Vanderbilt University

Living State Physics Group

Novel Insights on the Virtual Electrode Response

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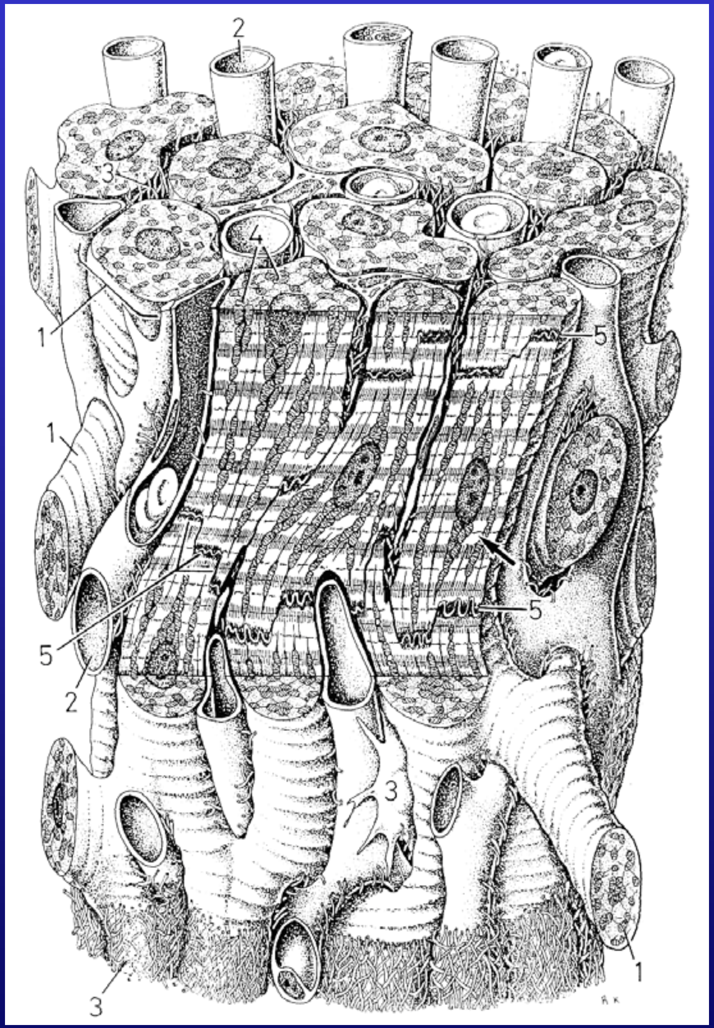
OUTLINE

- Review of bidomain model
- Excitation with a point electrode
  - Virtual cathodes and anodes
  - Make/break stimulation
  - Quatrefoil reentry
- Endocardial Shock Response
- Field Shock Response

The Cardiac Bidomain Model

- Homogeneous syncytium
- Separate intra- and extracellular spaces
- Differing electrical anisotropies
- Non-linear membrane
- Fiber curvature, heterogeneities, and discontinuities???



"Virtual Electrodes"

- The **Virtual Cathode** is the region of tissue adjacent to a stimulating electrode that is depolarized rapidly by electrotonic spread.
- The **Virtual Anode** is the region of tissue adjacent to a stimulating electrode that is hyperpolarized rapidly by electrotonic spread.

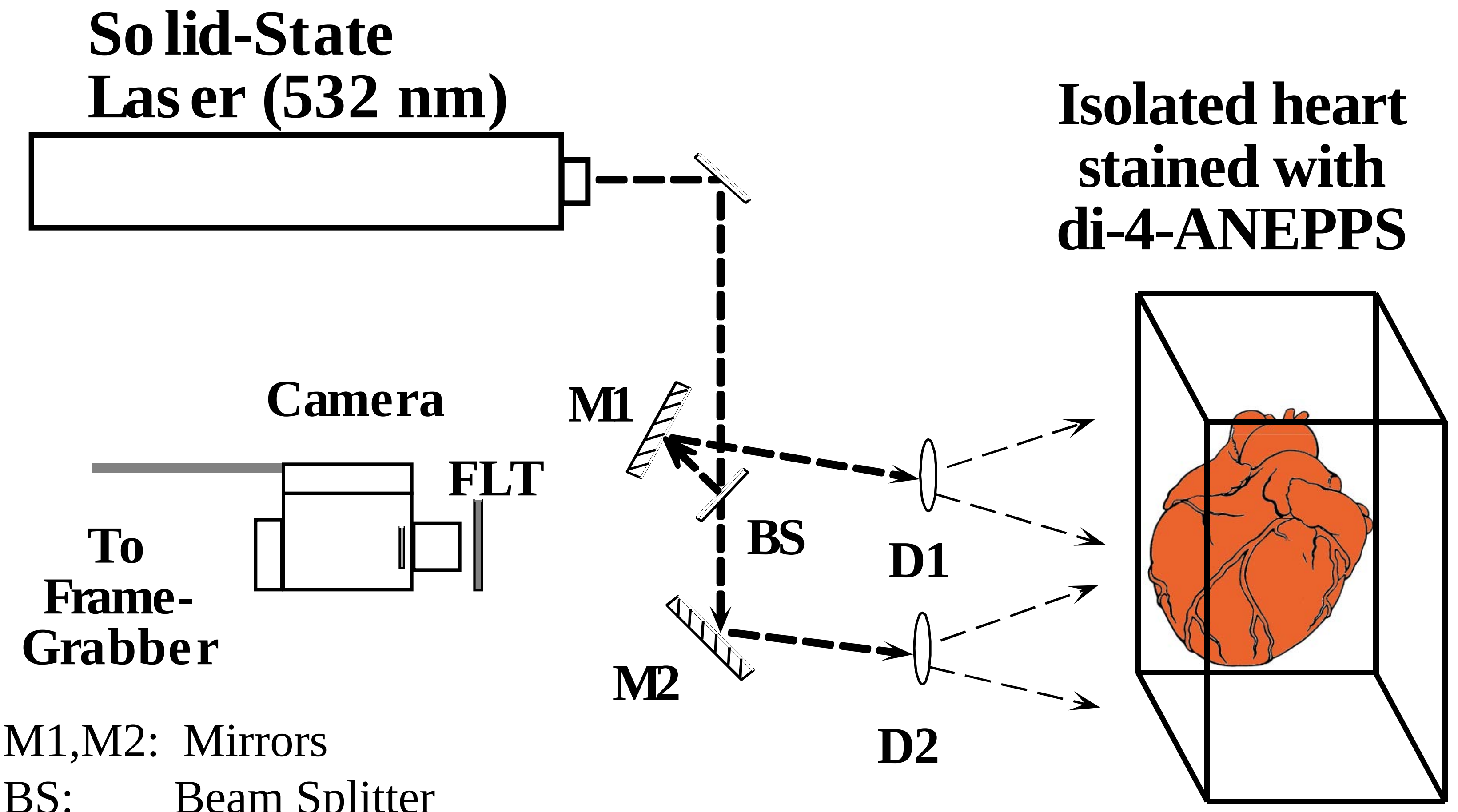
Phenomena unique to the cardiac bidomain with unequal intracellular and extracellular anisotropies

- Extended, quatrefoil current loops exist outside an expanding, activation wave front.
- Measurable, quatrefoil magnetic fields are produced by the extended current loops.
- The virtual cathode from strong, point stimulation has a dog bone shape.
- The virtual cathode exists in three dimensions, and rotates with depth due to the differing fiber orientations.
- The shape of the virtual cathode is altered pharmacological agents that block ion channels.
- Fiber rotation can alter the shape of the virtual cathode recorded on the epicardium.

Phenomena unique to the cardiac bidomain with unequal intracellular and extracellular anisotropies, con't

- Point stimulation produces longitudinal hyperpolarization.
- Point anodal stimulation can produce adjacent depolarization.
- Simultaneous virtual cathodes and anodes explain make and break stimulation.
- Bipolar stimulation produces complex areas of depolarization and hyperpolarization.
- Directionally-dependent time constant of the action potential foot.
- Uniform field defibrillation of hearts with curved fibers can polarize membranes deep within the myocardium.
- Strong point stimulation can produce quatrefoil spiral-wave reentry.

Optical Imaging Setup



M1,M2: Mirrors
BS: Beam Splitter
D1, D2: Diffusers
FLT: Long-Pass Filter (590 nm)

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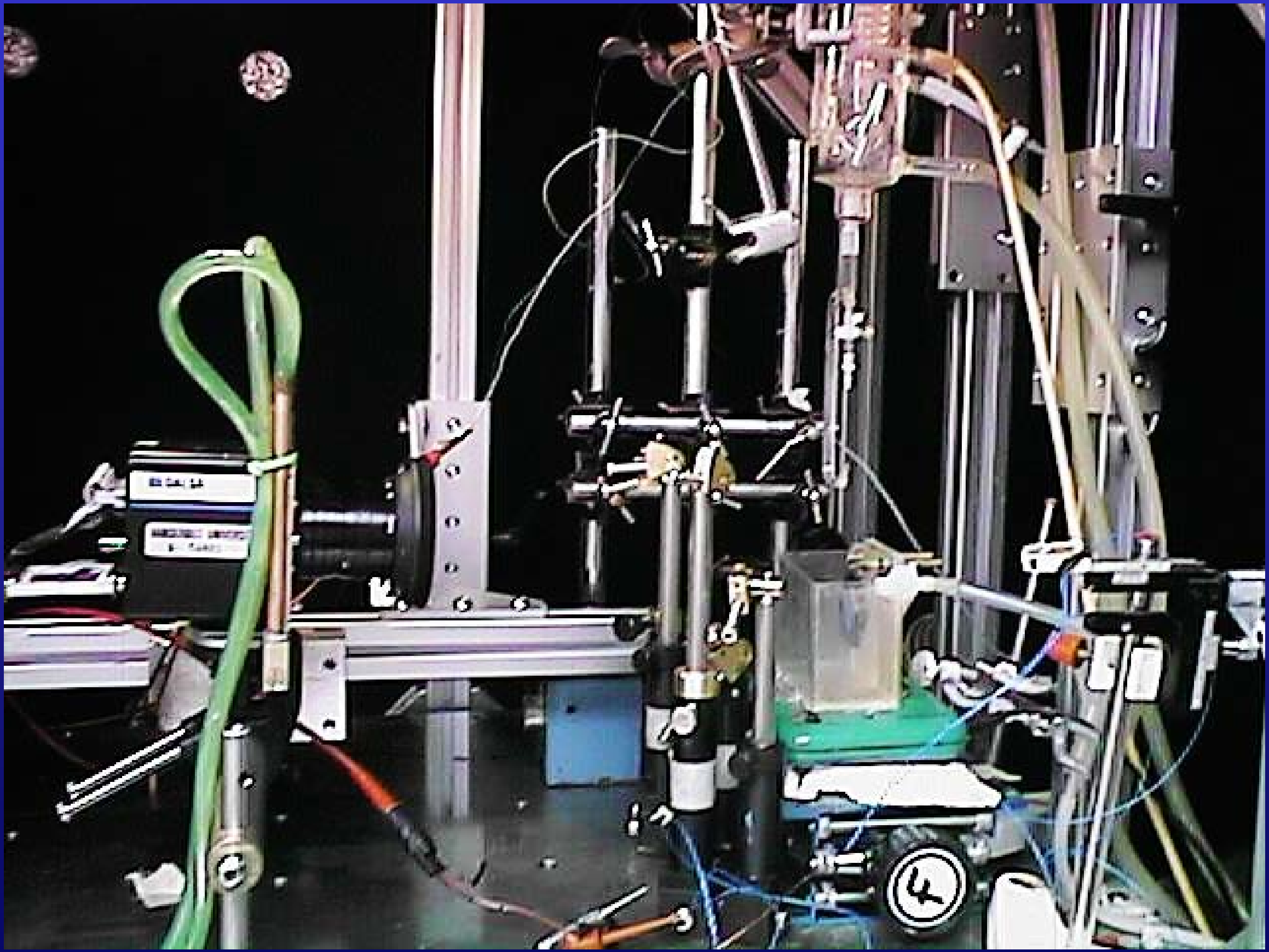
Vanderbilt Cardiac Imaging System

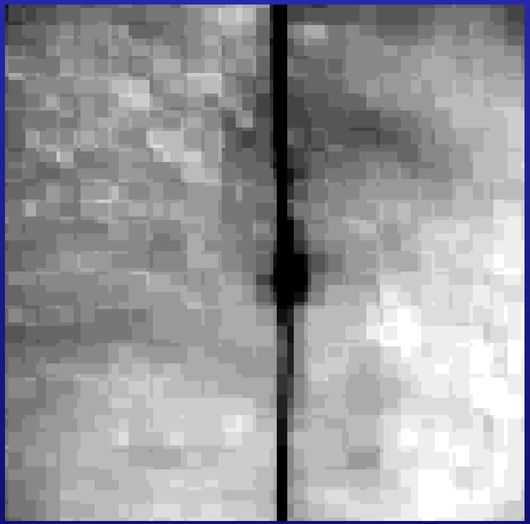


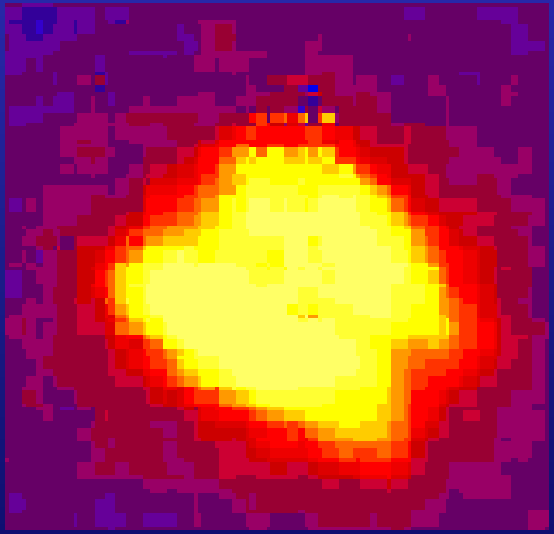
12-bit Resolution

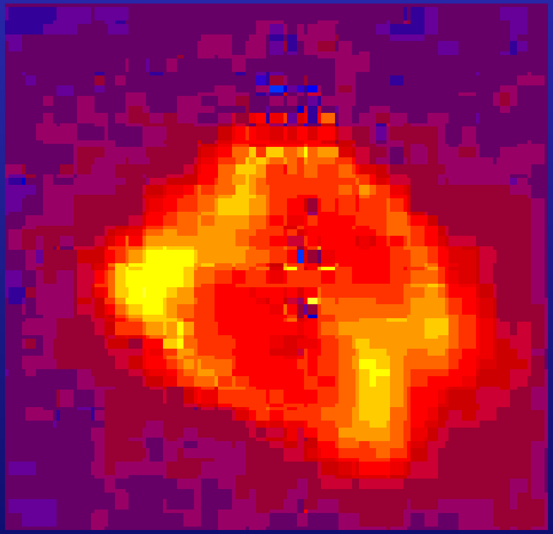
300 frames/sec
128x128 pixels
or
1200 frames/sec
64x64 pixels

Information from Imaging Data

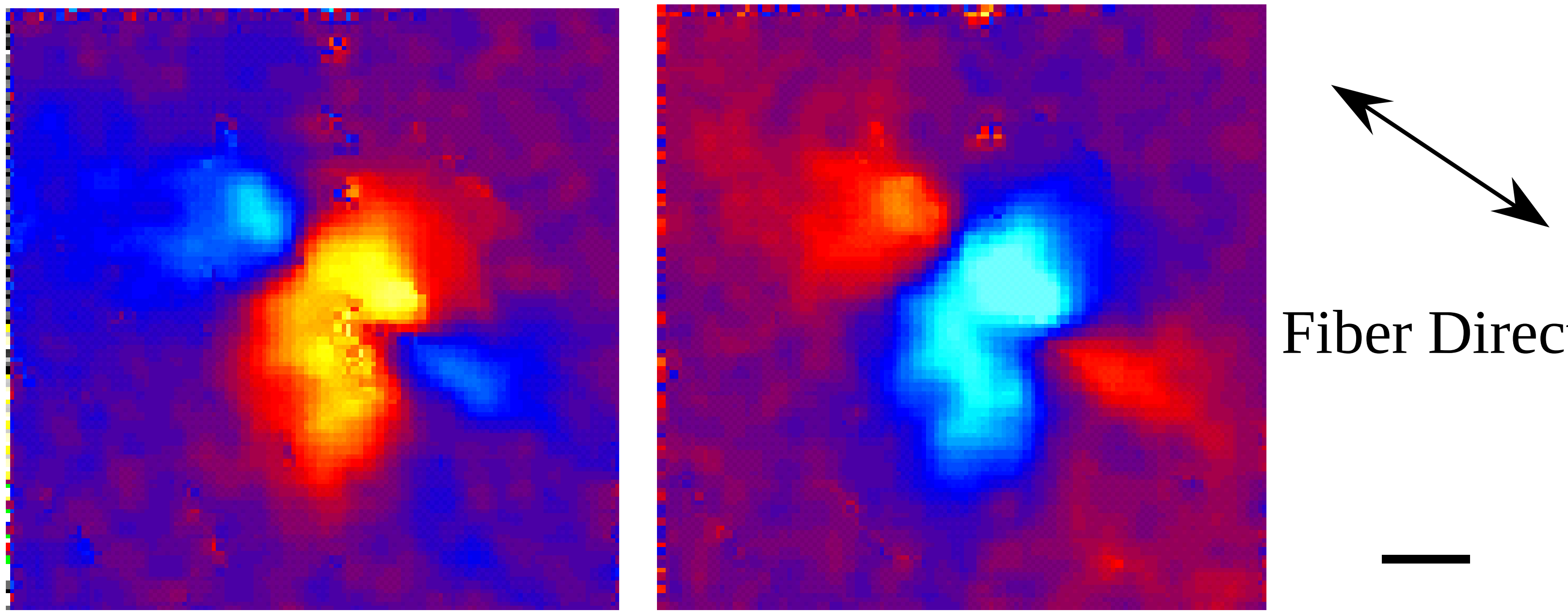
Structure **Function** **Dynamics**







Point-Electrode Excitation of Refractory Tissue



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Long-Standing Puzzle

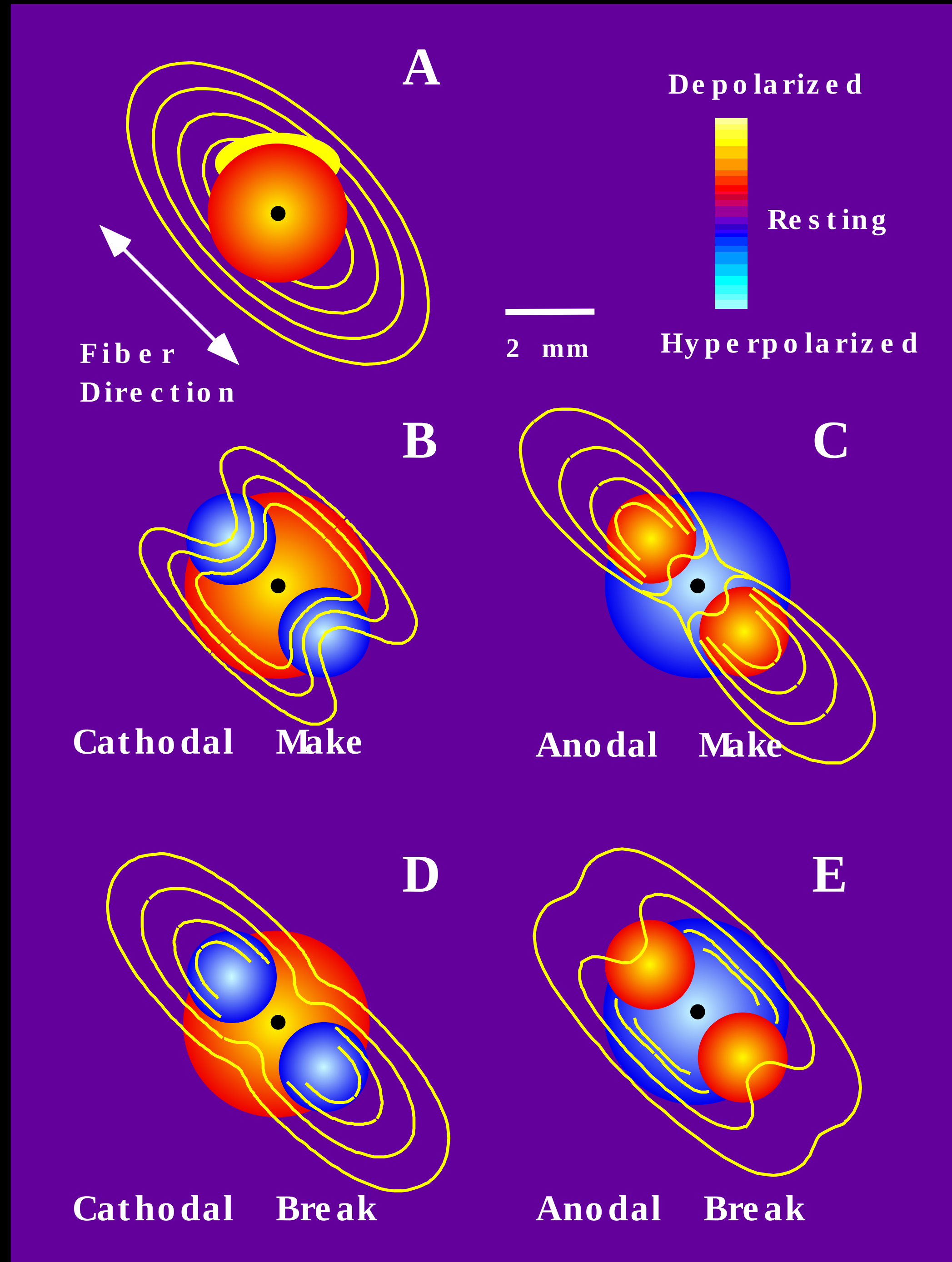
Why can the heart be stimulated electrically in four different ways?

- Turning-on of negative current (cathodal make)
- Turning-on of positive current (anodal make)
- Turning-off of negative current (cathodal break)
- Turning-off of positive current (anodal break)

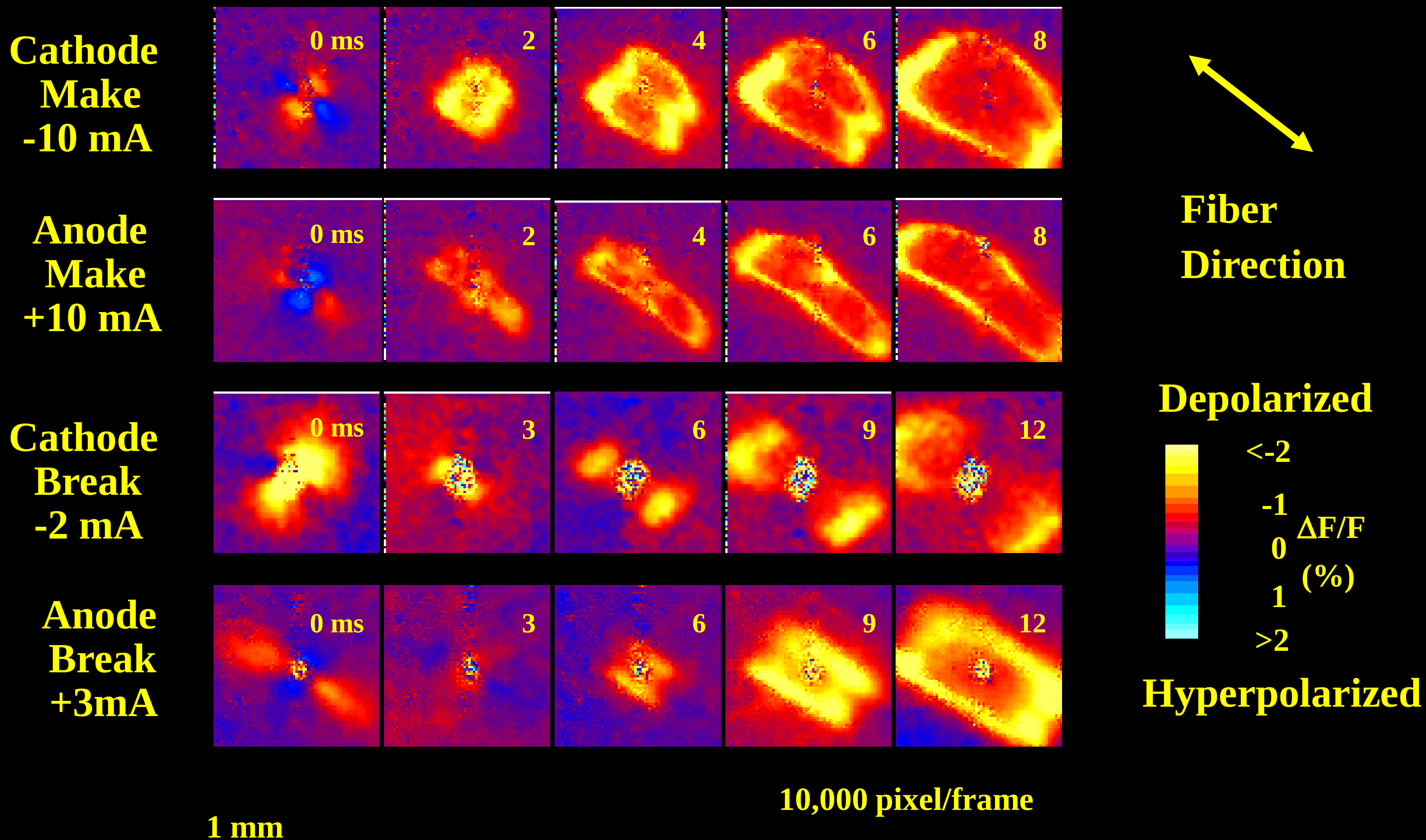
Four Modes of Cardiac Activation

Cathode Anode

Make Break



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



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

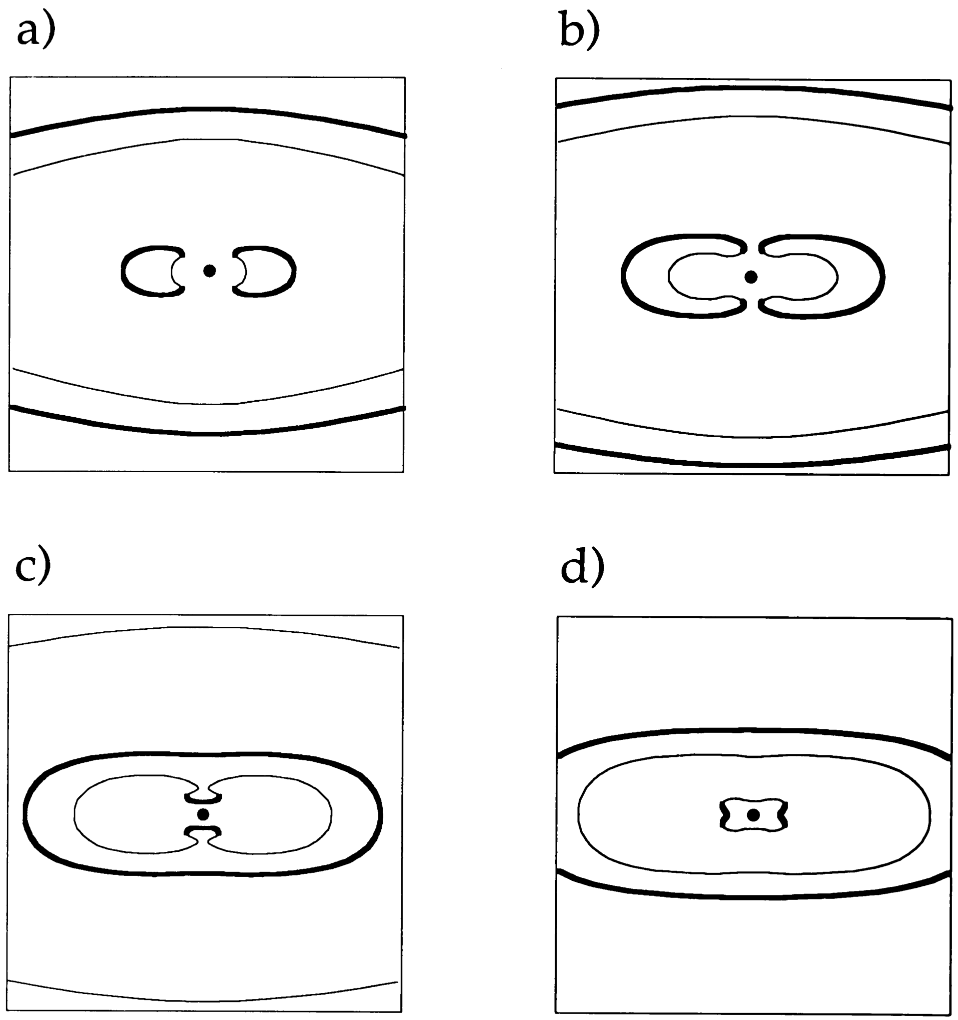
Prediction

In tissue with differing intracellular and extracellular anisotropies, a second, strong stimulus, delivered at the same location and during the vulnerable phase of the first wave front, results in a reentrant wave with four phase singularities.

- Thick line - depolarization phase
- Thin line - repolarization

" The formation of a re-entrant action potential wave front in tissue with unequal anisotropy ratios," B.J. Roth and J.M. Saypol, *International J. of Bifurcation and Chaos*, **1:** 927-928 (1991)

Prediction of Quatrefoil Reentry



(Saypol & Roth, 1992)

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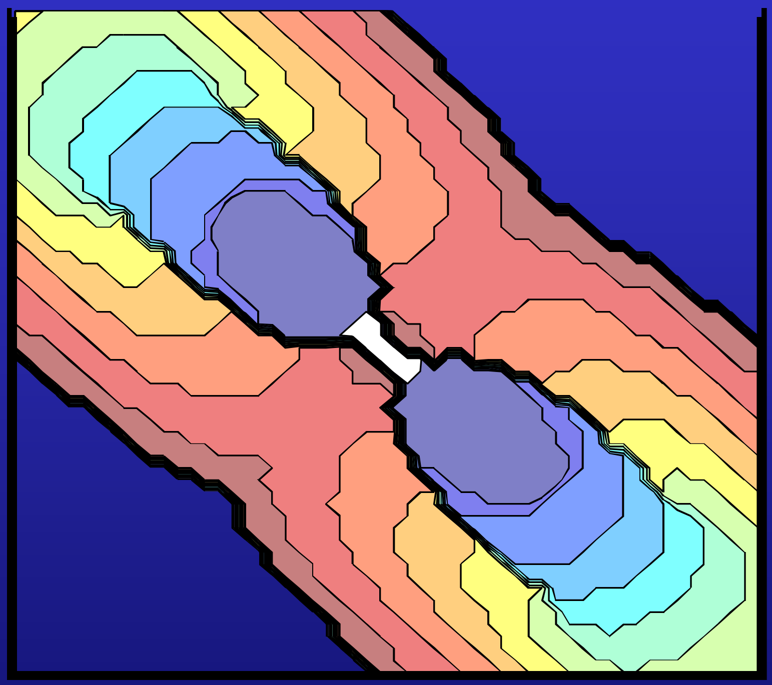
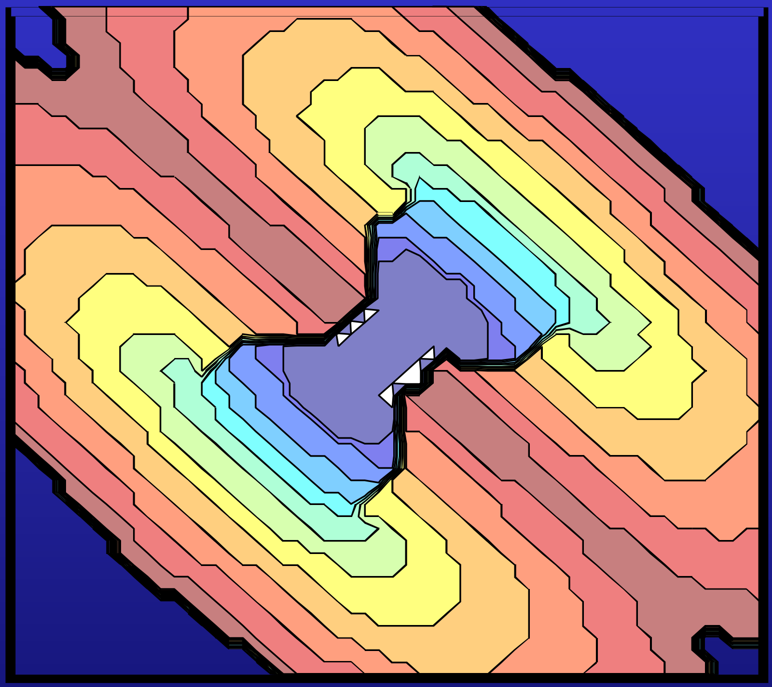
Quatrefoil Reentry Predicted by the Bidomain Model

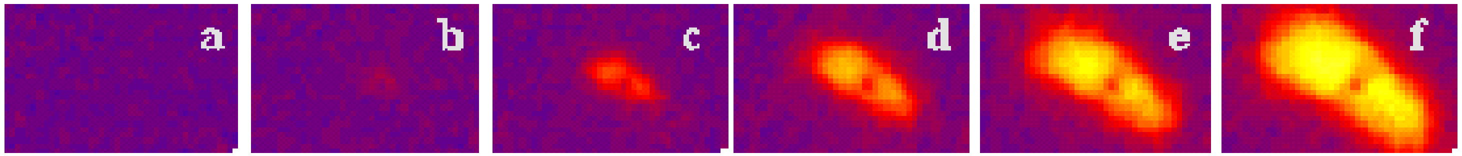




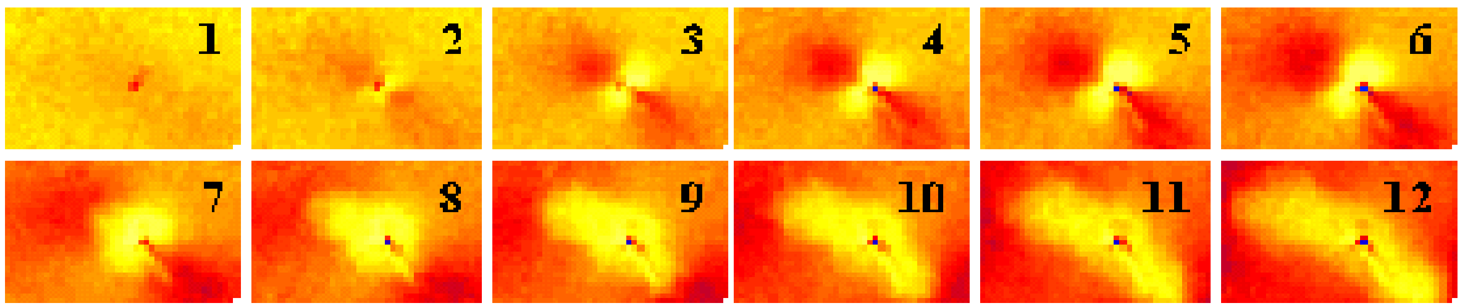
Fiber Direction

Activation Sequence

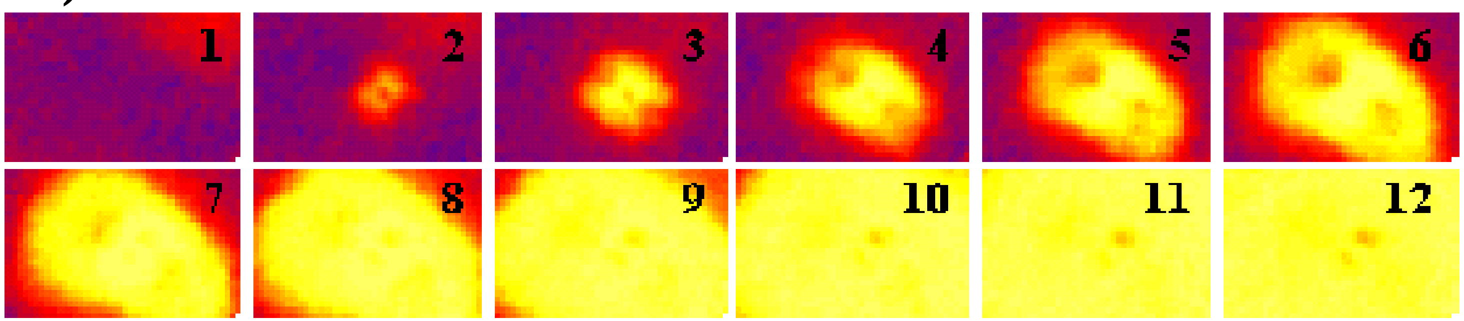
S1



S2 (CI: 140 ms) Cathode-break



S2 (CI: 180 ms) Cathode-make



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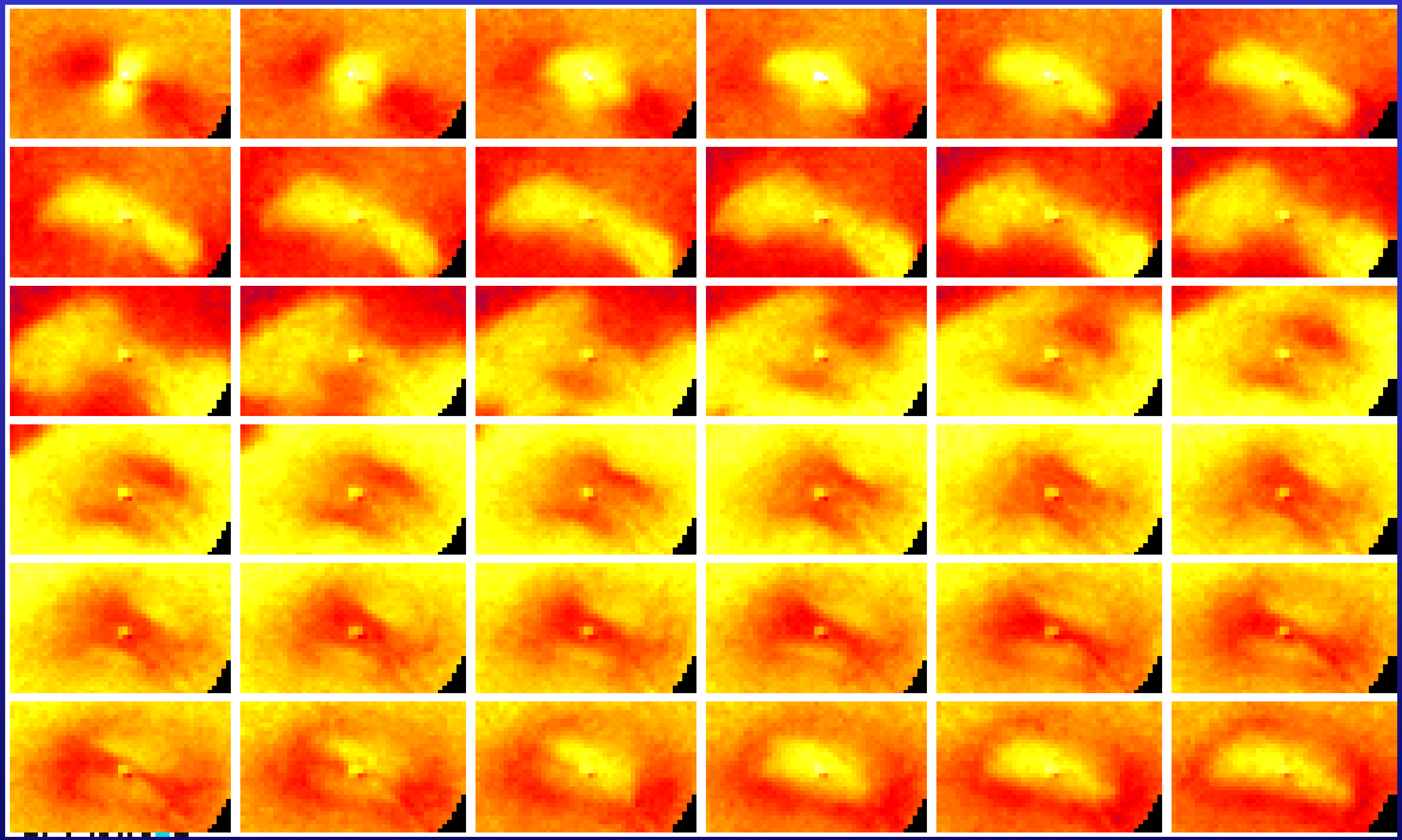
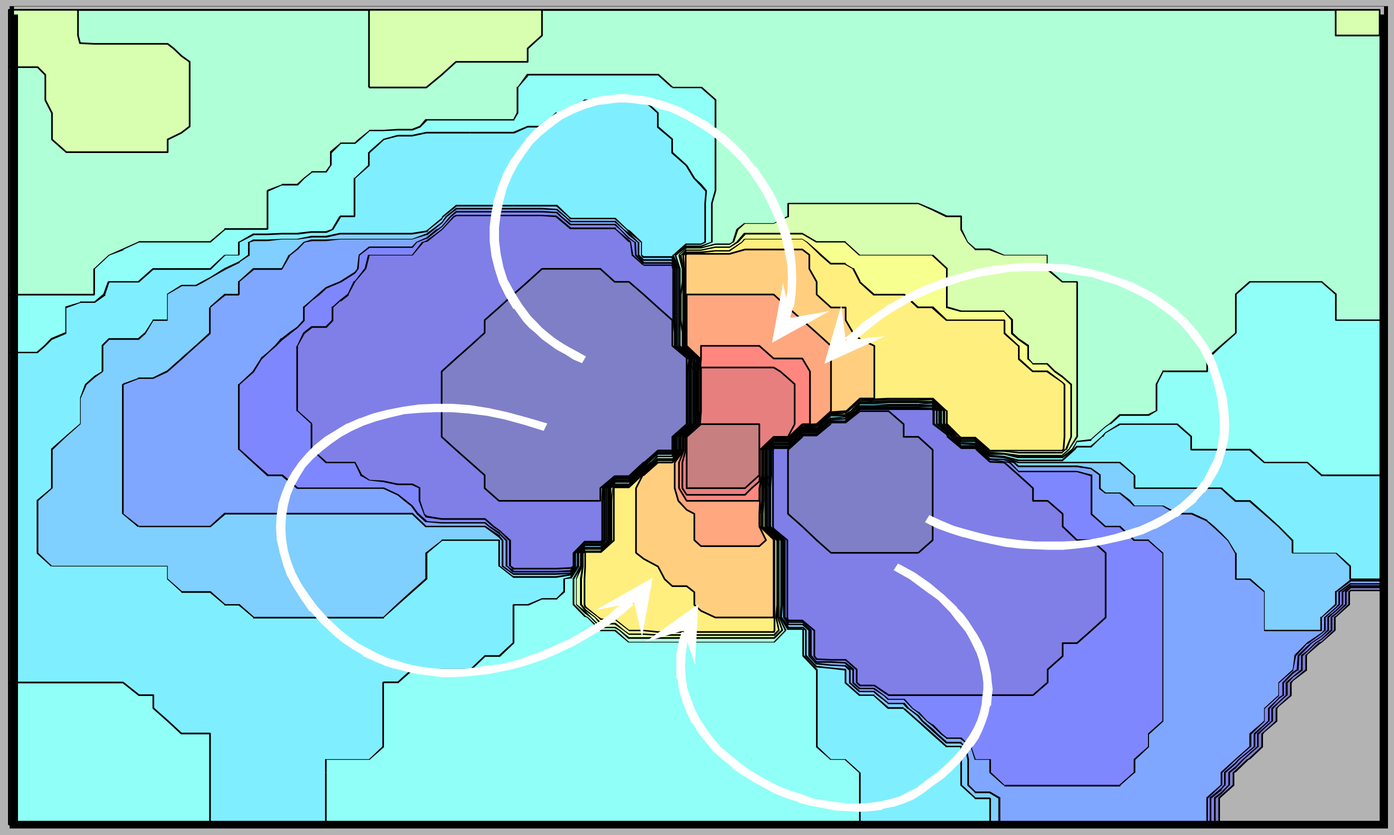
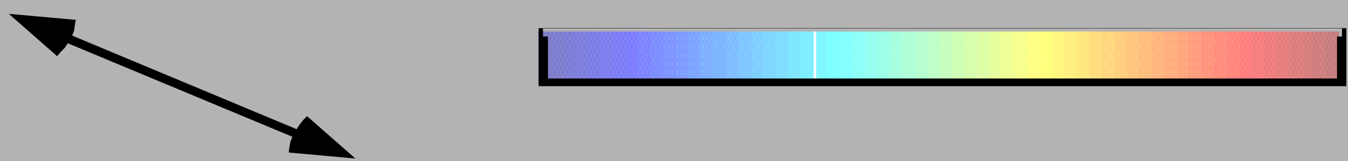
Quatrefoil Reentry from Cathodal Stimulation



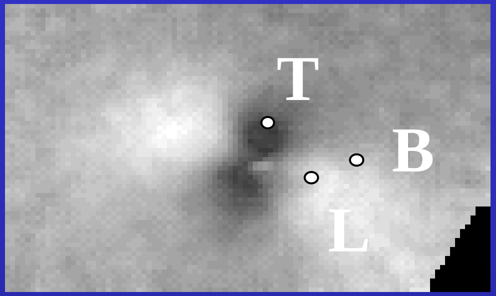
Isochronal Map of Quatrefoil Reentry (Cathodal S2)

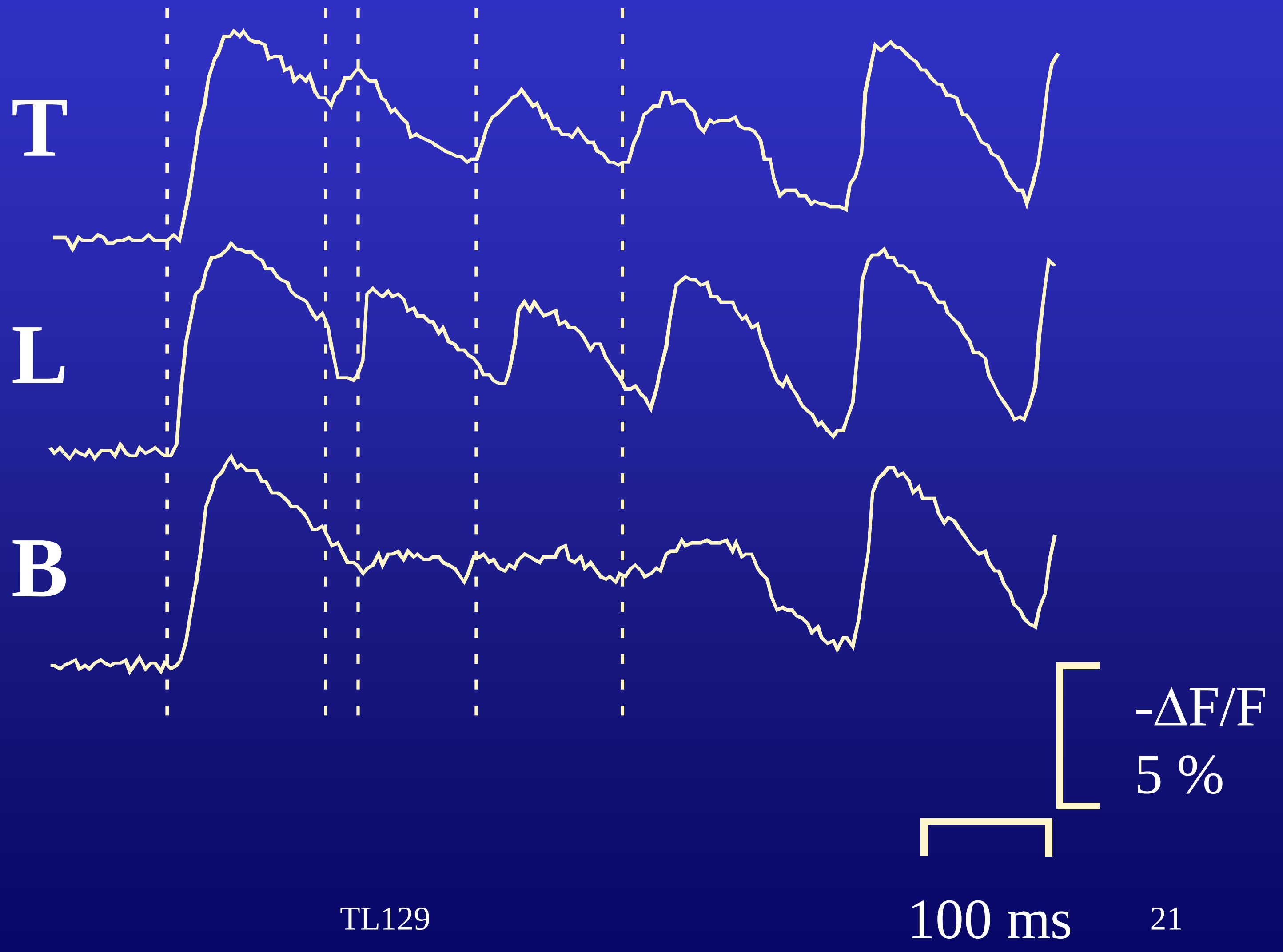




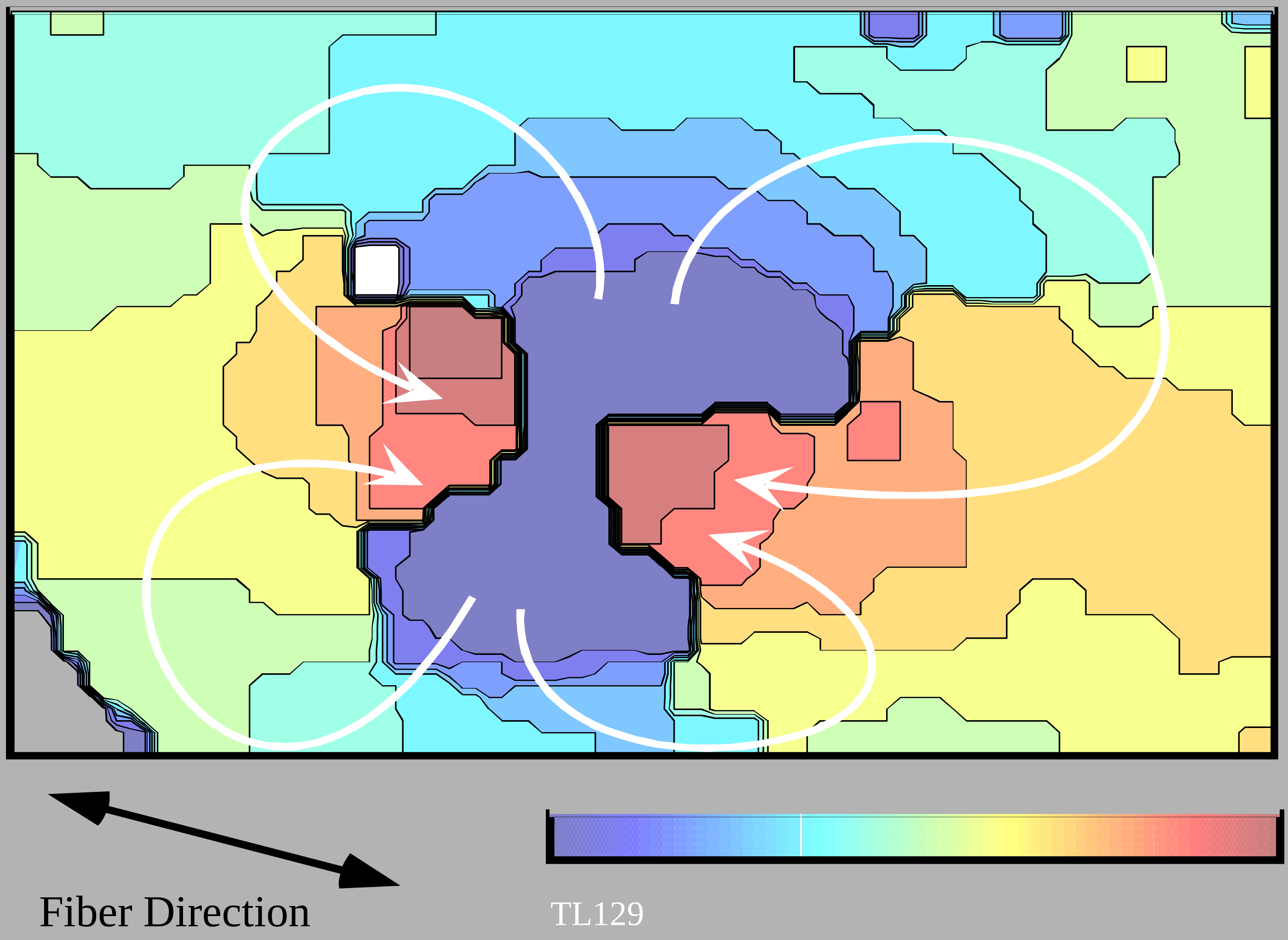
Fiber Direction

Functional Block is Characterized by Low-Amplitude Oscillation of V_m



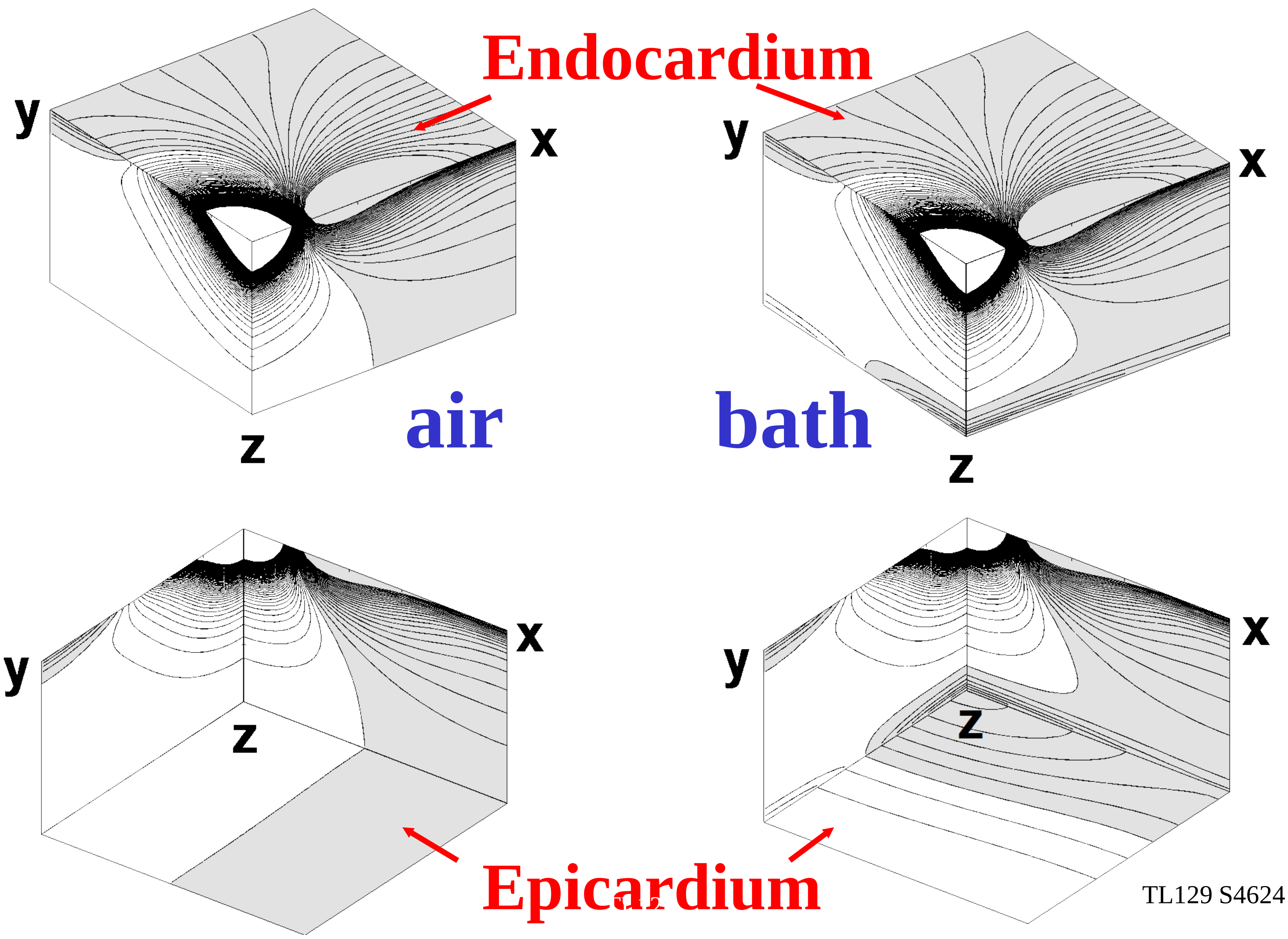


Isochronal Map of Quatrefoil Reentry (Anodal S2)



Prediction

- The <u>heart-medium interface</u>, *e.g.*, air versus a conducting bath, affects the distribution of stimulus and action currents
- The epicardial transmembrane potential distribution will differ greatly for endocardial stimulation of a heart in air or in a bath.


Endocardium
y
x
z
air
bath
y
x
z
y
x
z
y
x
z
Epicardium
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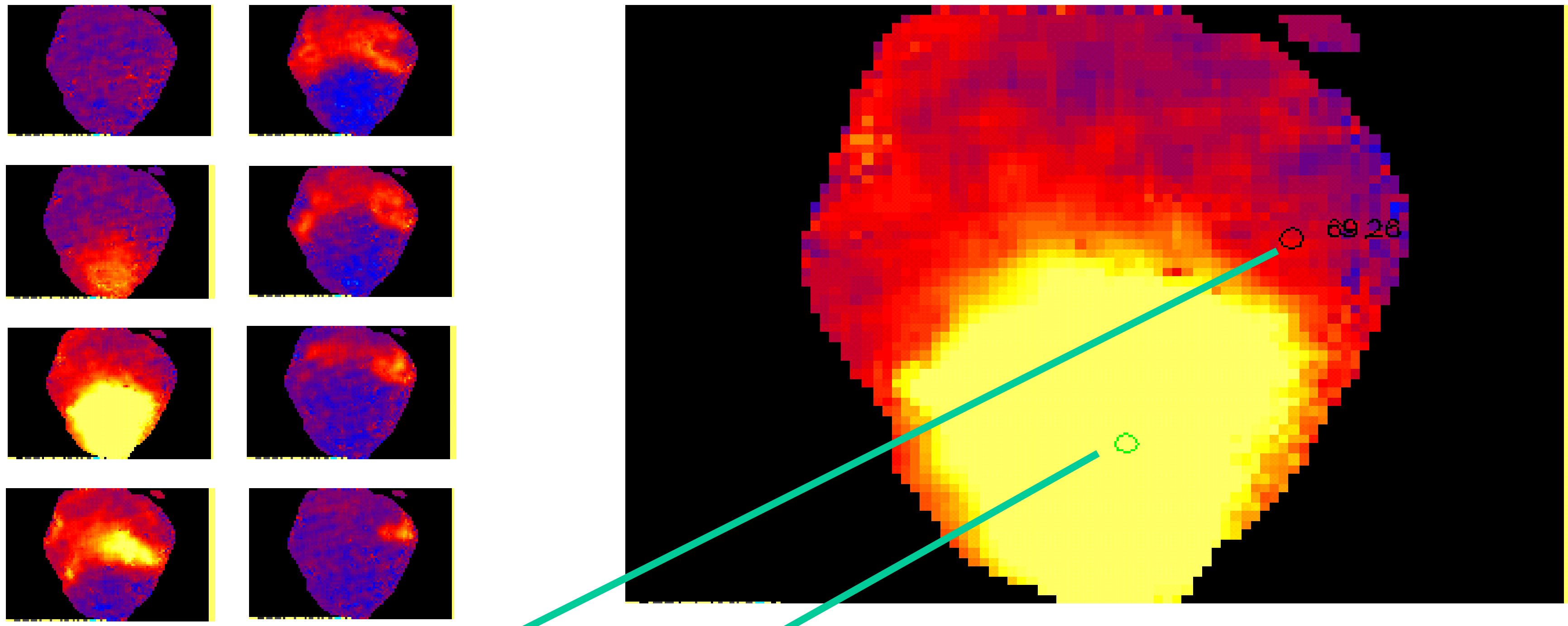
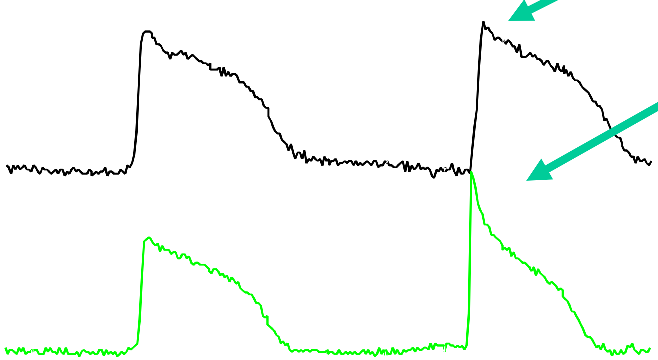
Heart Free in the Bath





A monophasic anodal shock (100 V/5 ms, CI: 500 ms) is delivered from the apex of LV with the heart in the bath WITHOUT against the frontal glass plate.   The response is dramatically different.

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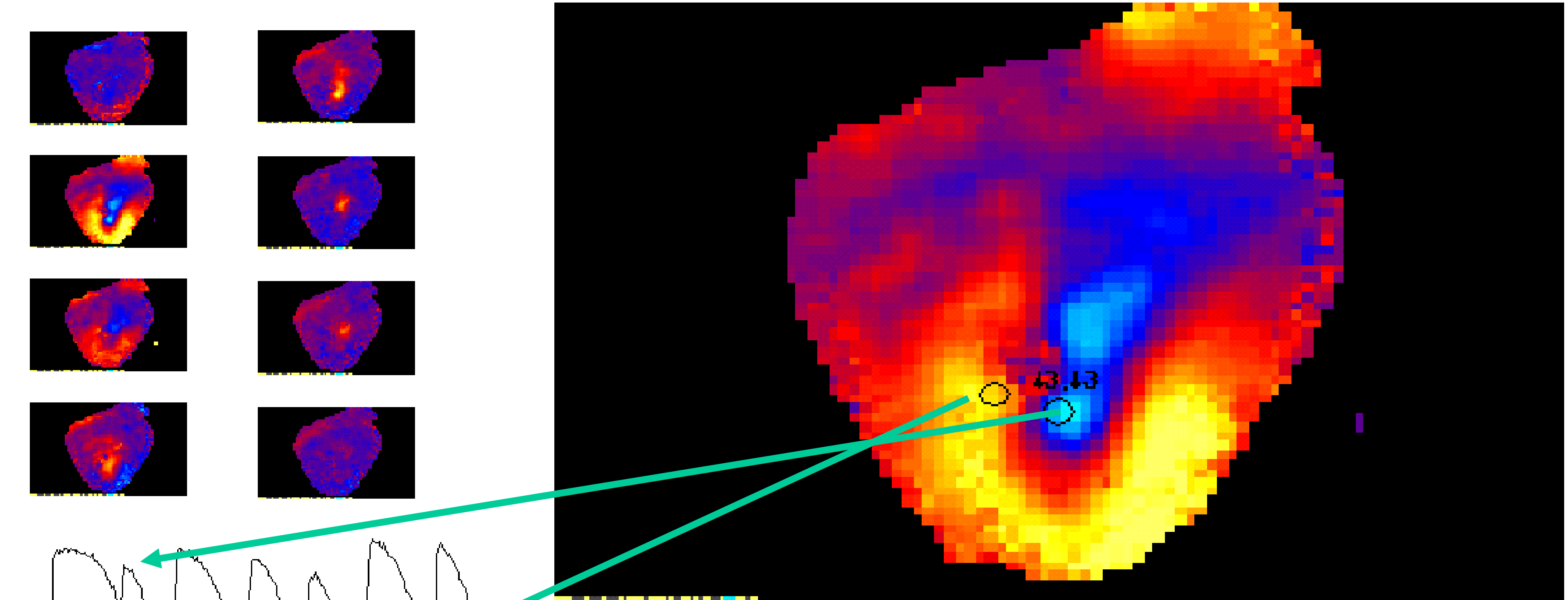
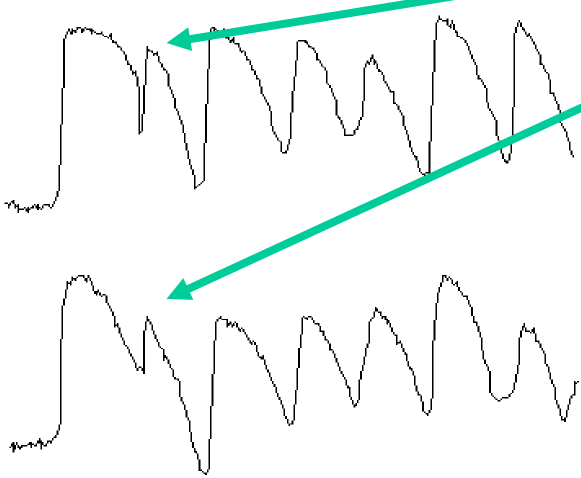
Heart Pressed against the Front Window





A monophasic anodal shock (100 V/5 ms, CI: 160 ms) is delivered from the apex of LV with the heart in the bath and pressed against the frontal glass plate.

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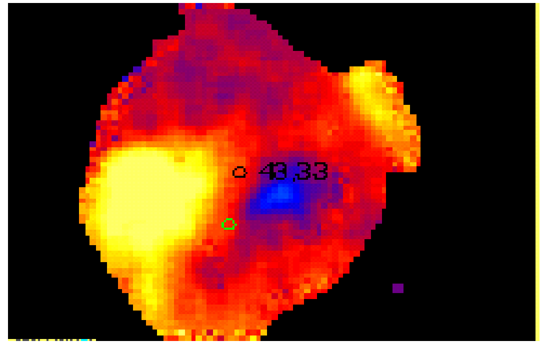
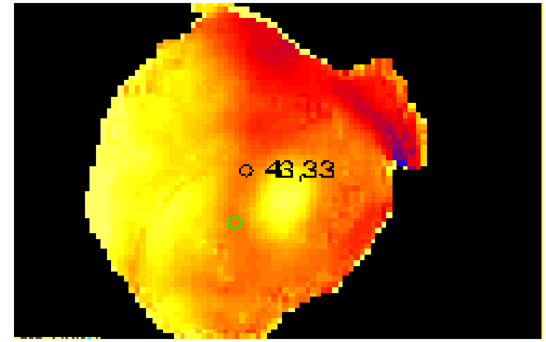
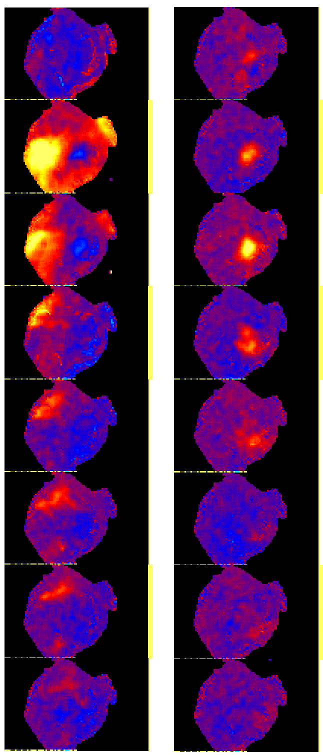
Propagationless, Post-Shock Charge-Diffusion

Excitation Pattern

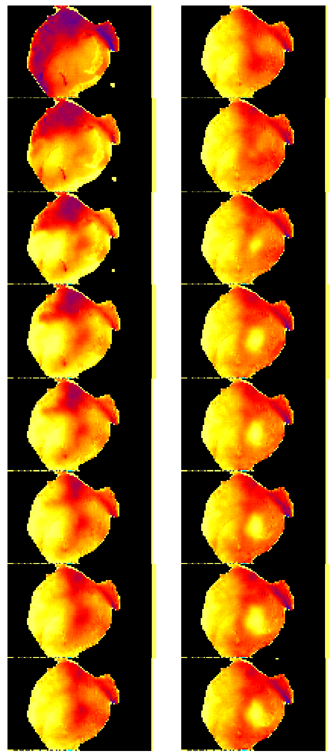


37 ms after the Shock

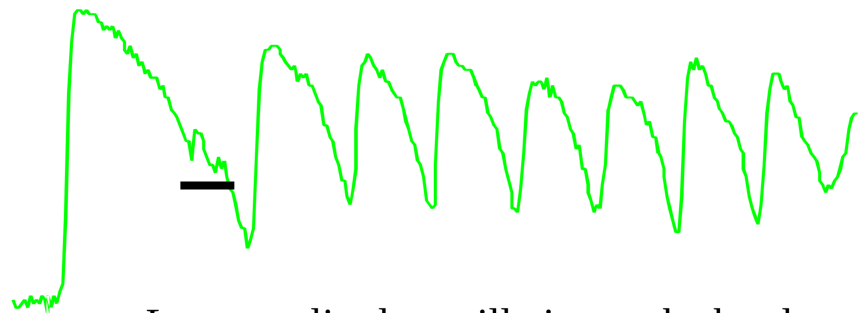




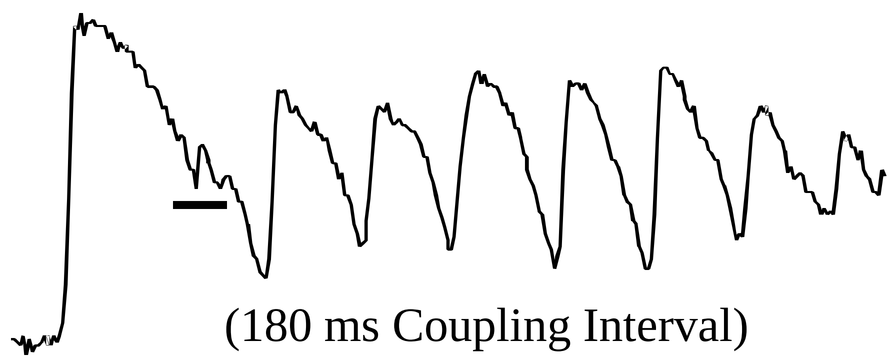
dVm/dt



Vm Distribution



Low-amplitude oscillation at the border



(180 ms Coupling Interval)

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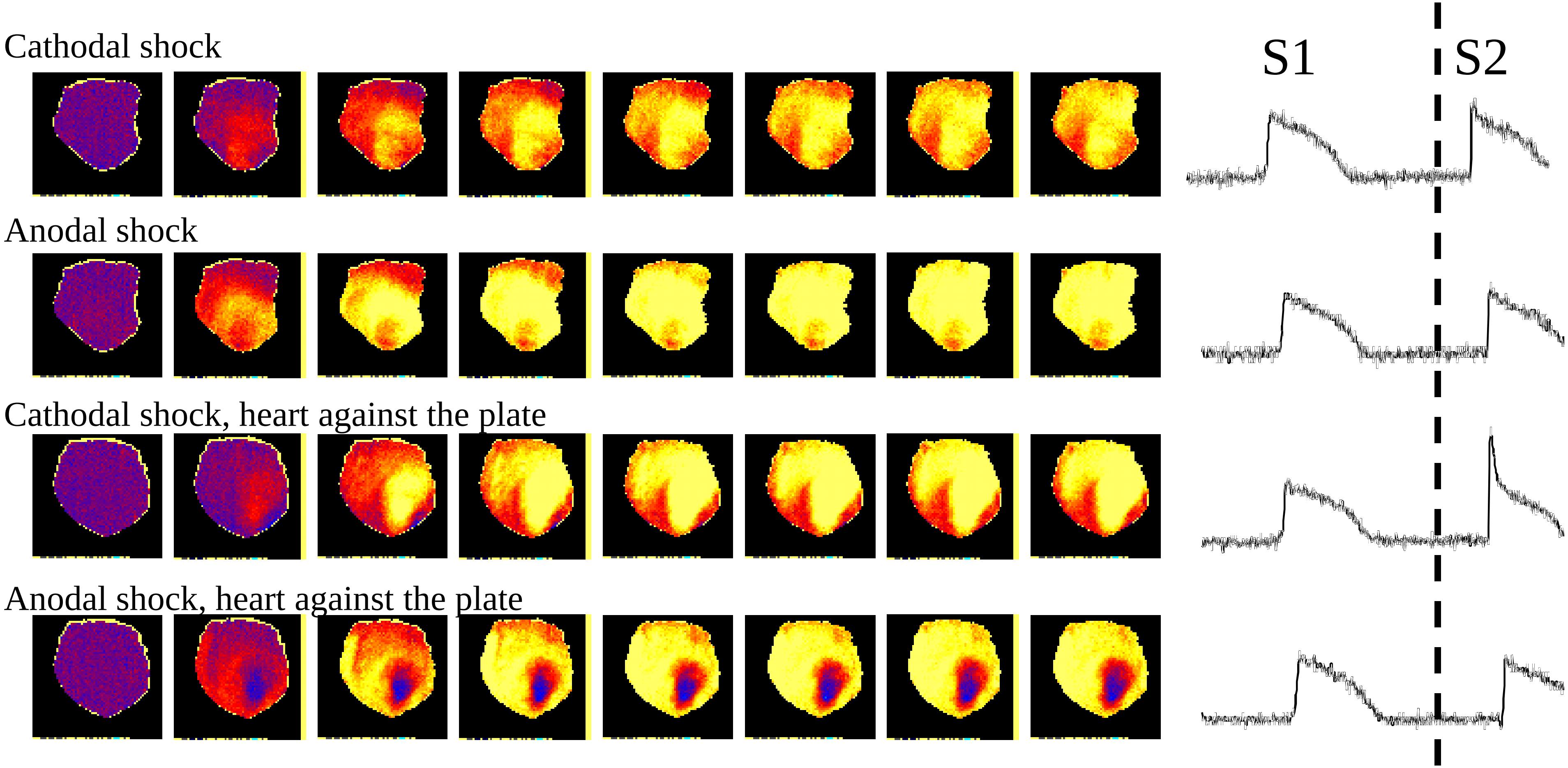
Response during a 200-V/5-ms Shock



Frame interval: 0.8 ms (1200 frames/sec)

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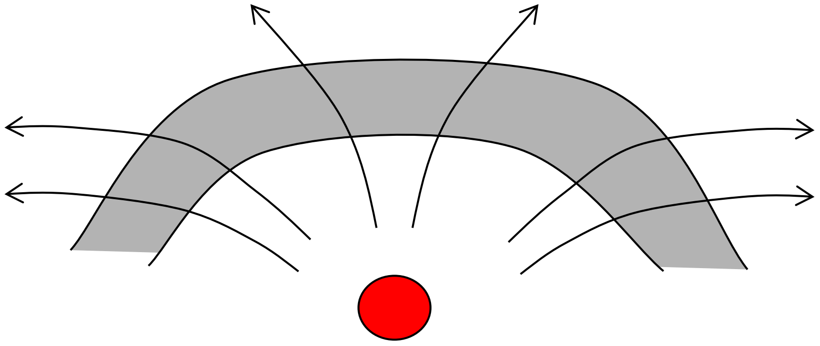
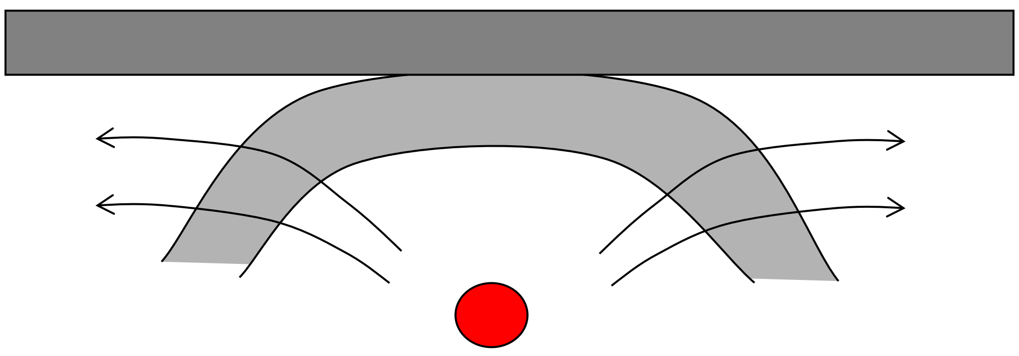
Preservation of Endocardial Response with Insulating Plate

A.



B.



The Problem of Defibrillation

If the heart is a cable with a length constant of 1-3 mm, the trans-membrane potential will fall below threshold within several length constants of the electrodes.

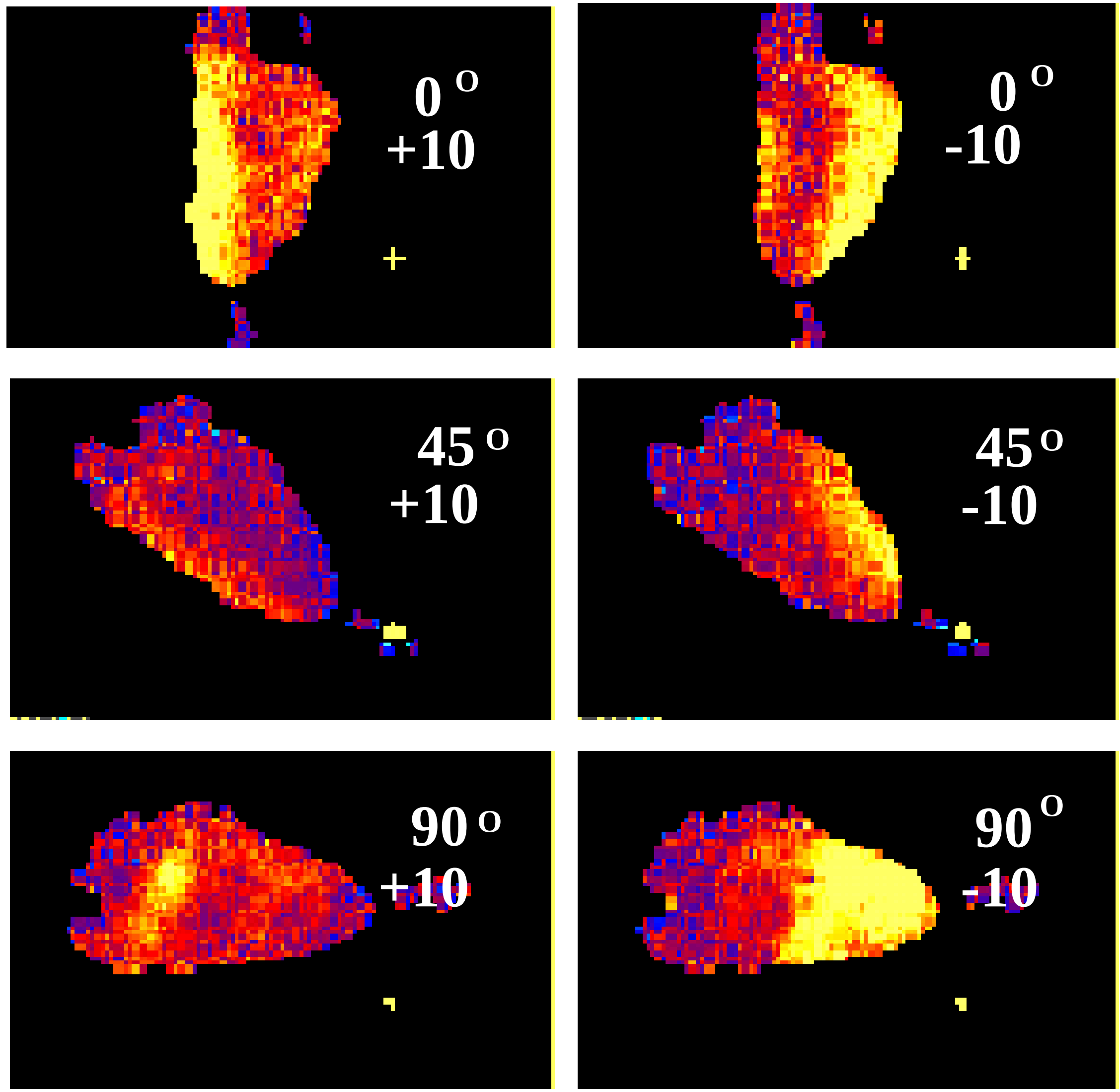
Possible Answers

- **Discrete mechanisms**
  - **Intracellular junctions**
  - **Uncoupled bundles**
  - **Patches of fat or collagen**

- **Continuous mechanisms**
  - **Cardiac surfaces**
  - **Fiber ends**
  - **Tissue anisotropy**
  - **Fiber curvature**
  - **Fiber branching**
  - **Strand taper**
  - **Fiber rotation**

"Cardiac tissue in an electrical field: A study in electrical stimulation," N.A. Trayanova and B.J.Roth, *Computers in Cardiology 1992*, (IEEE Computer Society Press, 1992) pp. 695-698.

Tissue Response to Field Shock



Conclusion

- Excitation with point electrode produces complex patterns of virtual electrodes
- Monophasic endocardial shocks elicit bipolar response through the heart wall
- Field shock produces initial bidomain response independent of fiber orientation
- Epicardial response from endocardial shock depends on the heart-medium interface
- Break excitation may be significant in defibrillation

Future Studies

- Biphasic shock
- Heterogeneous bidomain
- Knockout mice
- “Break” defibrillation mechanism