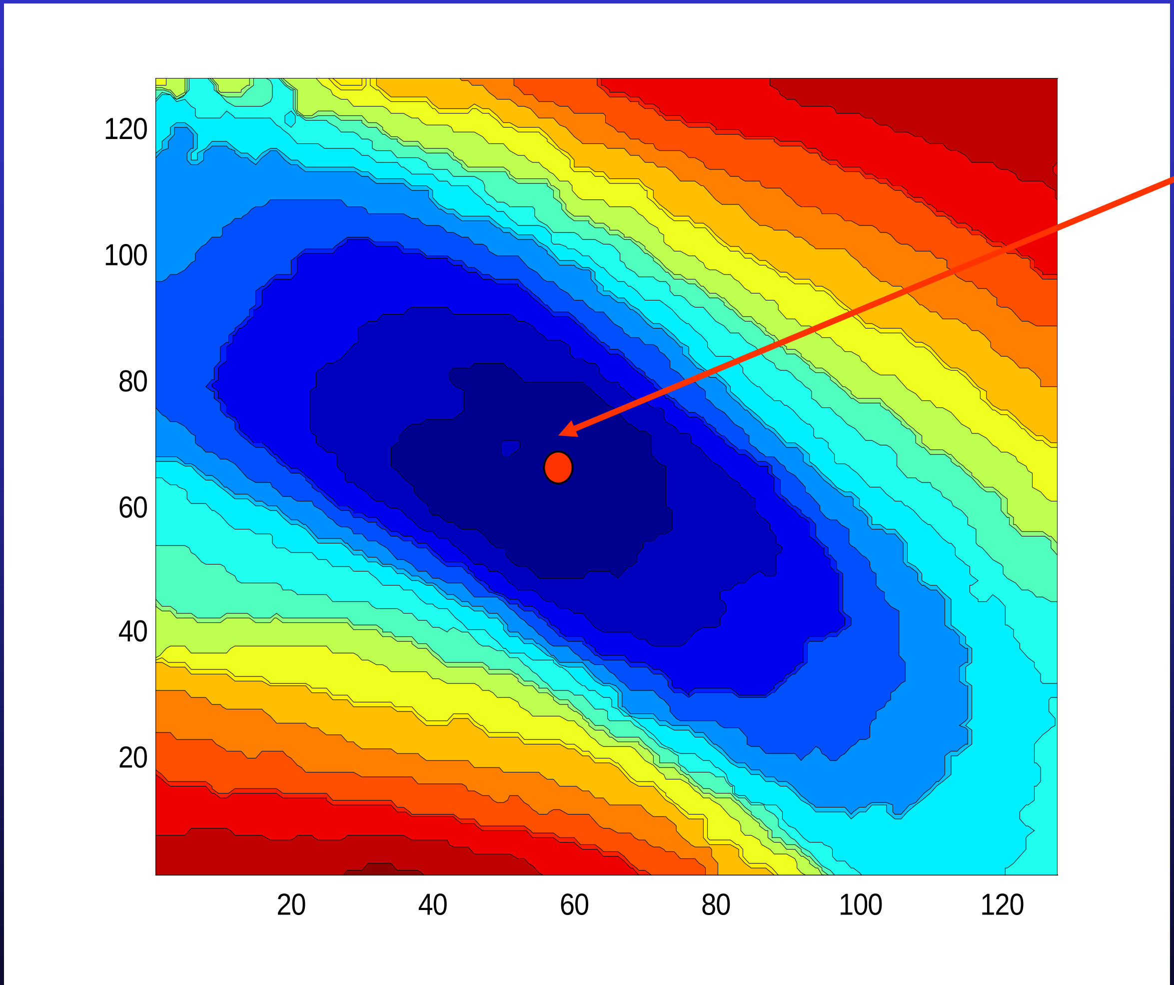


12 ms



18 ms

V_m Isochrones – LV Free Wall

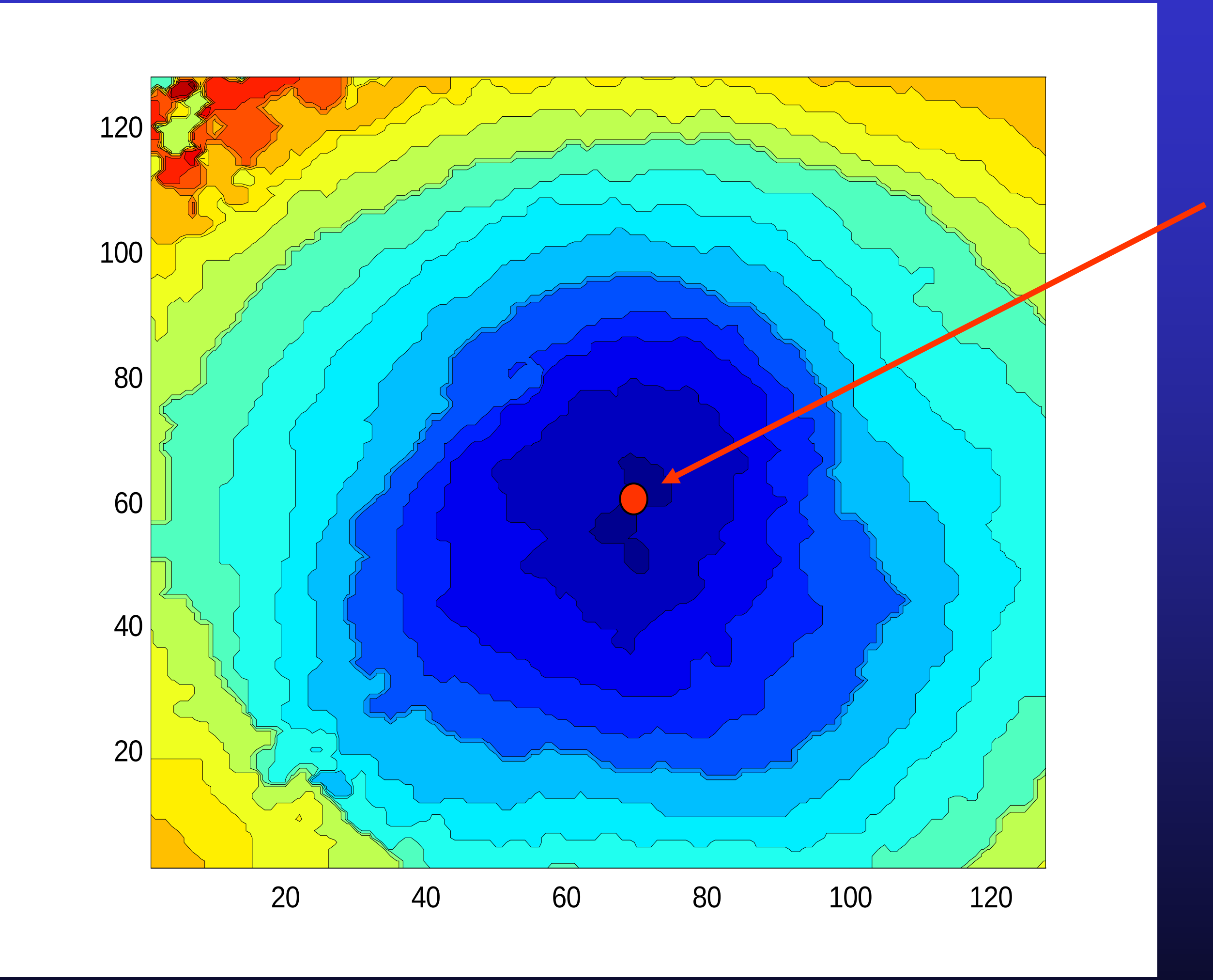


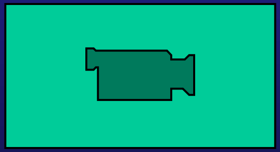
Point Stimulation

ventricle_propagation.mpg

Fiber Orientation

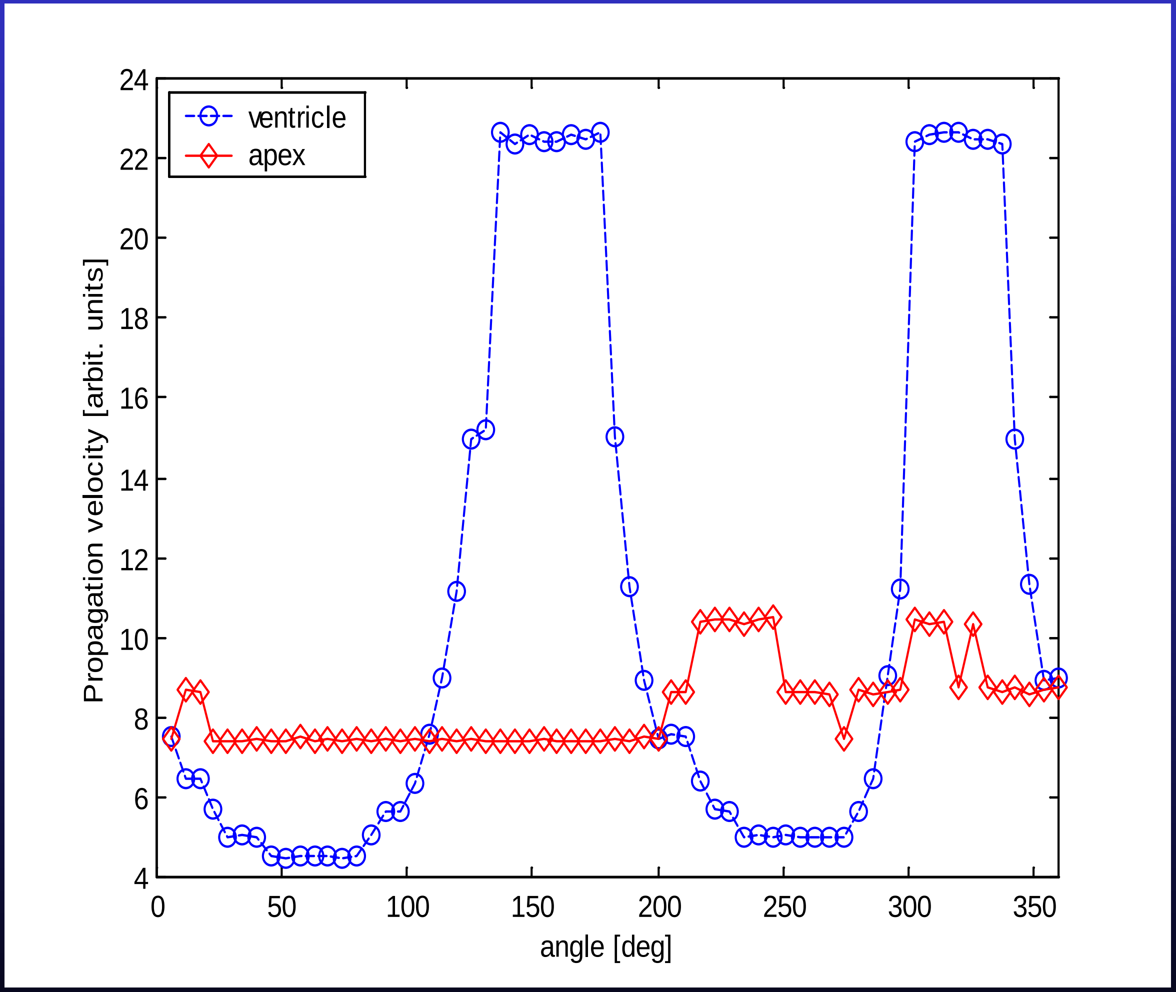
V_m Isochrones - Apex





apex_propagation.mpg

Velocities as a function of direction



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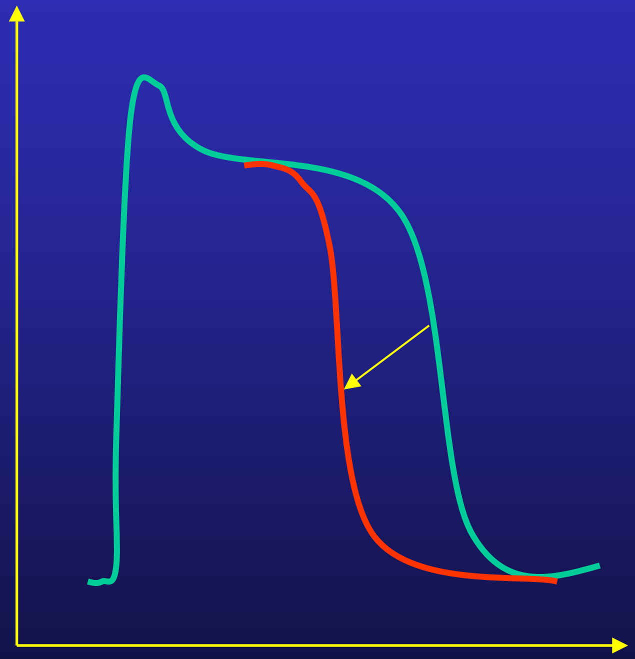
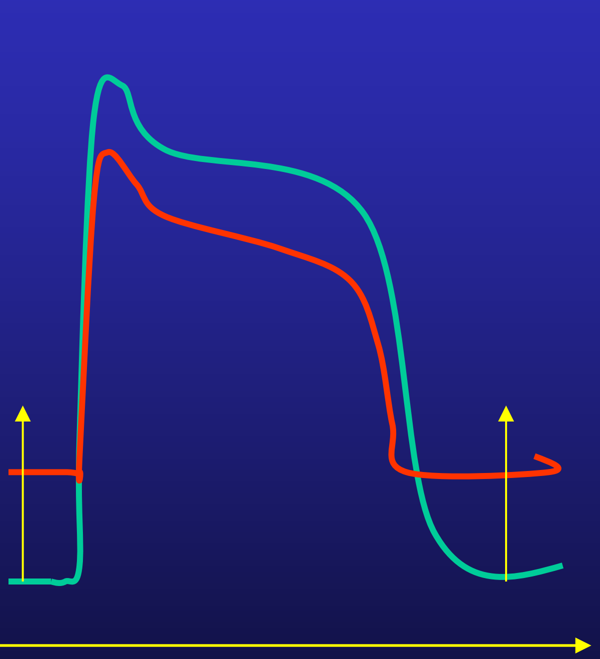
SQUID Senses Spatial V_m Gradients

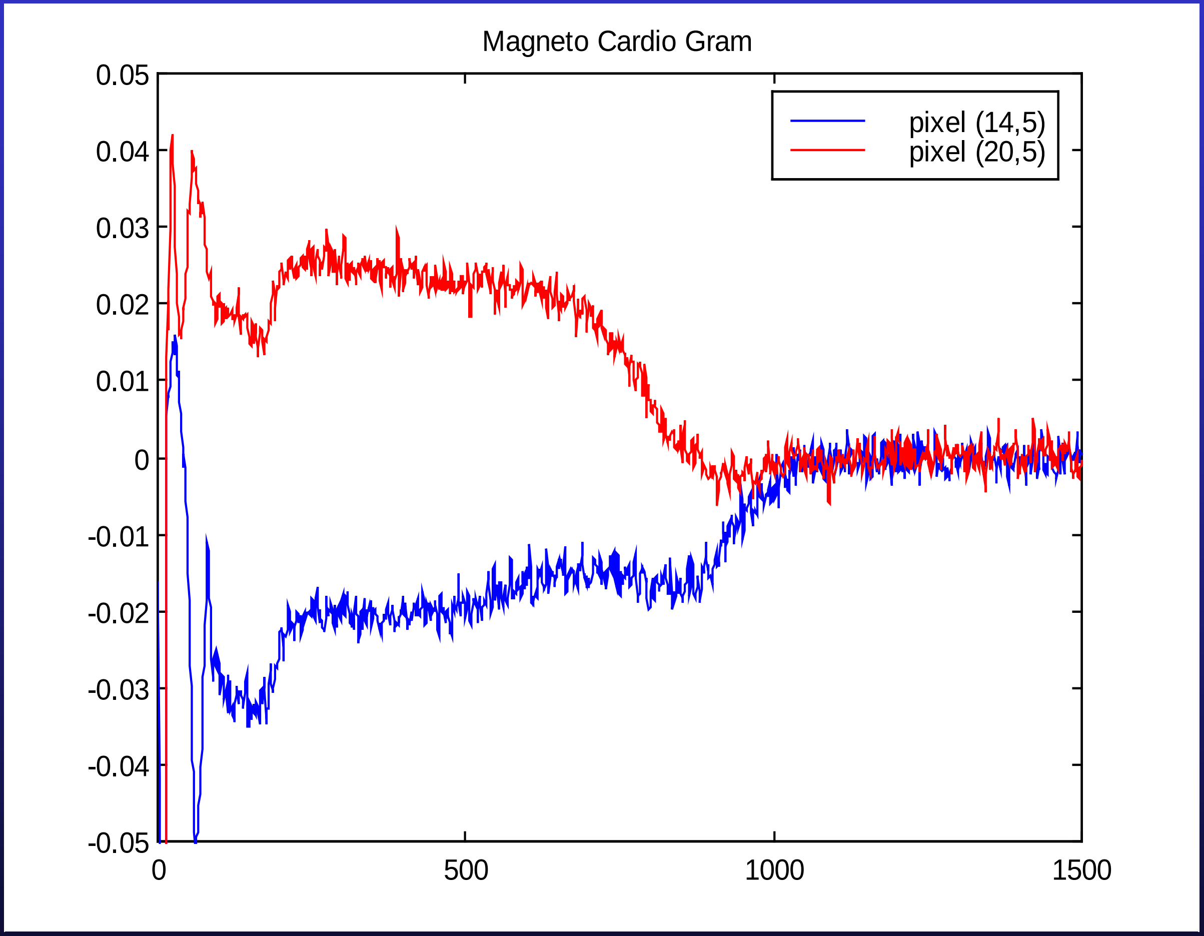
Repolarization



Injury Currents

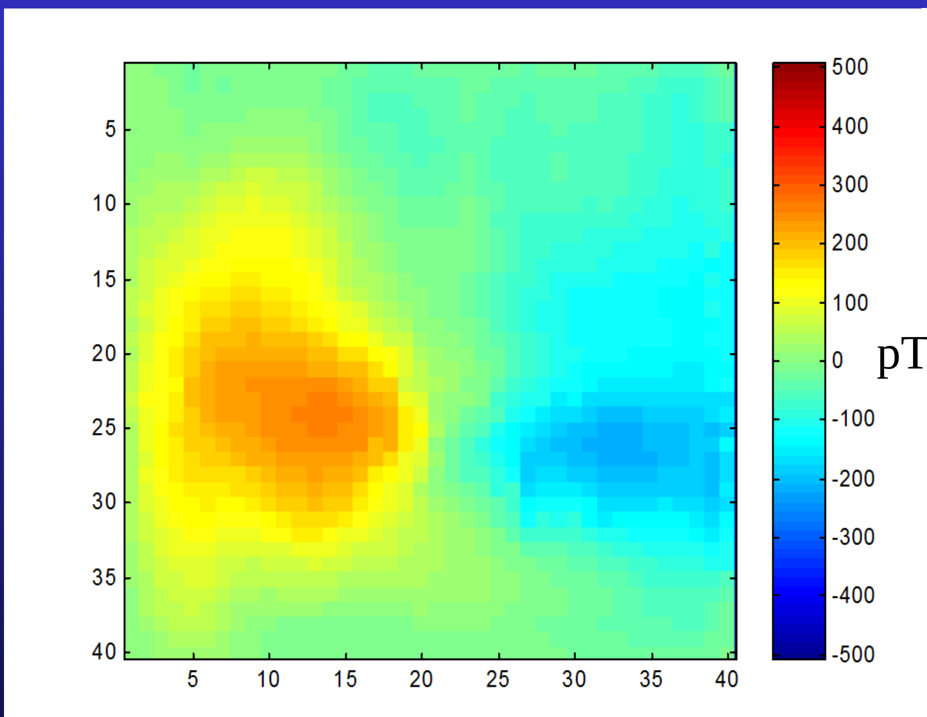


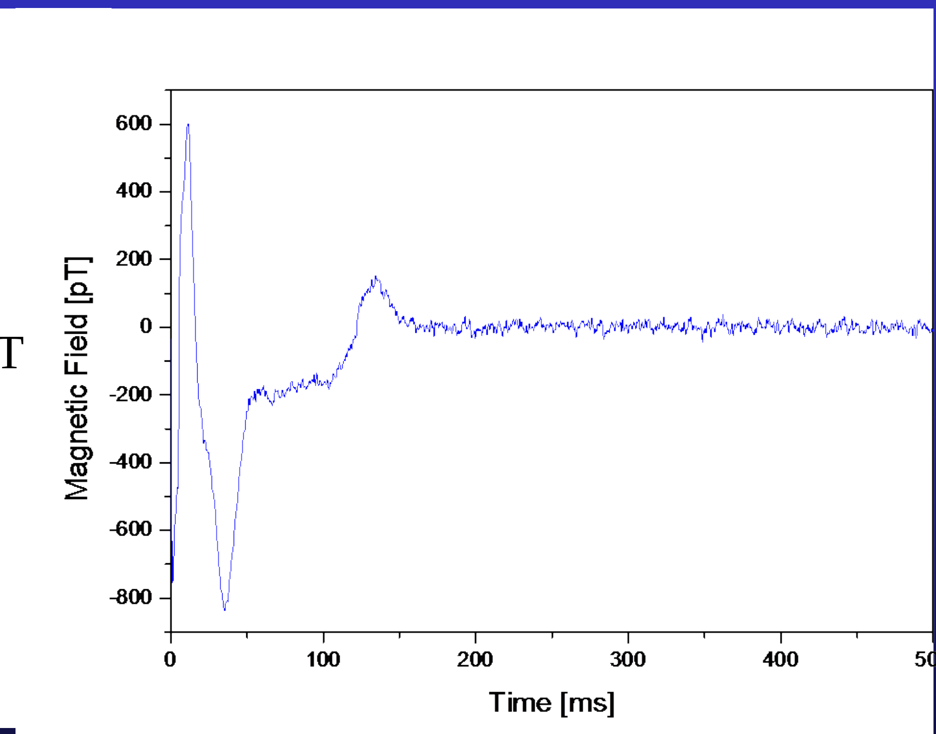
Gradients in Repolarization



repolarization.mpg

Dipole Signature in ST-segment





71 ms

b-frpo.mpg

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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