Vacuum Pair Production/Annihilation and Cardiac String Dynamics

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scroll_wave_breakup_fhnplus_high-res.mov

Acknowledgements

- Rubin Aliev
- **Mark Bray**
- Elizabeth Cherry
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- Mark Lin
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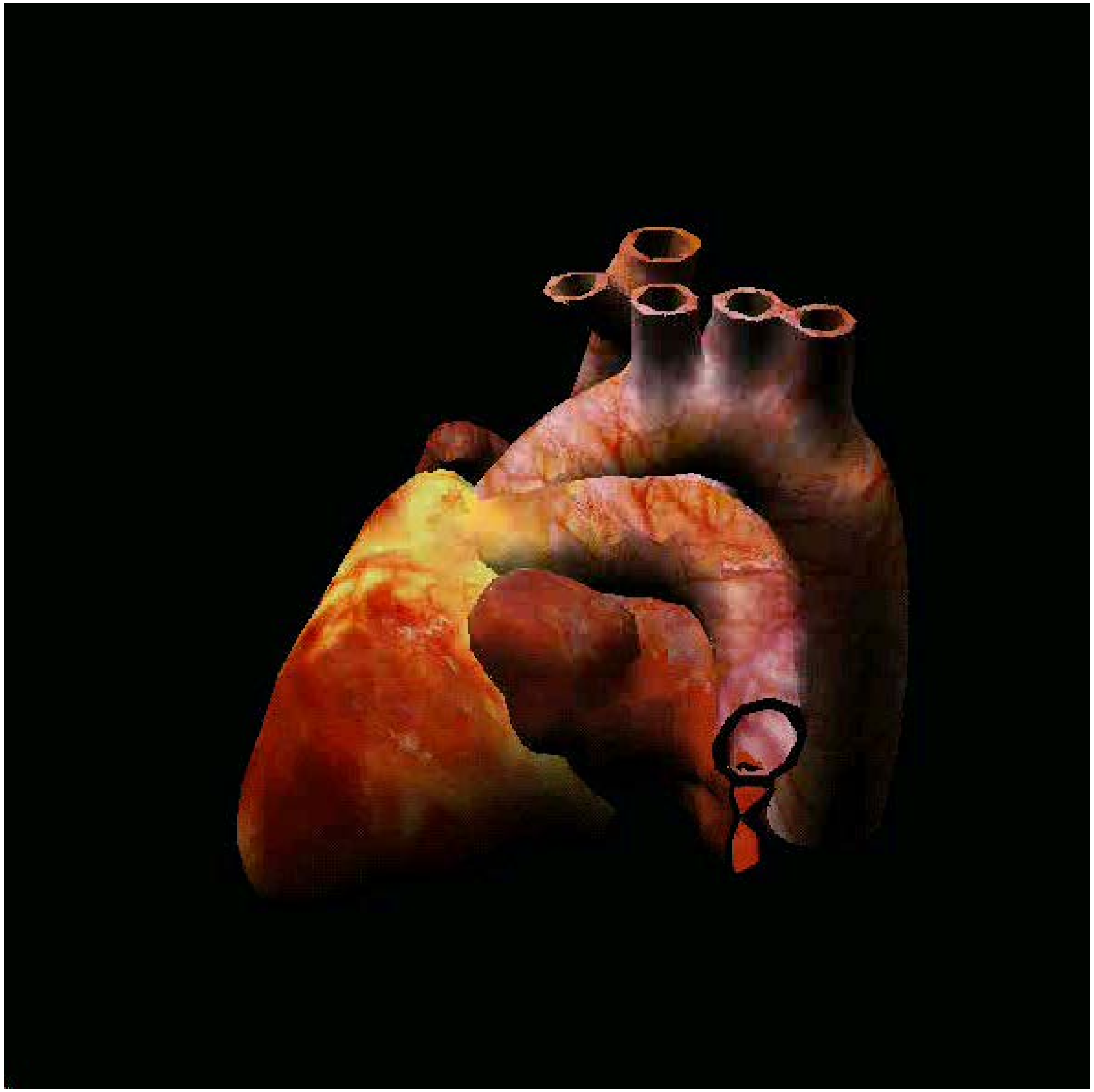
- Arkardy Pertsov
- Nathalie Virag
- Jim Weiss
- And many others

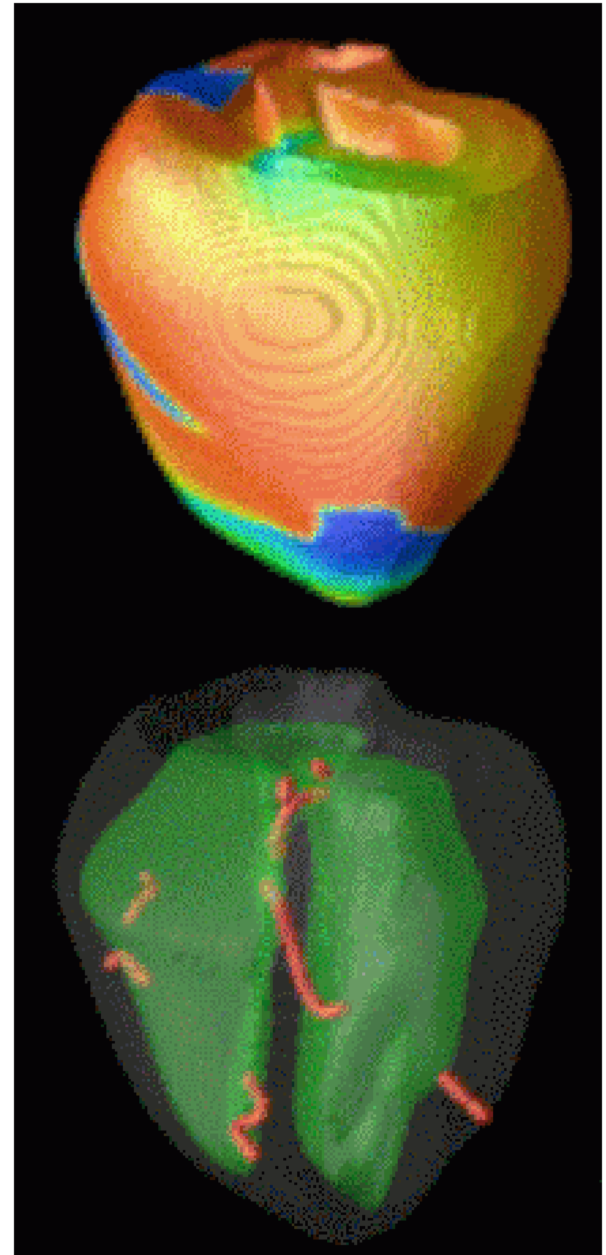


Courtesy of Peter Hunter, Auckland

textured-heart-spin.mpg

Where are the heart strings, and who is pulling them?

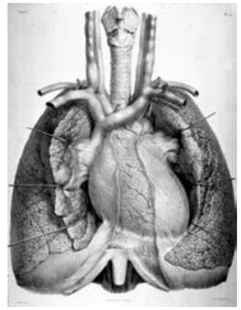
- The normal heart has none
- The presence of one string is serious
- The presence of several for a very few minutes is fatal



flavio_rabbit_vf.avi

Courtesy of Flavio Fenton, Hofstra

Outline



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  - Simple reentry
  - Fibrillation
- Singularity interactions
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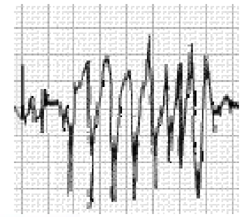
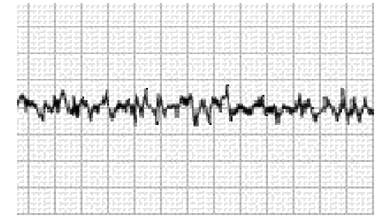
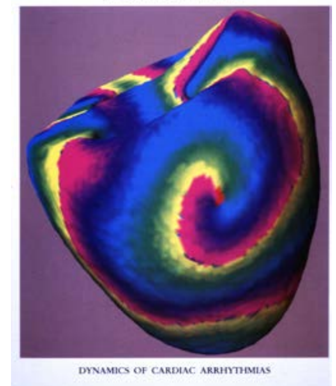
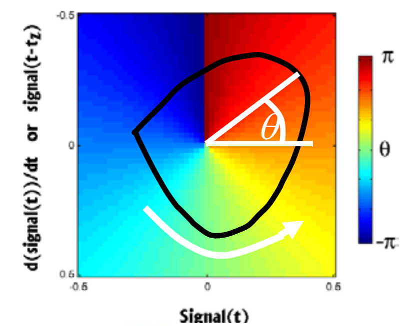
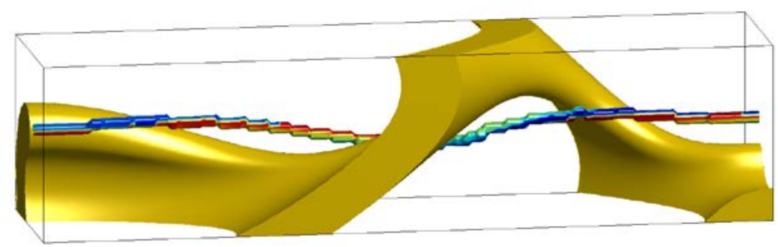
  - Annihilation
  - Creation
- What is needed?
  - Interaction potential
  - String creation operator

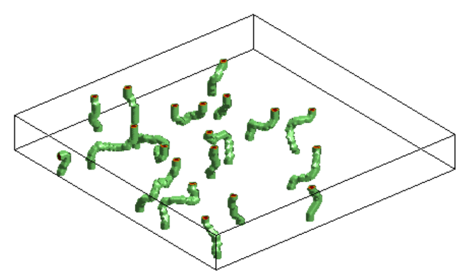






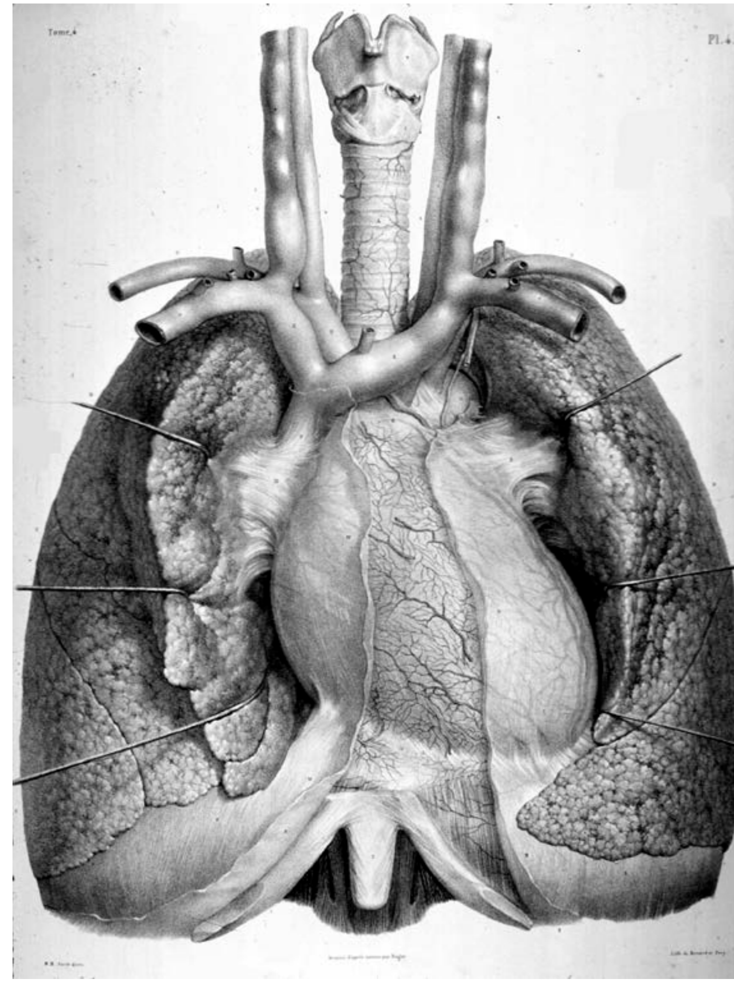






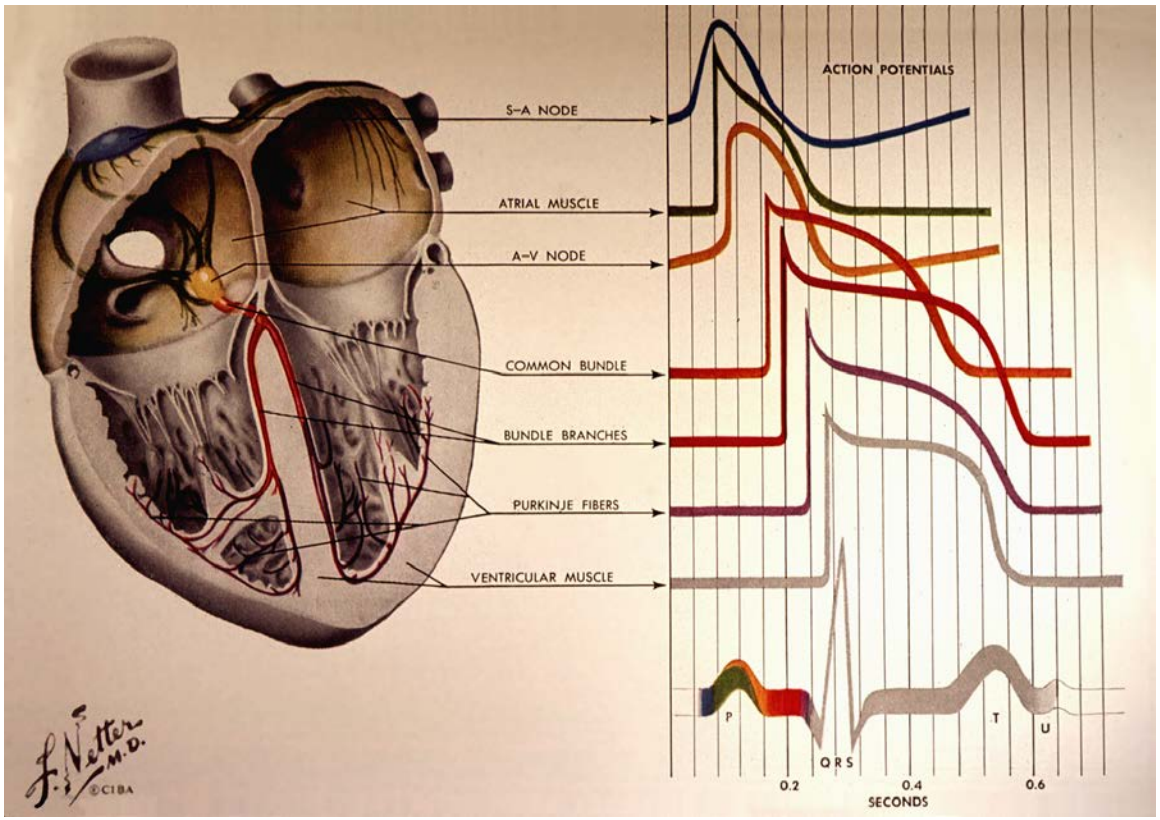
The Heart is a…

- Self-assembling,
- Biochemically powered,
- Electrically activated,
- Electrically non-linear,
- Pressure- and volume-regulated,
- Two-stage,
- Tandem,
- Mechanical pump
- With a mean time-to-failure of approximately two billion cycles.

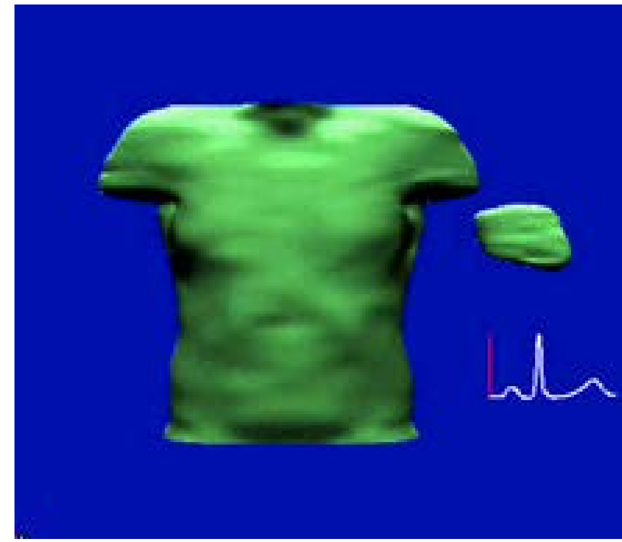


The heart is ...

electrically activated …



From: The Ciba Collection of Medical Illustrations: Heart, F. H. Netter, 1978



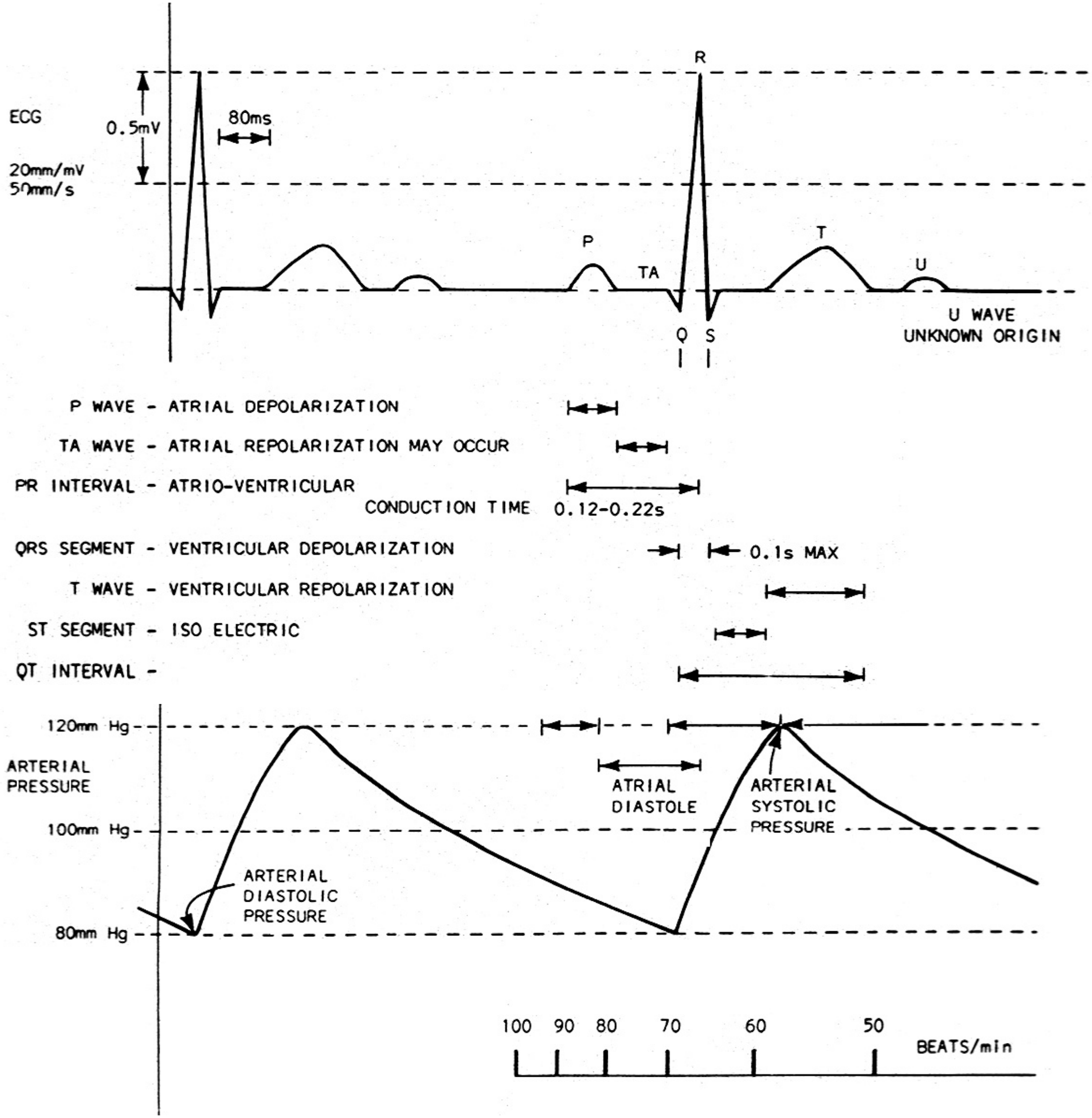
Courtesy of Peter Hunter, Auckland

normalbsm.mpg

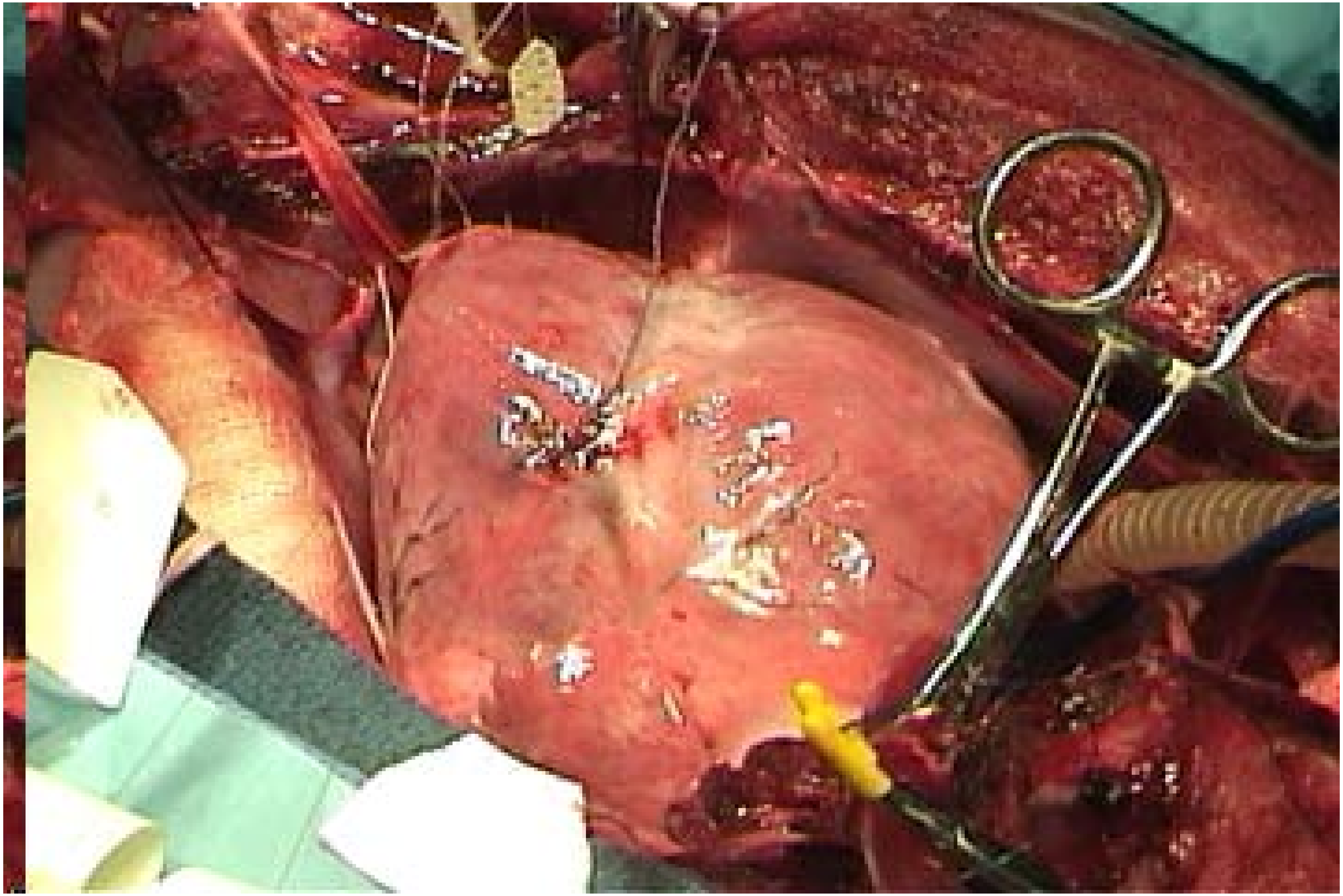
The heart is an …

- Electrically activated,

- Mechanical pump



The Normal Heart Beat



Courtesy of Rick Gray and CRML, U. Alabama Birmingham

SwineSinus.mov

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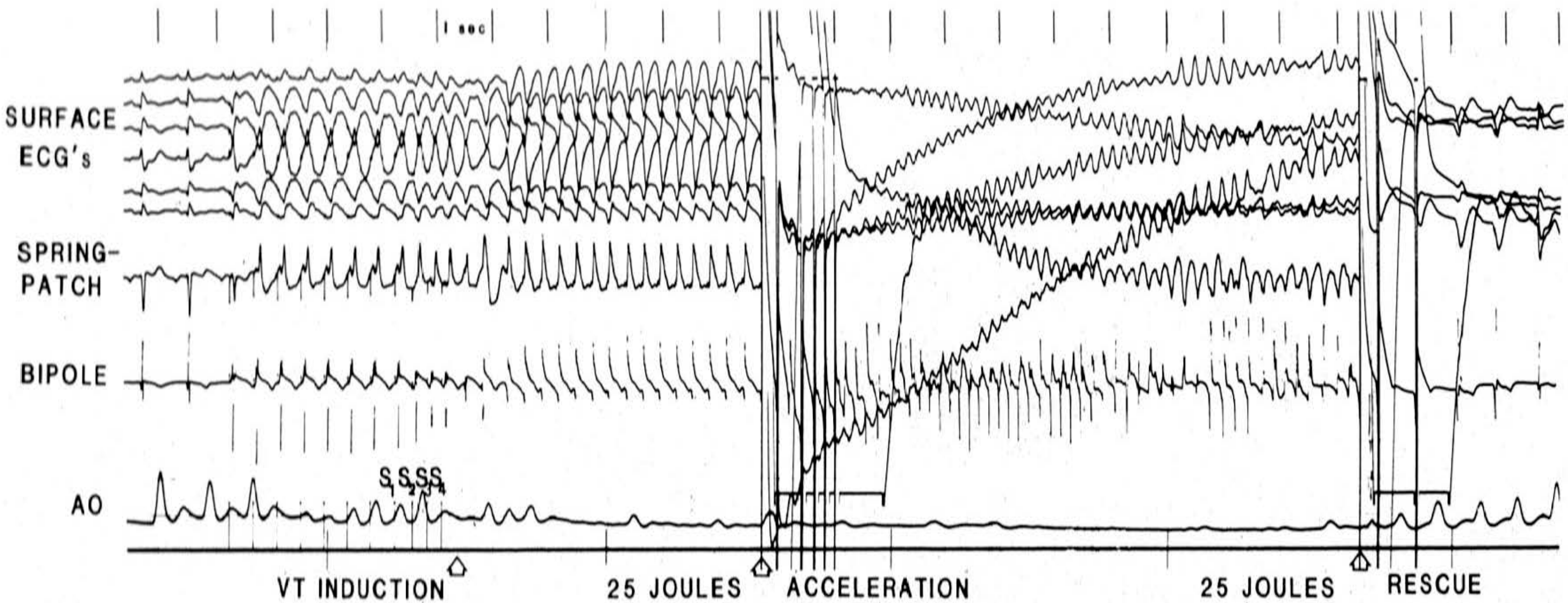
Courtesy of Flavio Fenton

The heart is an electrically activated mechanical pump

…with a mean time-to-failure of approximately two billion cycles….

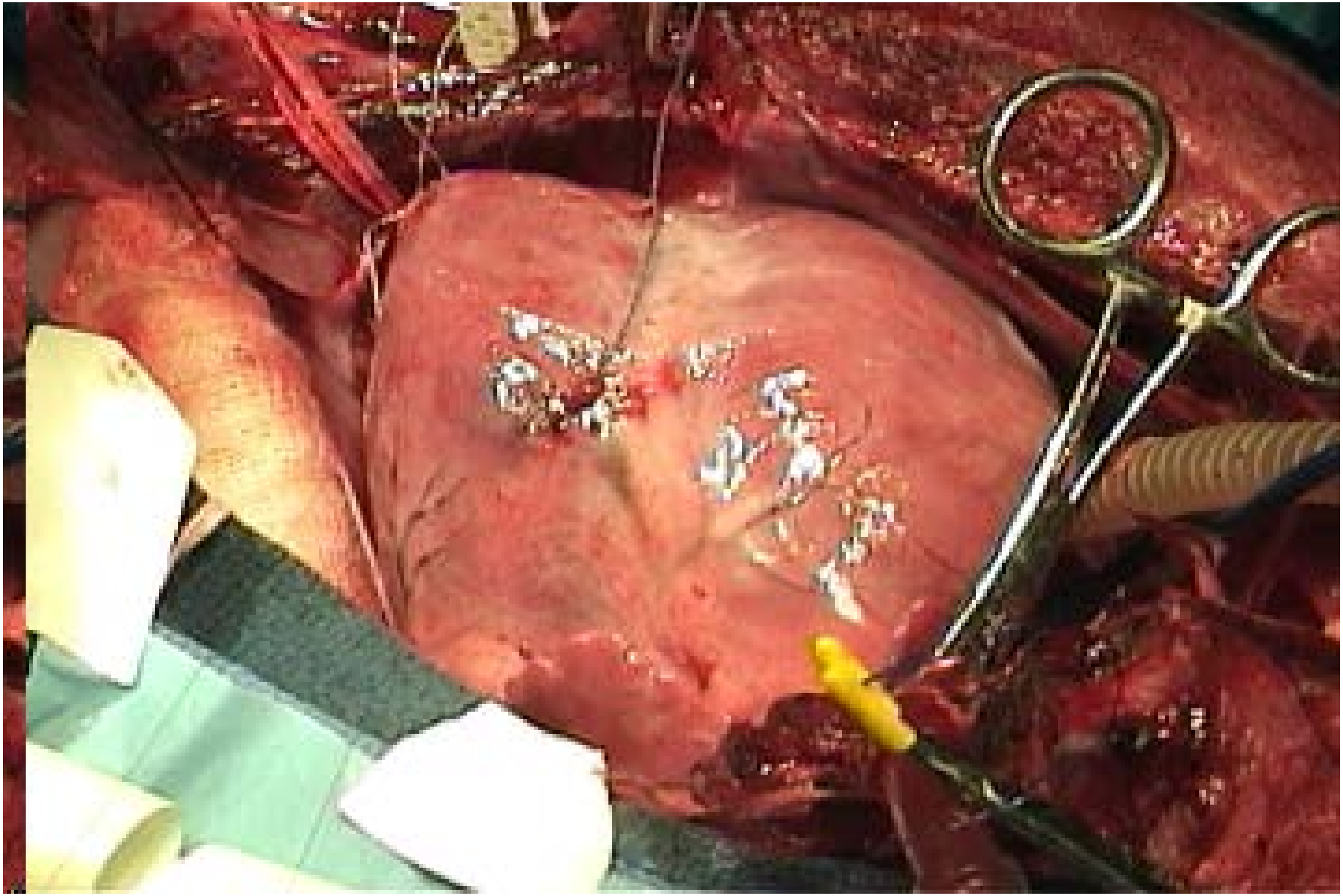


Courtesy of Debra Echt

Normal Tachycardia Fibrillation Defibrillation

s04105

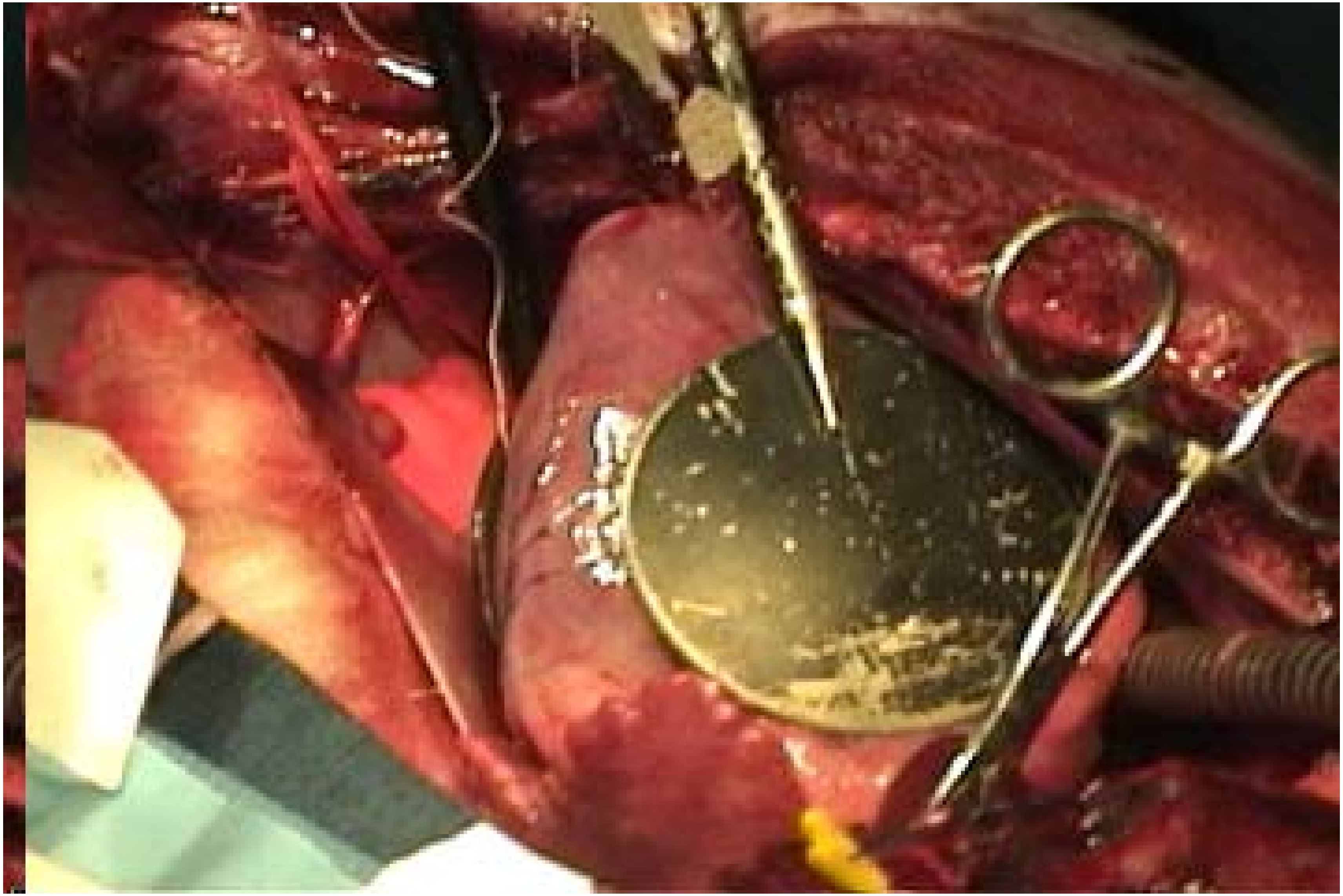
Induction of Fibrillation



Courtesy of Rick Gray and CRML, U. Alabama Birmingham

SwineSinusVF.mov

Termination of Fibrillation



Courtesy of Rick Gray and CRML, U. Alabama Birmingham

SwineVFShockSinus.mov

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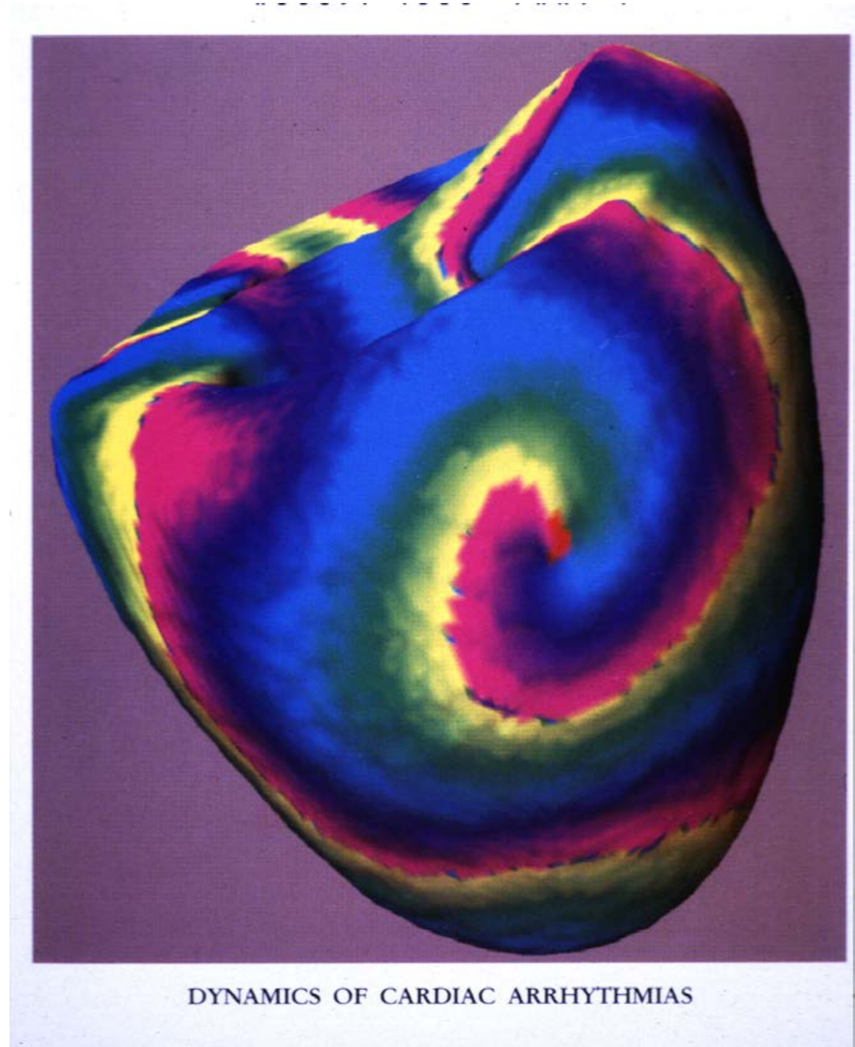
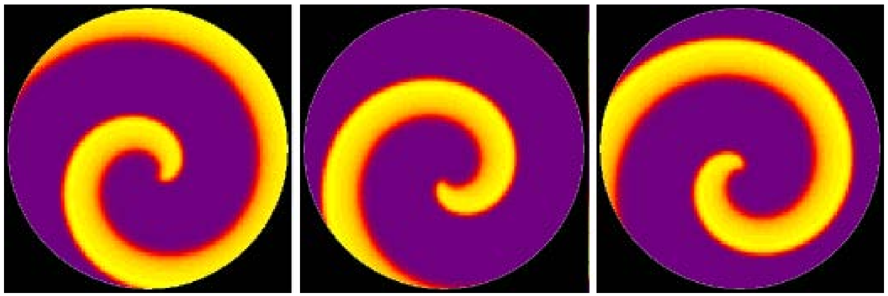
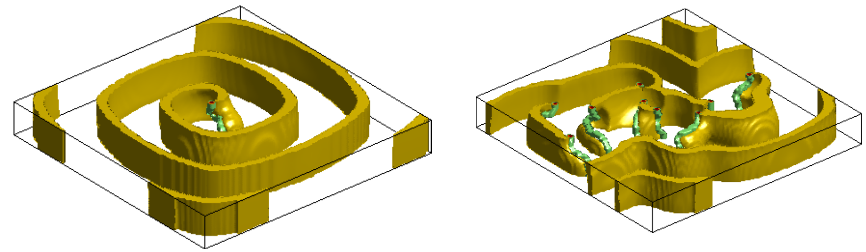


Leon Glass and *Physics Today*

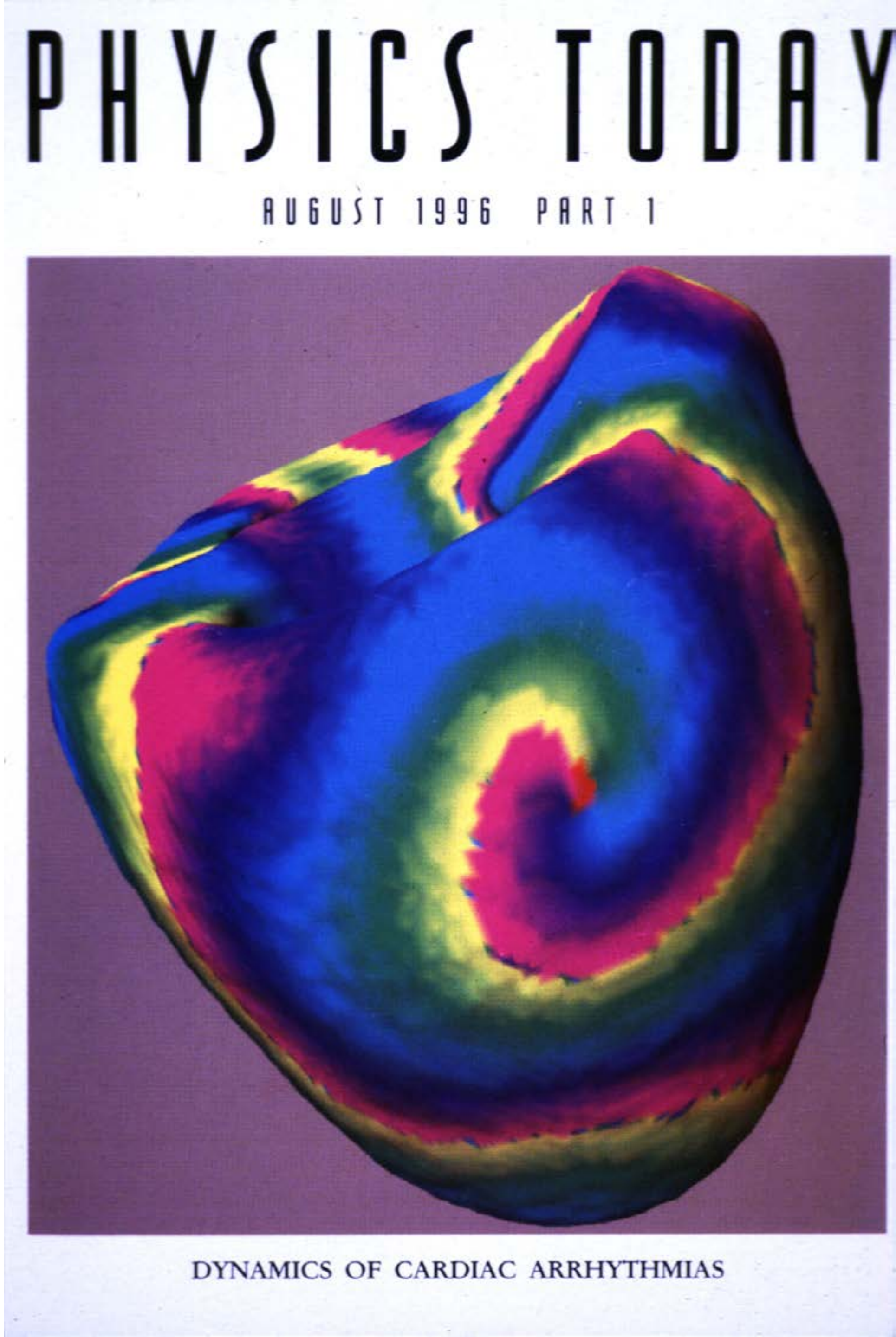
Spiral and Scroll Waves in Nature





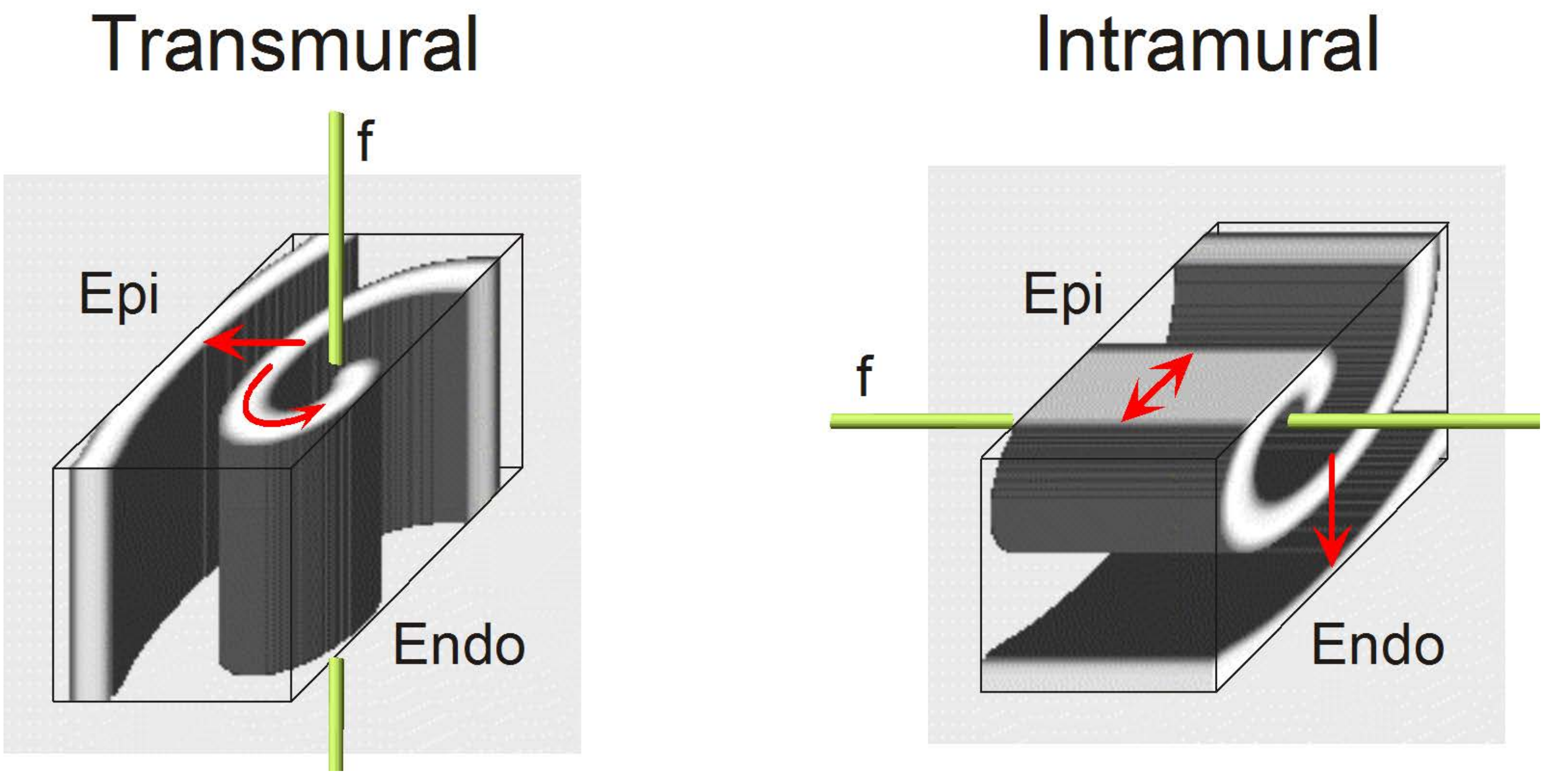
- A generic property of excitable media
- Have been shown to occur in
  - Circulating waves of bioelectric activity in cardiac and retinal tissue
  - Autocatalytic chemical reactions, such as Belousov-Zhabotinsky reaction (BZ)
  - cAMP waves in slime mold *Dictyostelium discoideum*
  - Intracellular calcium release in oocytes
  - Oxidation of CO on crystal surfaces in ultrahigh vacuum conditions
- Cardiac fibrillation involves multiple scroll waves in 3-D

Cardiac fibrillation occurs at the spatial scale of the entire heart, and involves multiple, interacting spiral and/or scroll waves!



Physics Today and Leon Glass, Montreal

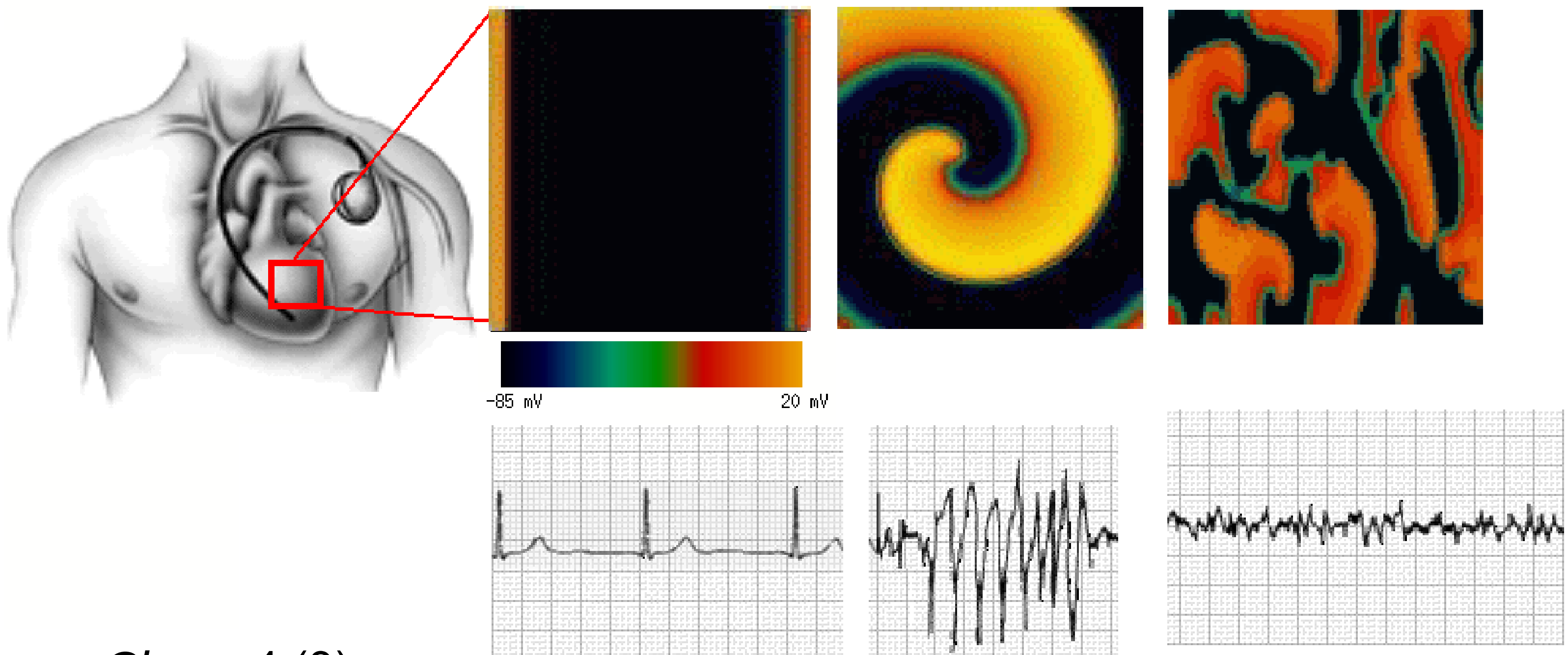
Transmural versus intramural scroll waves in reentrant arrhythmias and fibrillation



- Transmural waves can exist in 2-D (thin) or 3-D (thick)
- Intramural waves require ~1 cm wall thickness

Courtesy of Arkady Pertsov, Syracuse

Transition from Normal Rhythm to Ventricular Tachycardia to Ventricular Fibrillation



A. Karma, *Chaos* 4 (3): 461-472, 1994

Normal Rhythm **VT** **VF**

Single spiral wave = Tachycardia

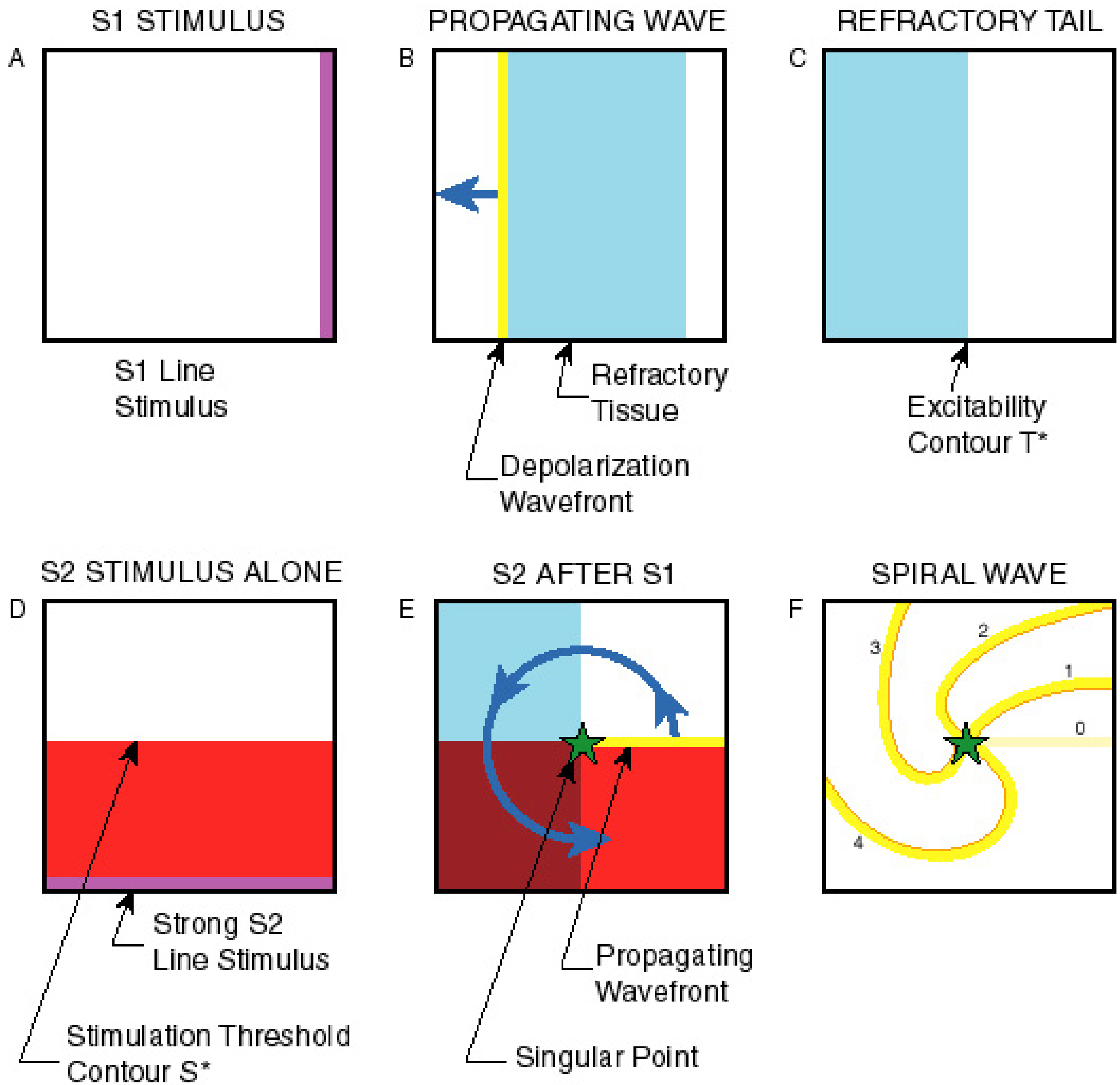
Multiple spiral waves = Fibrillation = SCD

Movies courtesy of Flavio Fenton

SA.avi SBB.avi scclong.avi

Initiation of Spiral Wave Reentry

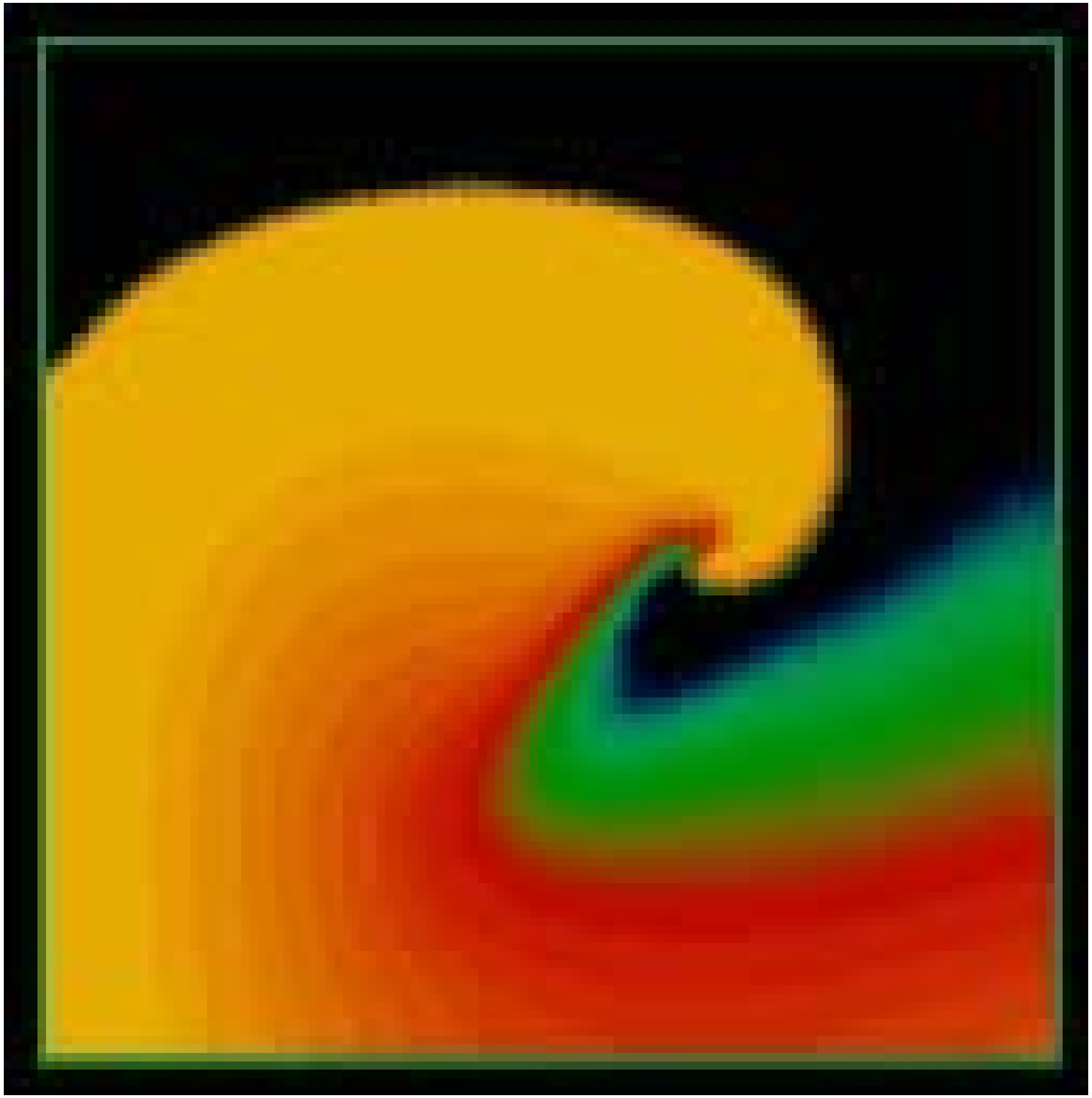
S1-S2 crossed-field stimulation



A “Simple” Spiral Wave

The nature of the spiral is set by the non-linear properties of the excitable medium

- Linear core
- Epicycloidal meander
- Circular core



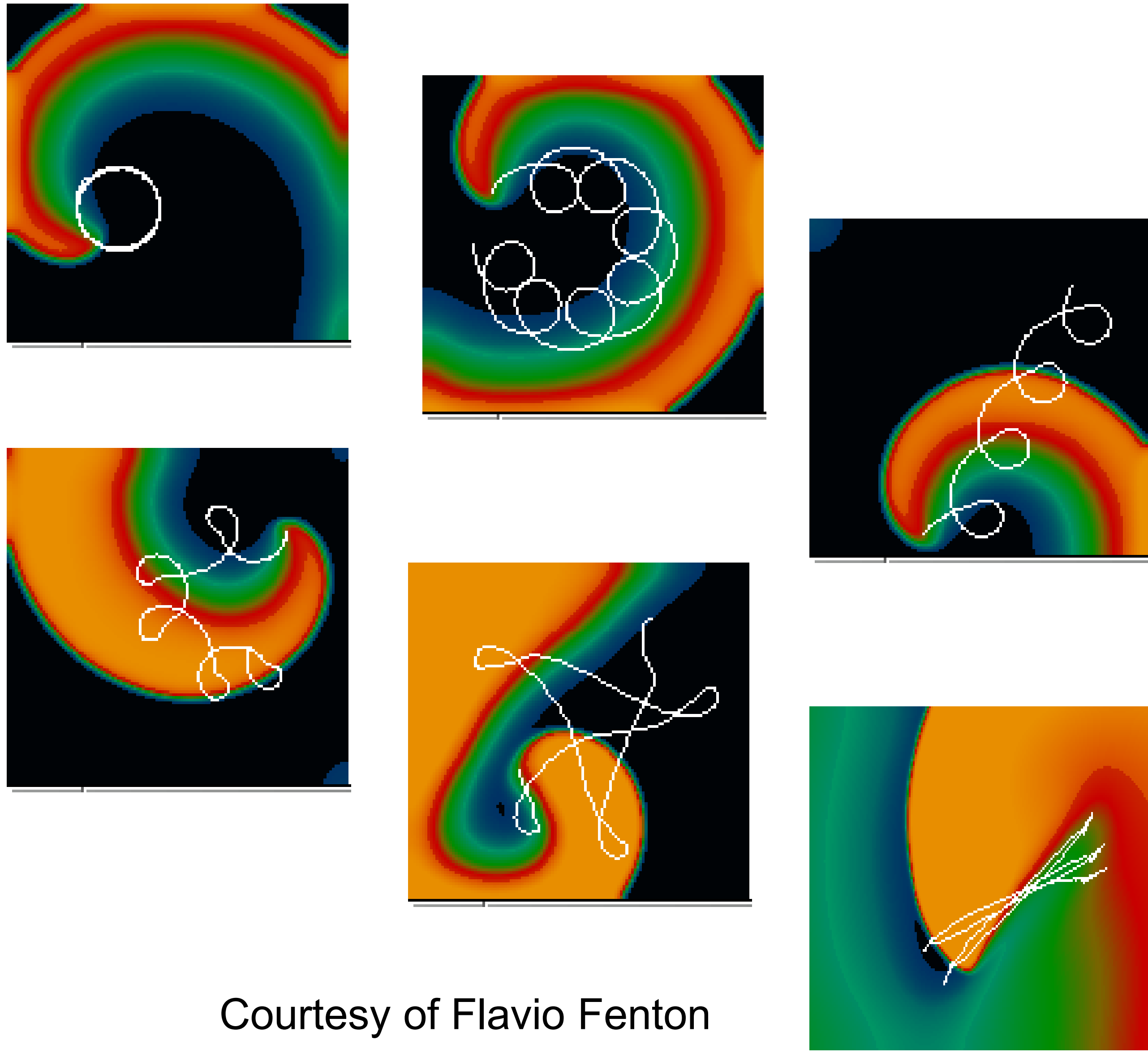
tspiralgs.avi

Courtesy of Flavio Fenton

Nonlinear Properties Determine the Trajectories

- Six Phenotypes
  - Circular
  - Epicycloidal
  - Cycloid
  - Hypercycloidal
  - Hypermeander
  - Linear core

- Winfree, Krinsky, Barkley, Efimov, Jalife, Pertsov, Gray, Roth, Fenton, Garfinkel, Chen …



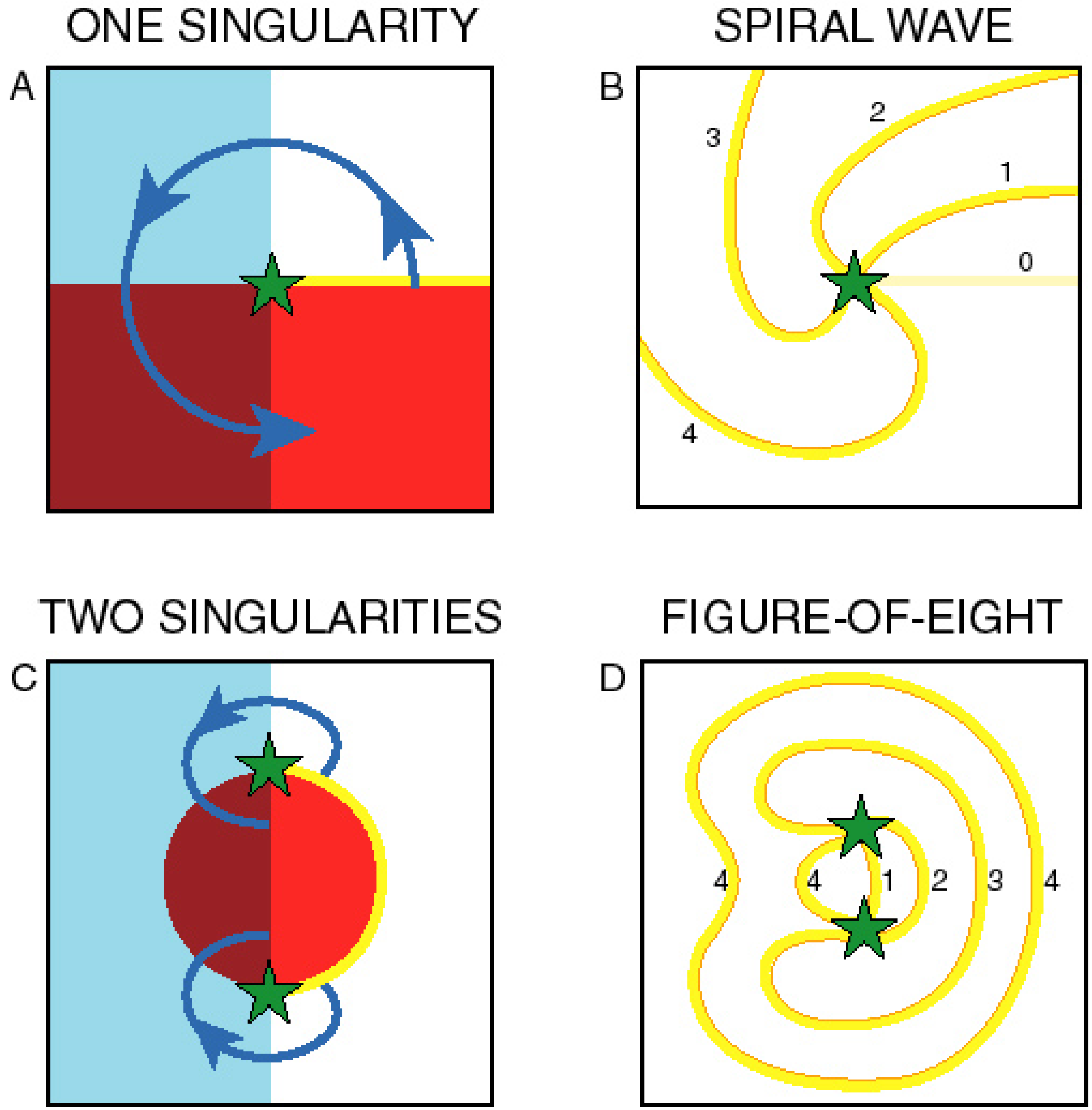
Courtesy of Flavio Fenton

Non-linear dynamics of <u>reentry</u>, fibrillation, and defibrillation

- <u>Reentry</u> -- Self-sustained excitation due to propagating activation wave fronts in the heart that continue to re-excite different regions of tissue rather than terminating after a single excitation
- <u>Anatomical reentry</u> -- activation wave fronts that travel in one direction around an anatomical obstacle
- **<u>Functional reentry</u> -- activation circulate around a dynamical phase singularity**

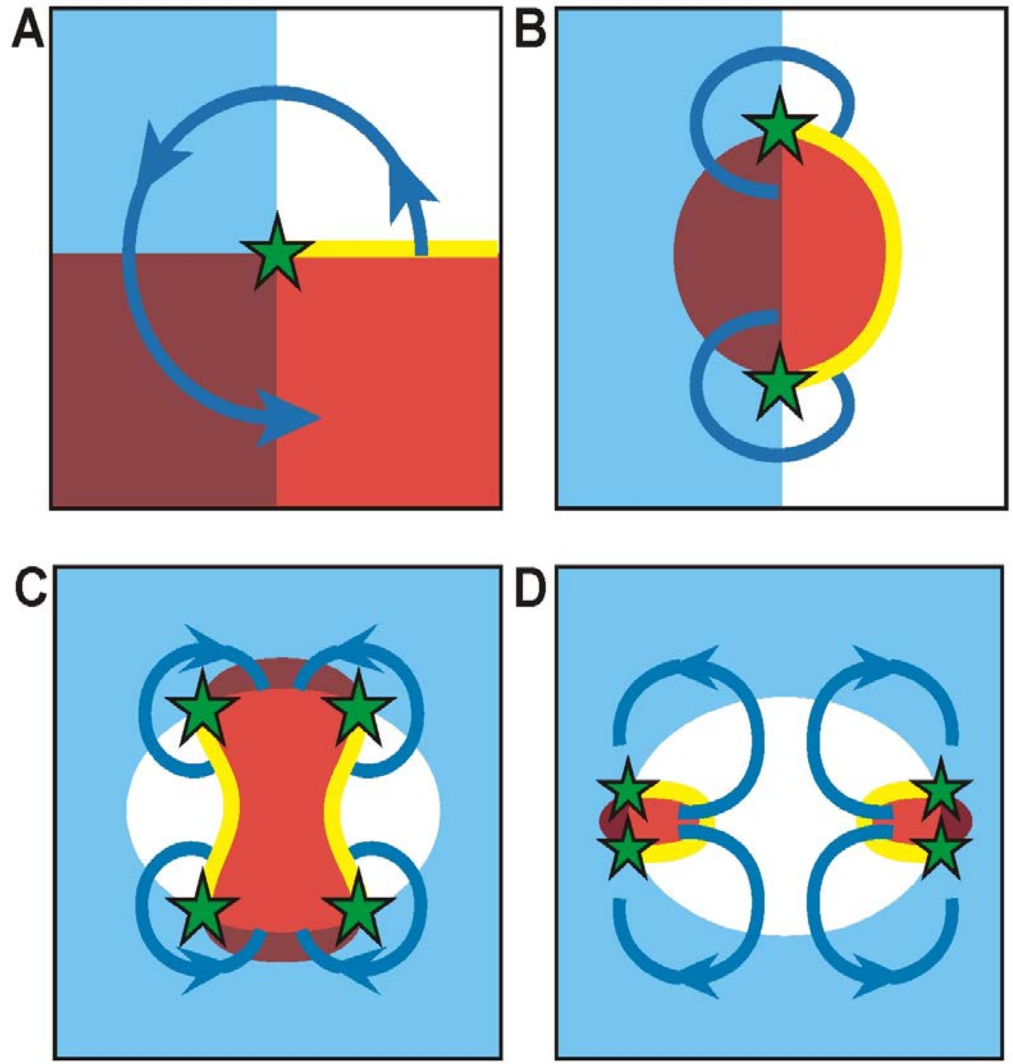
Spiral Wave and Figure-of-Eight Reentry

- Spiral Wave:
  - S1 vert line
  - S2 horiz line
- Figure-of-Eight
  - S1 vert line
  - S2 point

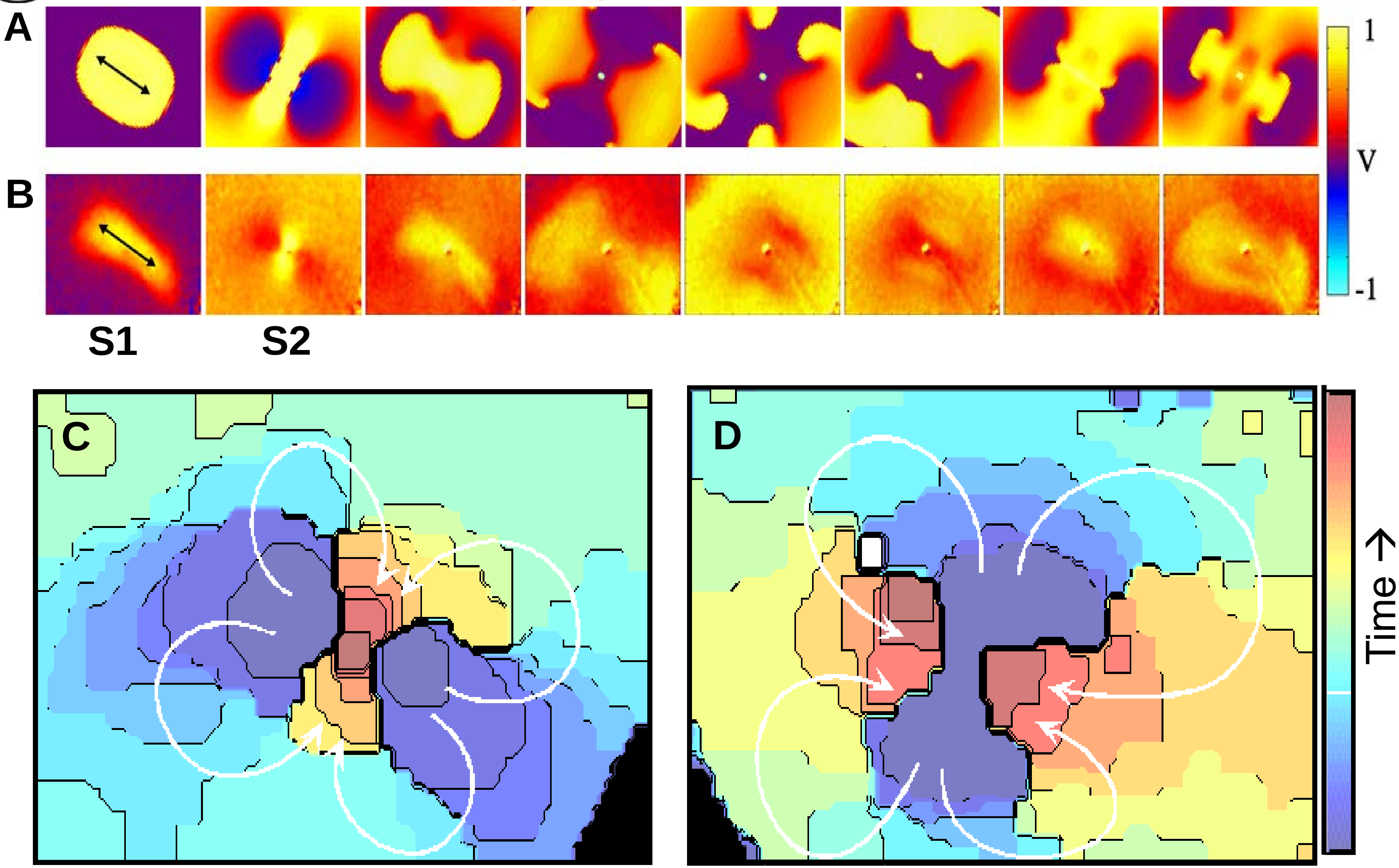


Spiral Wave, Figure-of-Eight, and Quatrefoil Reentry

- **Spiral Wave (A)**
  - S1 vertical line
  - S2 horizontal line
  - One singularity (plus boundary)
- **Figure-of-Eight (B)**
  - S1 vertical line
  - S2 point
  - Two singularities
- **Quatrefoil (C & D)**
  - Anisotropic cable
  - S1 point
  - S2 point
  - Cathodal (C) or anodal (D) have opposite rotations
  - Four singularities



Optical Imaging of Quatrefoil Reentry



Cathodal-Break Isochrones

Anodal-Break Isochrones

SF Lin, BJ Roth, and JP Wikswo. J. Cardiovasc. Electrophysiol. 10(4): 574-586, 1999

M-A Bray, S-F Lin, RR Aliev, BJ Roth, and JP Wikswo, J. Cardiovasc. Electrophysiol. 12(6): 716-722, 2001.

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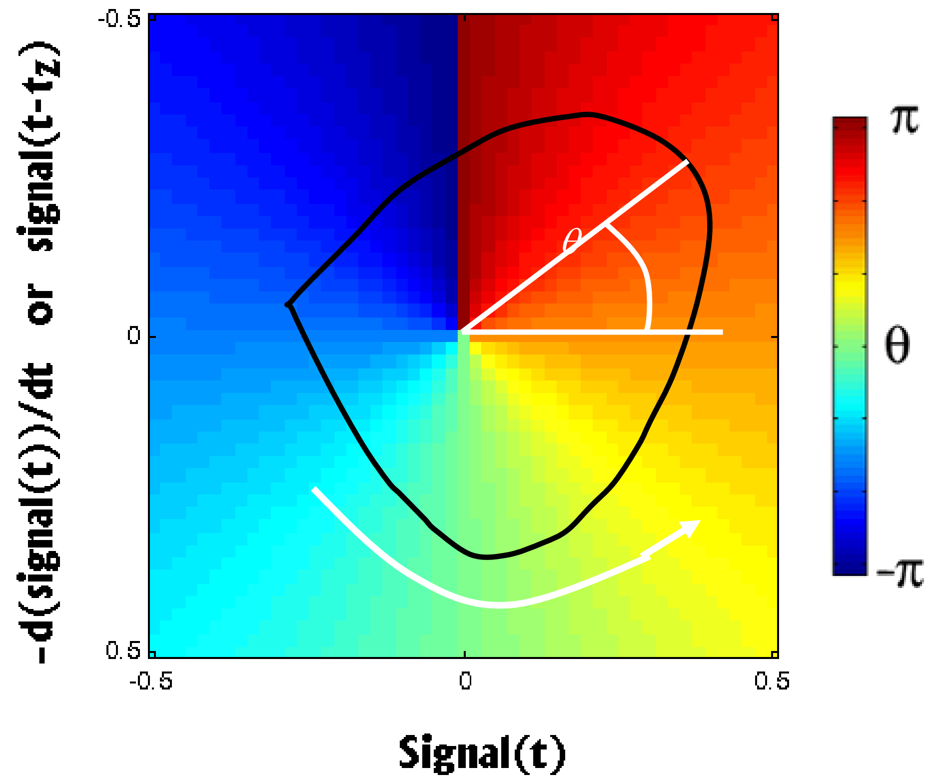
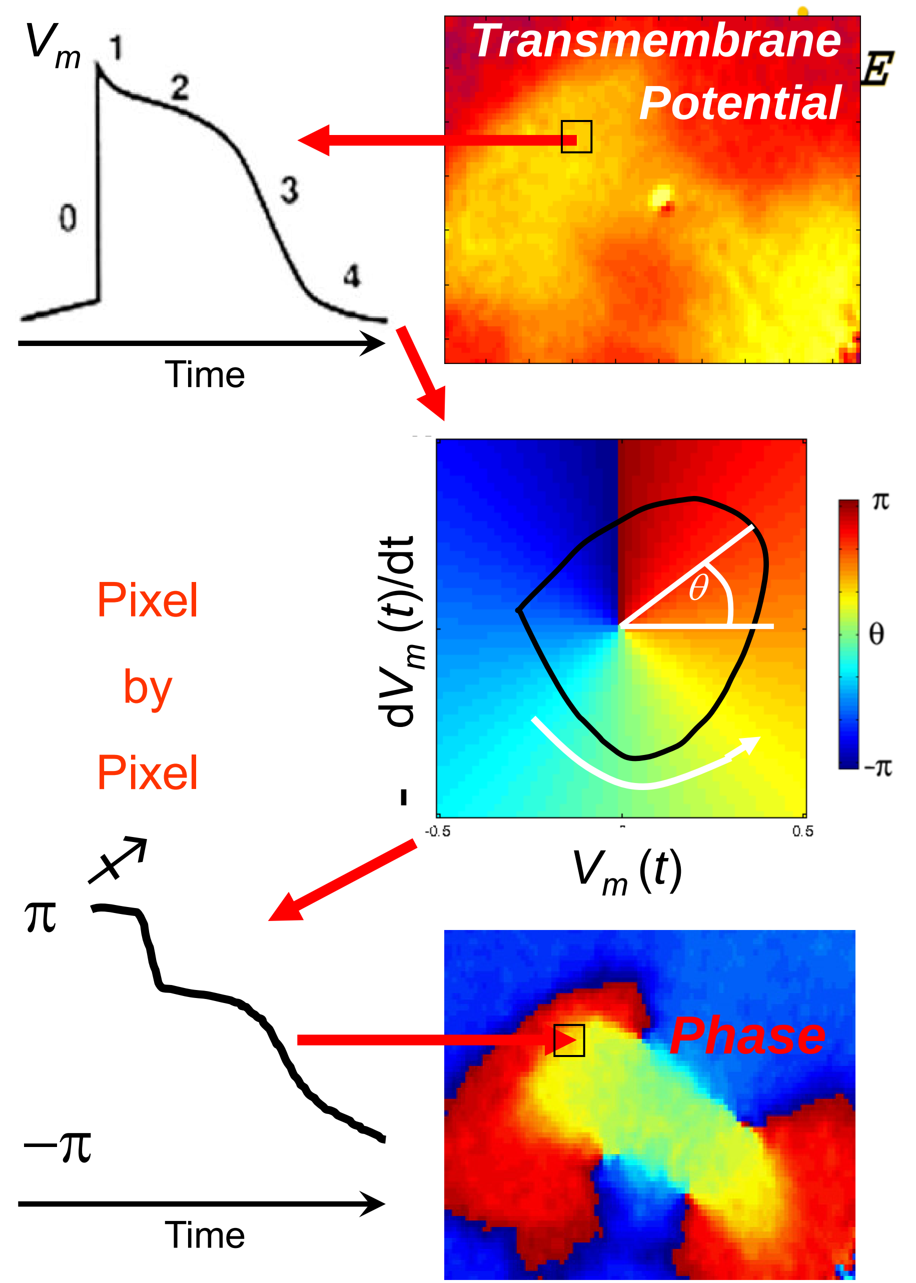


Courtesy of Mark Bray

Transform into Phase Space

- **<u>The problem</u>: a given voltage can either be rising or falling**
- <u>The solution</u>: represent the cardiac action potential in terms of "phase" in the cardiac cycle:
  - 0, 1, 2, 3 …
  - 1%, 2%, 3%, 3%, 5%, …
  - 0°, 5°, 10°, 15°, 20°, 25°, …
- One definition of phase (of many):

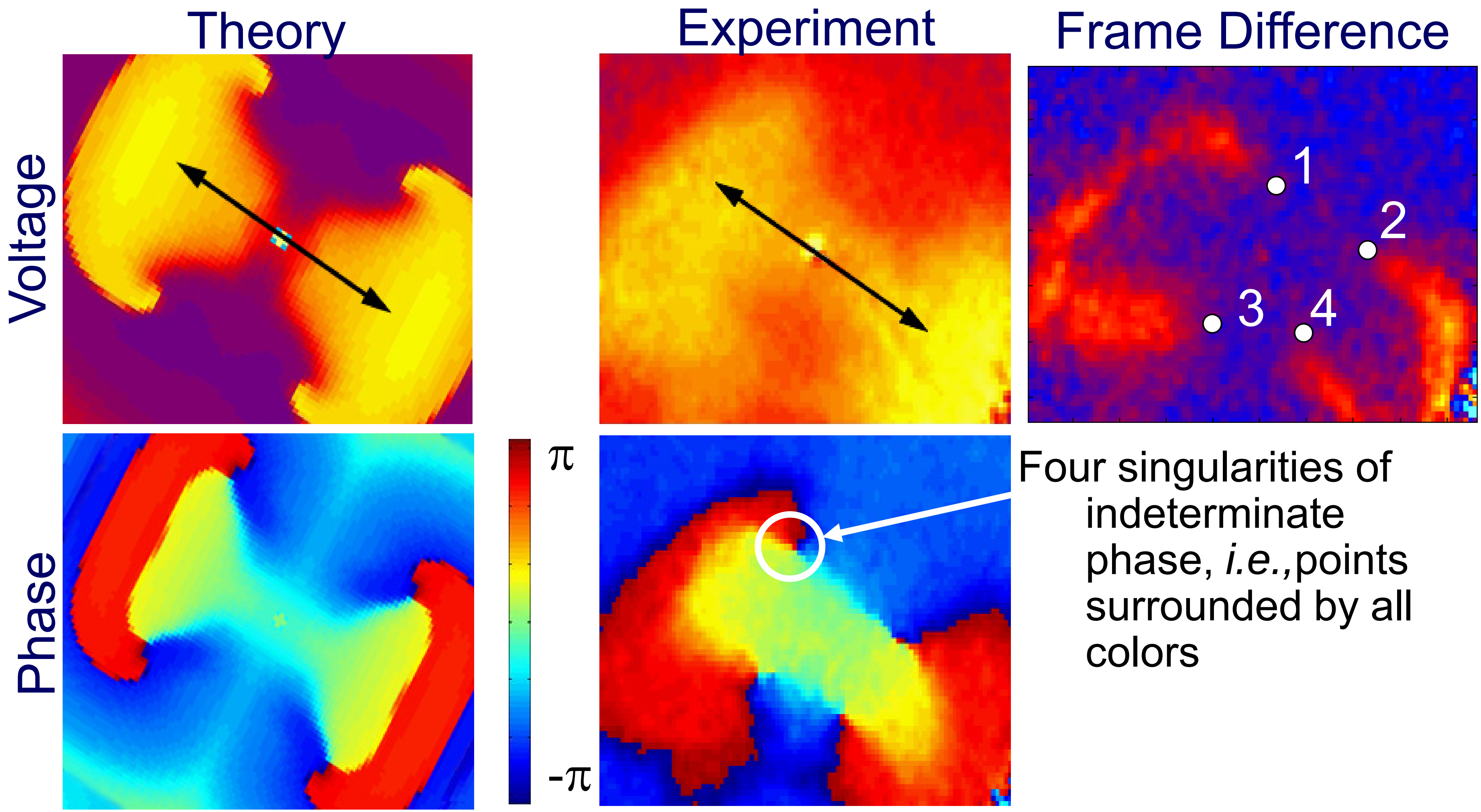
$$\boxed{\phi(x,y,t) = \tan^{-1}\left[\frac{V_m(x,y,t)}{dV_m(x,y,t)/dt}\right]}$$



Pictures by Mark Bray

Method by RA Gray, AM Pertsov, and J Jalife, Nature **392:** 75 (1998)

From Voltage to Phase Space



Four singularities of indeterminate phase, *i.e.,*points surrounded by all colors

M-A Bray, S-F Lin, RR Aliev, BJ Roth, and JP Wikswo, *J. Cardiovasc. Electrophysiol.* 12(6): 716-722, 2001.

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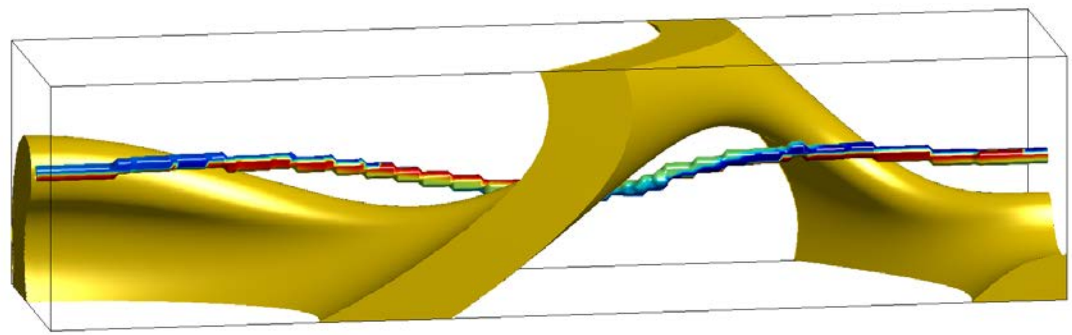
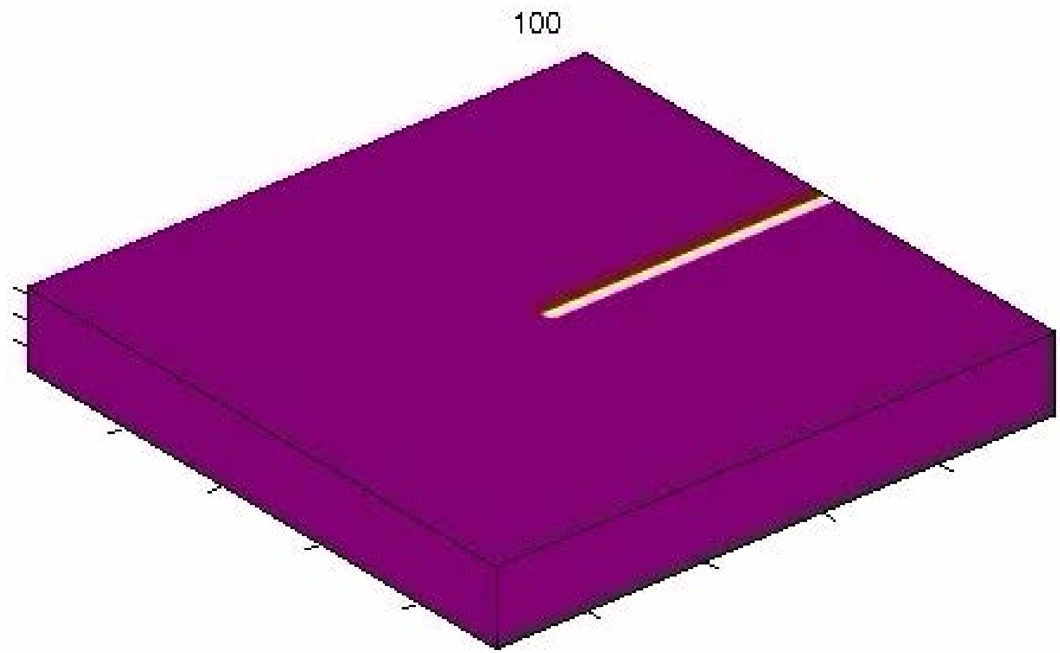


Mark Bray

Why look for strings?

- Movies of the surface potentials are complicated
- It is not clear how much of the information is needed

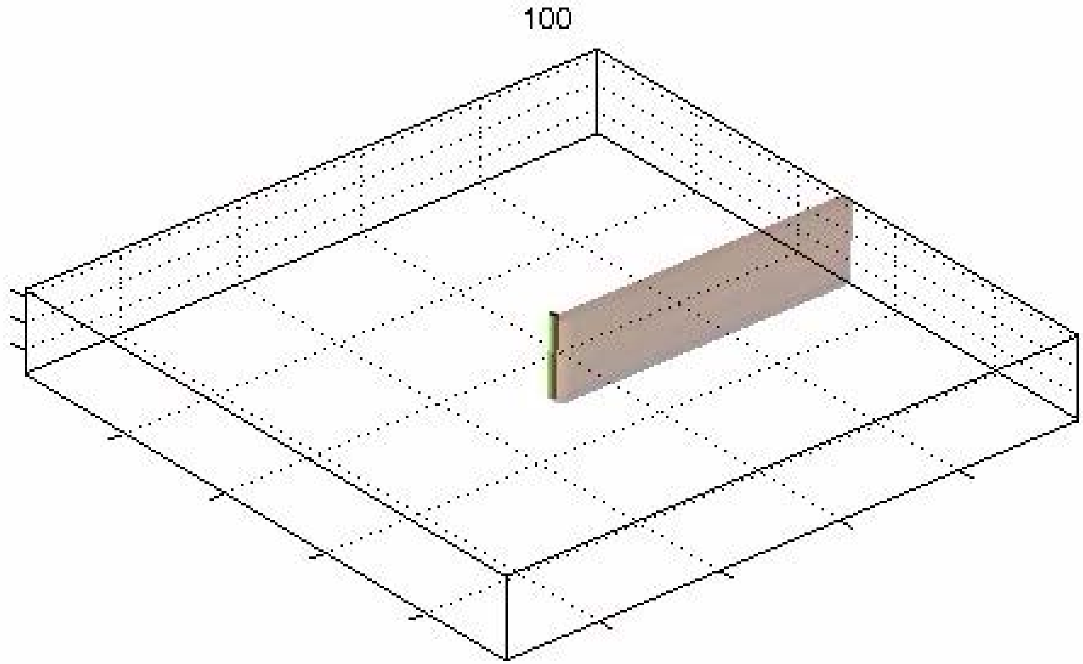


- Model based upon
  - –R.R. Aliev and A.V. Panfilov, A. V., *Chaos, Solitons, & Fractals*, 7(3): 293-301 (1996)
  - –Gray, R. A. and Jalife, J., *Chaos*, 8(1): 65-78 (1998)
- Movies by Mark Bray

fhnplus_scroll_wave_breakup_surface_fps60.avi

Wavefronts are Better

- The wavefronts are better
- Require description of the dynamics of the entire system

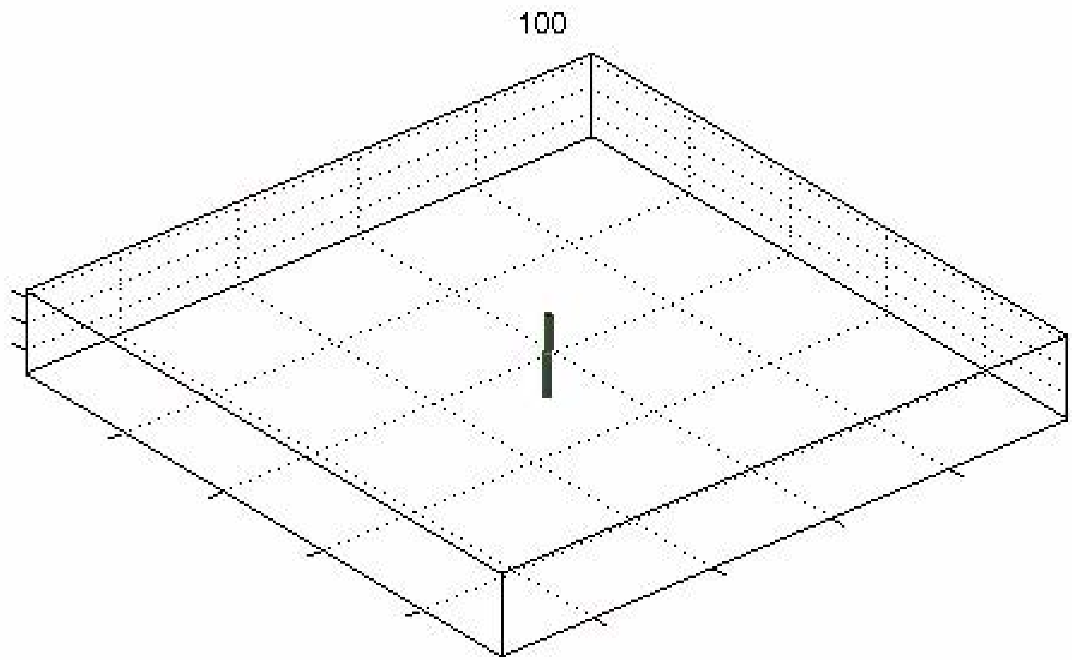


fhnplus_scroll_wave_breakup_filament_plus_wavefront_fps60.avi

Mark Bray

Strings Alone May Be Best

- Surface singularities are simpler
- Filaments (strings) are the best
- Do they interact in a manner that can allow us to ignore the rest of the problem?
- **HOW DO WE FIND THEM??**



fhnplus_scroll_wave_breakup_filament_fps60.avi

Mark Bray

Local Phase and the Wave Vector $\vec{k}$

- The spatial gradient of the phase ϕ is the wave vector $\vec{k}$

$$\vec{k} = -\nabla\phi(x, y)$$

Topological Charge $\vec{k}$

$$n_t \equiv \frac{1}{2\pi} \oint_c \nabla\phi \cdot \vec{d\ell} \ ,$$

$$n_t \equiv \frac{-1}{2\pi} \oint_c \vec{k} \cdot \vec{d\ell} \ ,$$

Phase and Topological Charge

- *Curl k* is proportional to the topological charge!

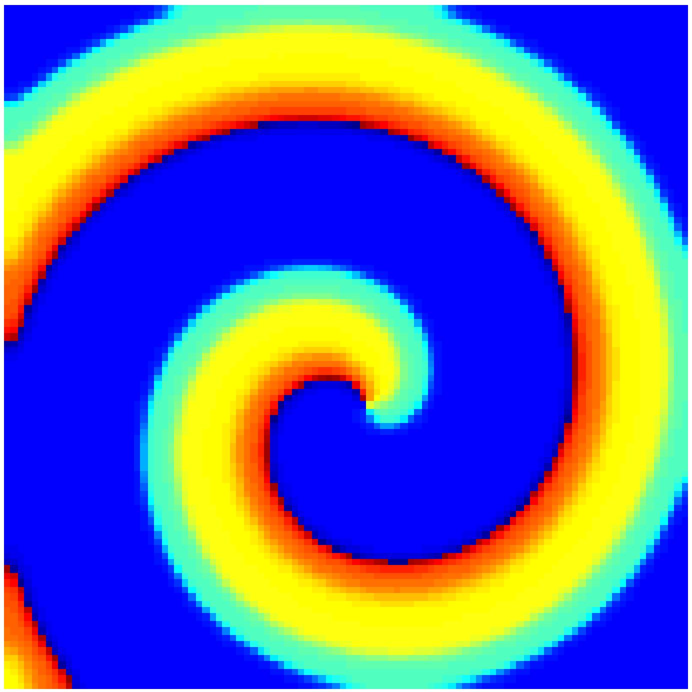
$$\hat{z}\cdot[\nabla\times\vec{k}(\vec{x})] = \frac{\partial k_y}{\partial x} - \frac{\partial k_x}{\partial y} = \lim_{\Delta S\to 0}\frac{1}{\Delta S}\oint_c \vec{k}(\vec{r})\cdot d\vec{\ell}$$

- It can be shown that the differential curl evaluates as exactly zero, except at the singularity, where it is undefined.
- At the singularity, the line integral around the singularity must be used directly to find the topological charge.

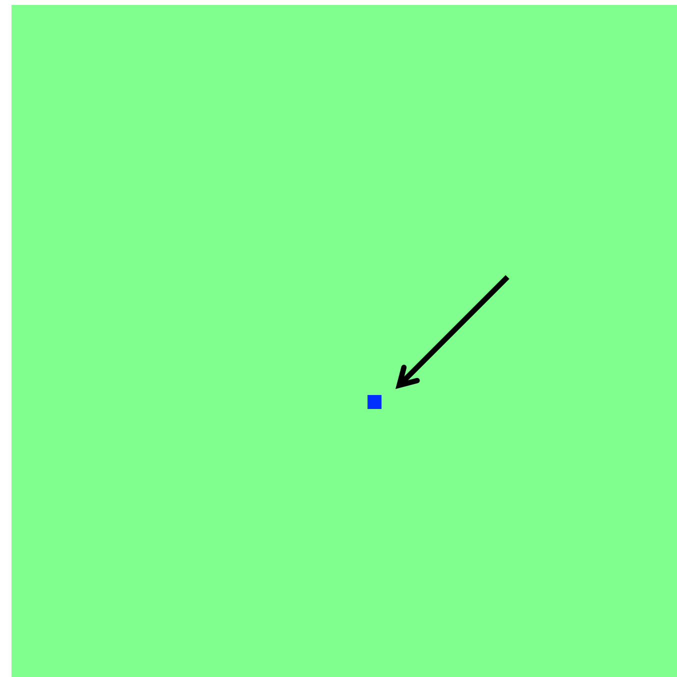
"Use of Topological Charge to Determine Filament Location in a Numerical Model of Scroll Wave Activity," M.-A. Bray and J.P. Wikswo, Jr., IEEE Trans BME, in press

Phase Singularities in Cardiac Reentry

Phase (ϕ) plot



$Curl\ k = Curl\ (\nabla\phi)$



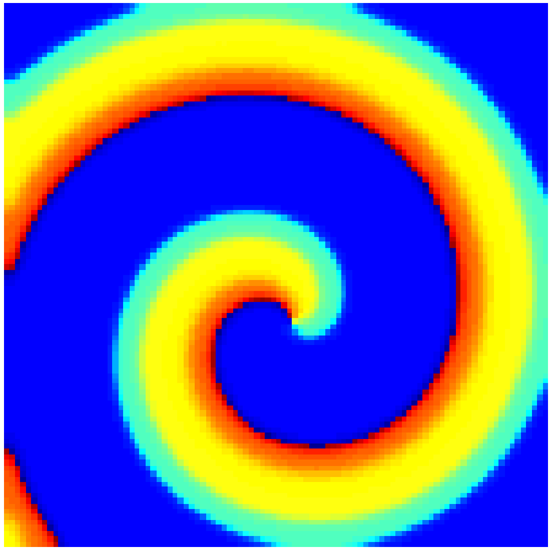
The phase singularities can be identified by computing the curl of the gradient of the phase distribution

Mark Bray

Topological Charge

$$n_t \equiv \frac{1}{2\pi} \oint_c \nabla \phi \cdot \vec{d\ell} \quad ,$$

$$n_t \equiv \frac{1}{2\pi} \oint_c \vec{k} \cdot \vec{d\ell} \quad ,$$

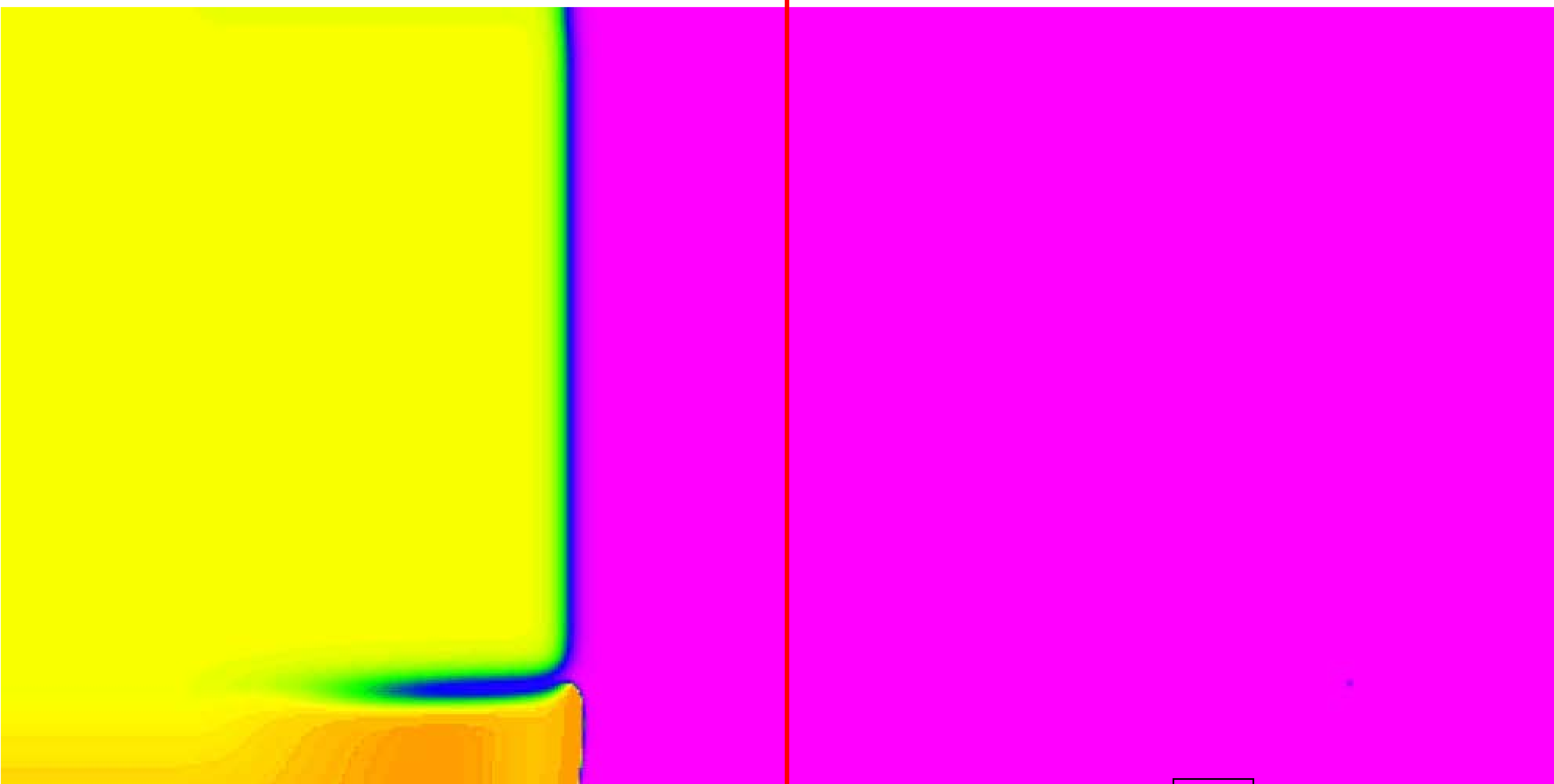

Phase(x,y)

- Topological charge n_t is zero about any closed path that does not encircle a phase singularity
- n_t is +1 or -1 for a path that encircles a singularity with a single arm
- Topological charge is conserved, *i.e.*, singularities are created and destroyed in pairs.

Singularity Motion During Spiral Wave Breakup

Voltage

Curl of Phase

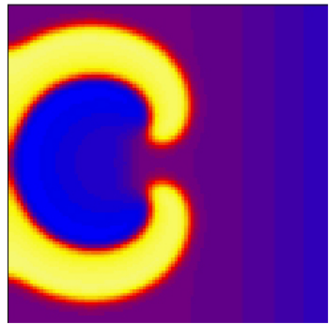


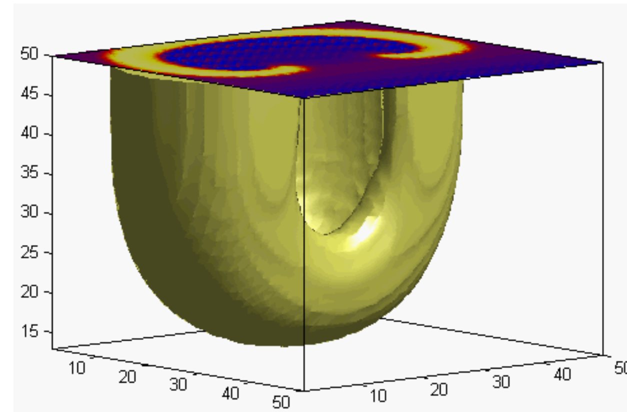
Courtesy of Rick Gray

BRDR.avi

Filaments in Three Dimensions

What looks like a figure-of-eight reentrant wave from the surface...





...is actually a 3-D scroll wave in the underlying myocardium with a filament connecting the two singularities

- Filaments are the 3-D analogue of the 2-D phase singularity

Mark Bray

Topological charge

- *Curl k* may be approximated by

  1) a differential operator, or

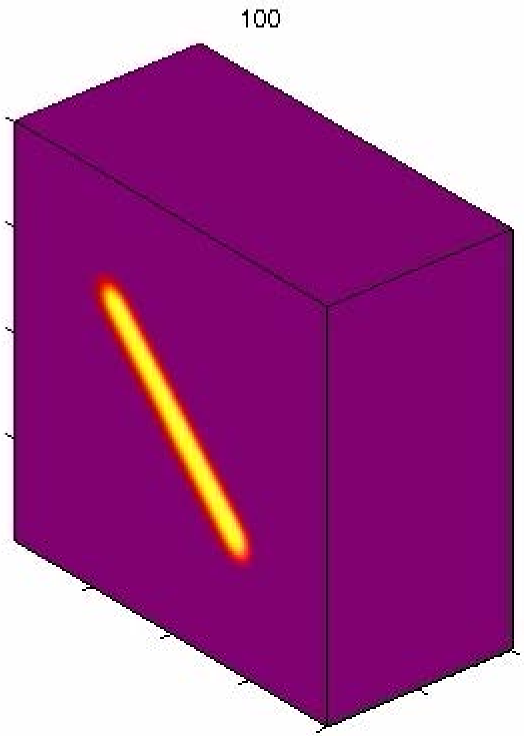
  2) as a discretized contour interval that is in fact a convolution operation of an image with two Nabla windows

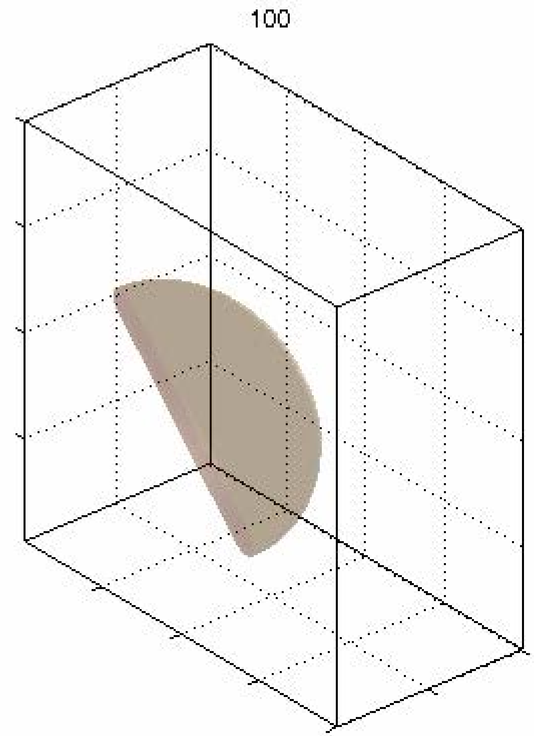
$$\left(\nabla \times \vec{k}\right) \cdot \hat{z} \propto \nabla_x \otimes k_y + \nabla_y \otimes k_x,$$

$$\nabla_x = \begin{bmatrix} +1 & +1 & +1 \\ 0 & 0 & 0 \\ -1 & -1 & -1 \end{bmatrix} \quad \nabla_y = \begin{bmatrix} -1 & 0 & +1 \\ -1 & 0 & +1 \\ -1 & 0 & +1 \end{bmatrix}$$

Bray, Lin, Aliev, Roth, and Wikswo, *J. Cardiovasc. Electrophysiol.* 12(6): 716-722, 2001.

Filaments in Three Dimensions



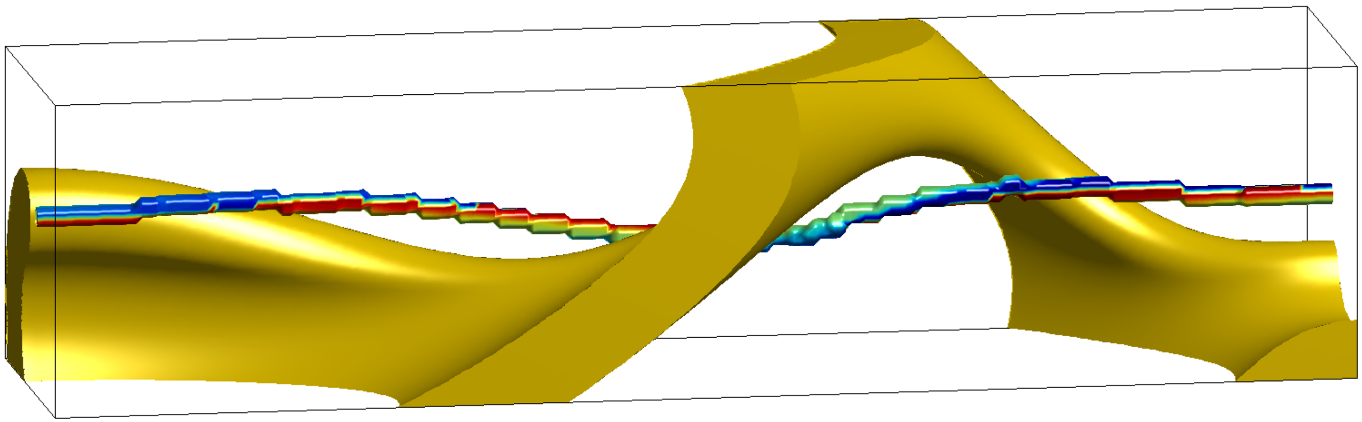


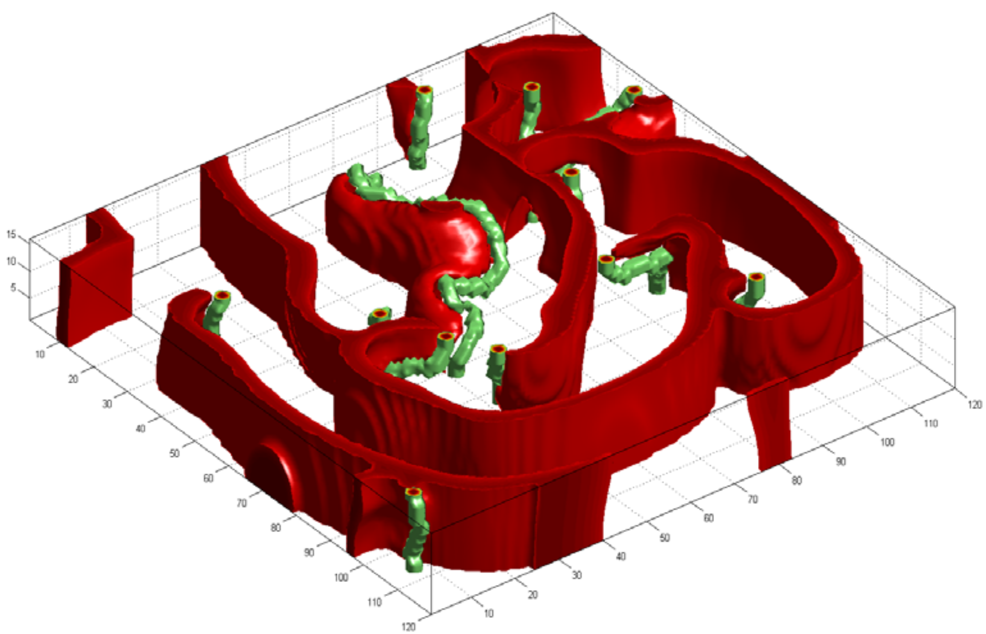
- Filaments are the 3-D analogue of the 2-D phase singularity

bz_scroll_ring_surface.avi
bz_scroll_ring_filament_plus_wavefront.avi

Mark Bray

3-D Filaments



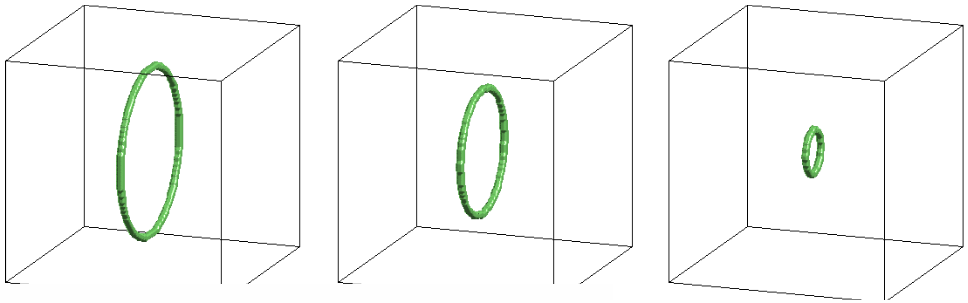


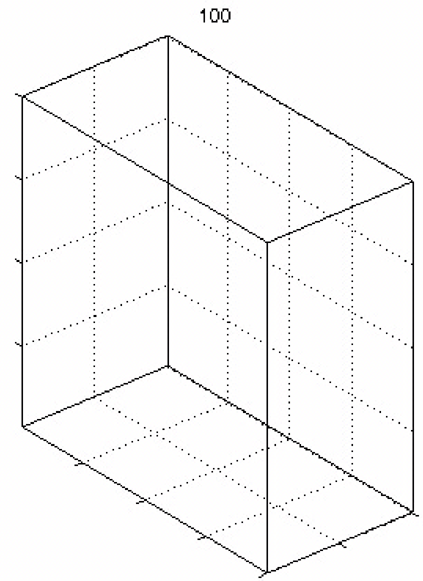
Because curl is a three-dimensional vector operator, this convolution approach can can be extended readily to 3-D in order to visualize scroll wave filaments

Mark Bray

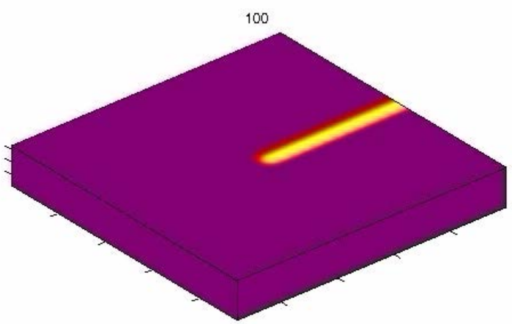
String Dynamics

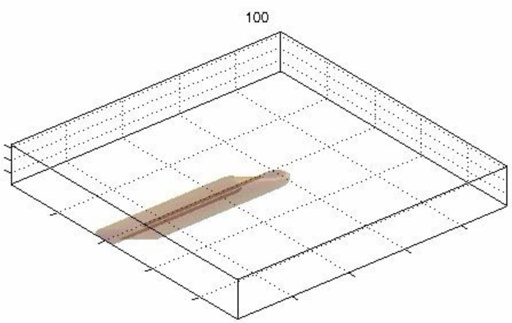
- Strings with positive line tension shrink (Paniflov, Rudenko and Krinsky, Biophysics, 31: 926 (1986))

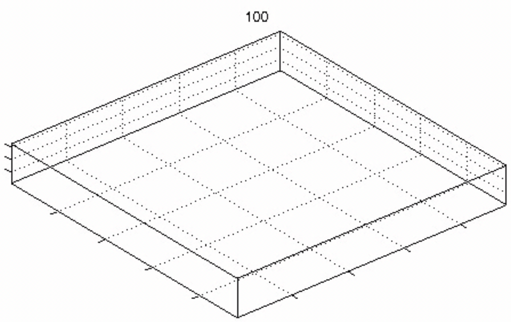




bz scroll ring (filament).avi





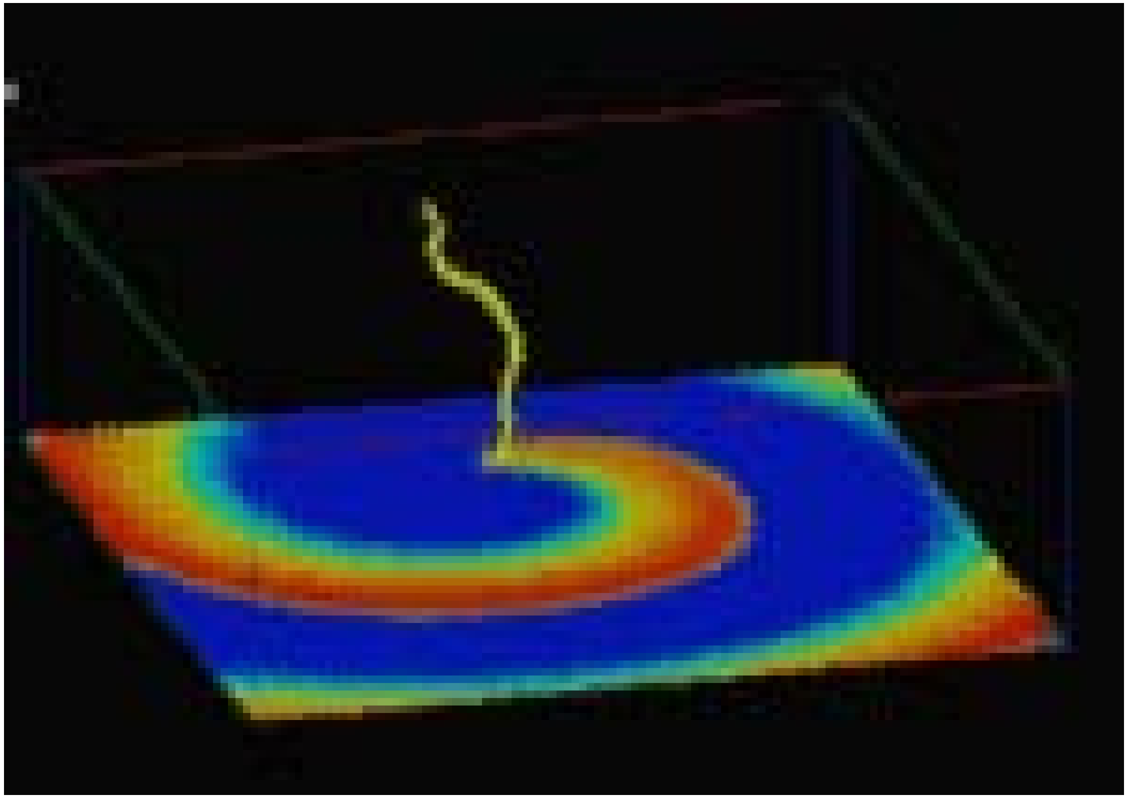


bz_scroll_wave_stable_surface_fps60.avi
bz_scroll_wave_stable_filament_plus_wavefront_fps60.avi
bz_scroll_wave_stable_filament_fps60.avi

Mark Bray

String Dynamics

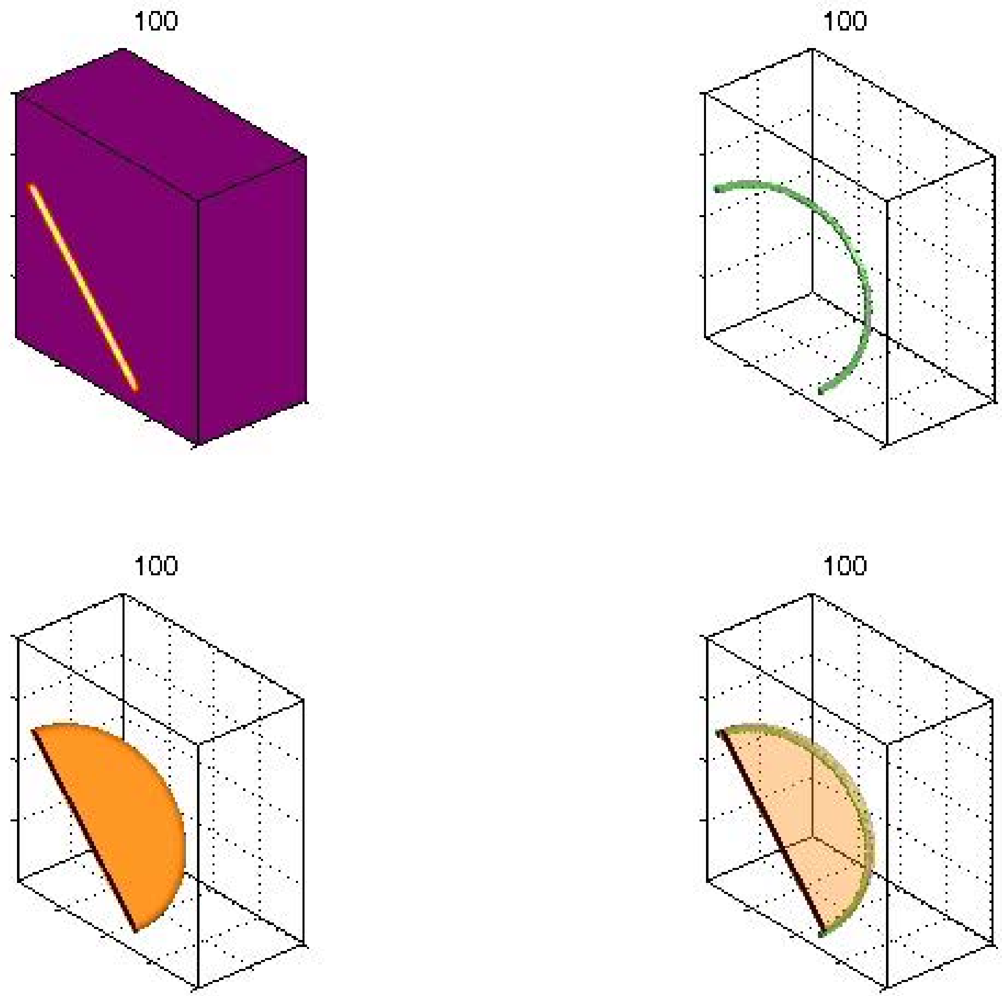
- Strings with negative line tension grow and buckle (see V.N. Biktashev, A.V. Holden, and H. Zhang. *Phil. Trans. Royal Soc. London, Series A* 347: 611-630, 1994)
- If they touch a surface, a pair of singularities is produced
- Topological charge is conserved



Movie Courtesy of Flavio Fenton

T8.avi

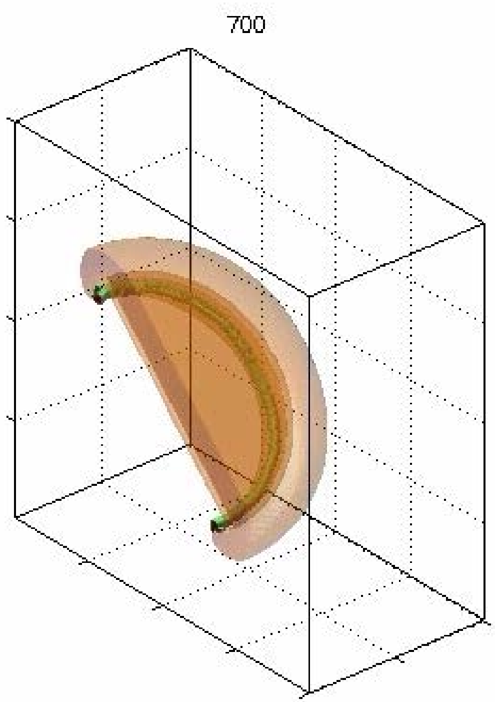
A Little Negative Line Tension

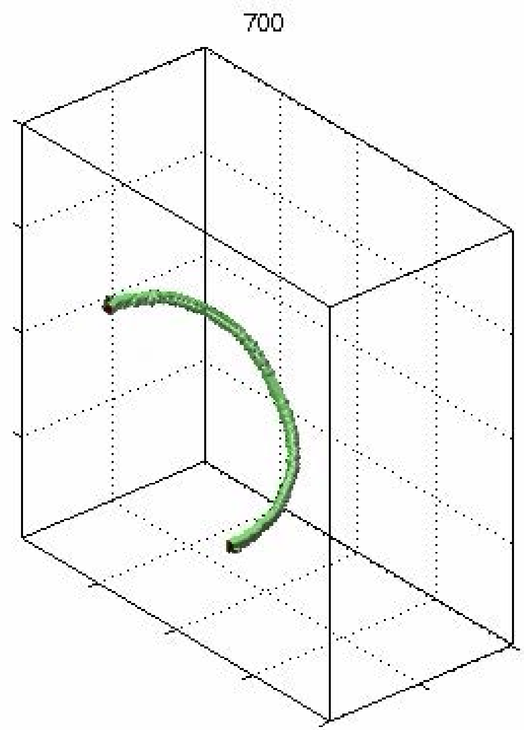


fhnplus_scroll_ring_k8_4panel.avi

Mark Bray

A Lot of Negative Line Tension



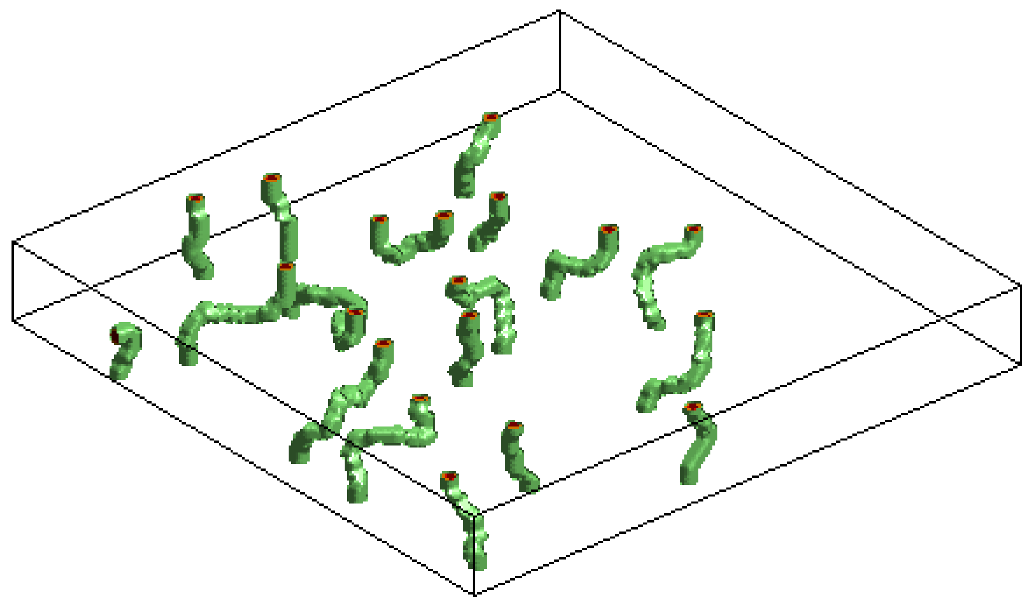


fhnplus_scroll_ring_k40_filament_plus_wavefront.avi
fhnplus_scroll_ring_k40_filament.avi

Mark Bray

Outline

- The heart is a …
- Cardiac fibrillation
- Spiral waves in the heart
  - Two dimensions – Spiral waves
  - Three dimensions – Scroll waves
- Phase plane analysis
- Singularity identification
  - Simple reentry
  - Fibrillation
- Singularity interactions
  - Attraction vs repulsion versus oscillation
  - Annihilation
  - Creation
- What is needed?
  - Interaction potential
  - String creation operator

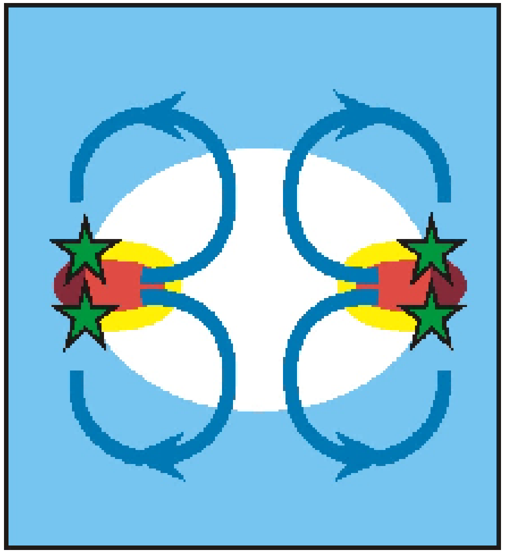


Courtesy of Mark Bray

Quatrefoil Reentry

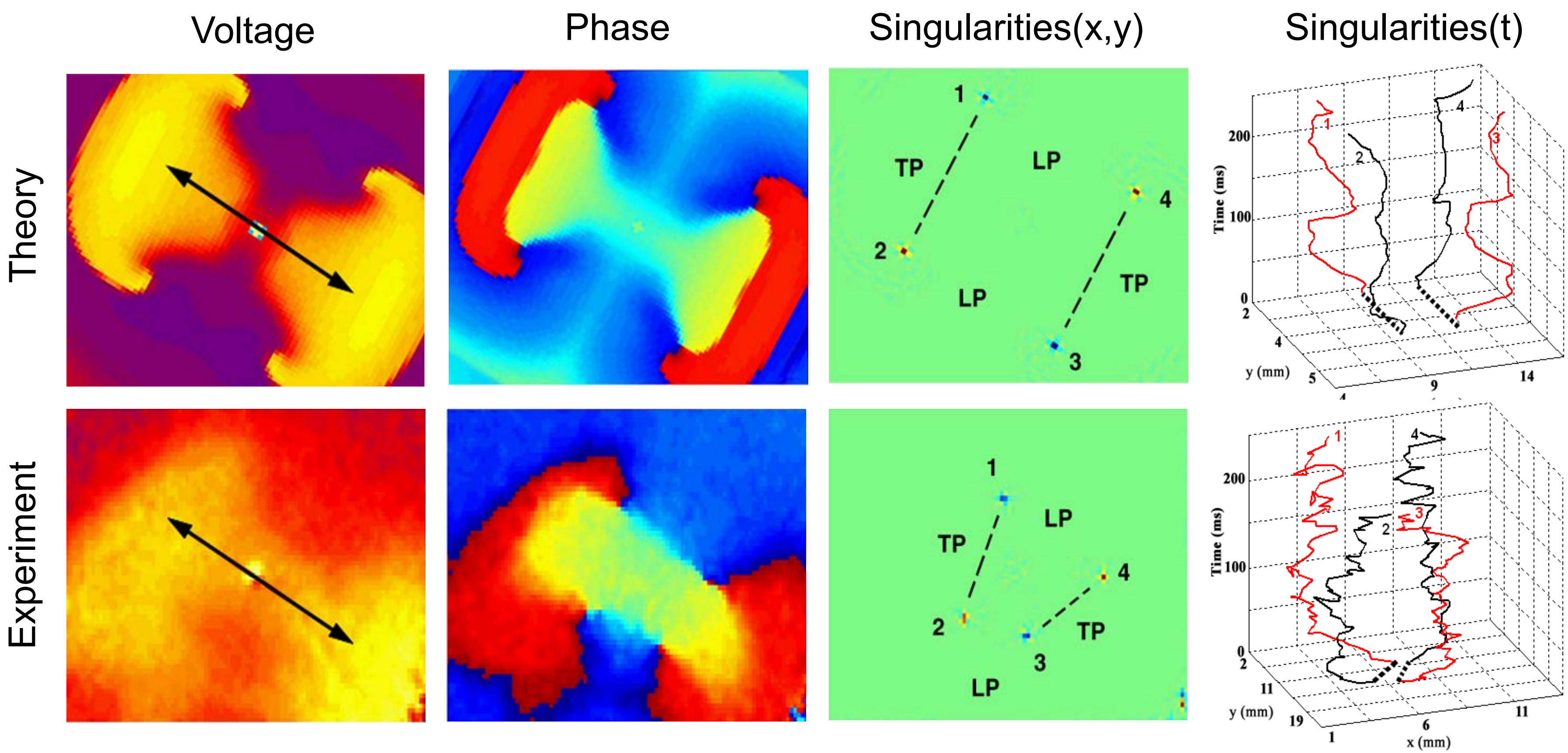
- Follows repeated stimuli applied at a single site
- Has been used to demonstrate the importance of unequal bidomain anisotropies in cardiac electrodynamics
- **Provides a reproducible, controlled system for study of the interactions of phase singularities and their accompanying filaments**

Cathode break



Anode break

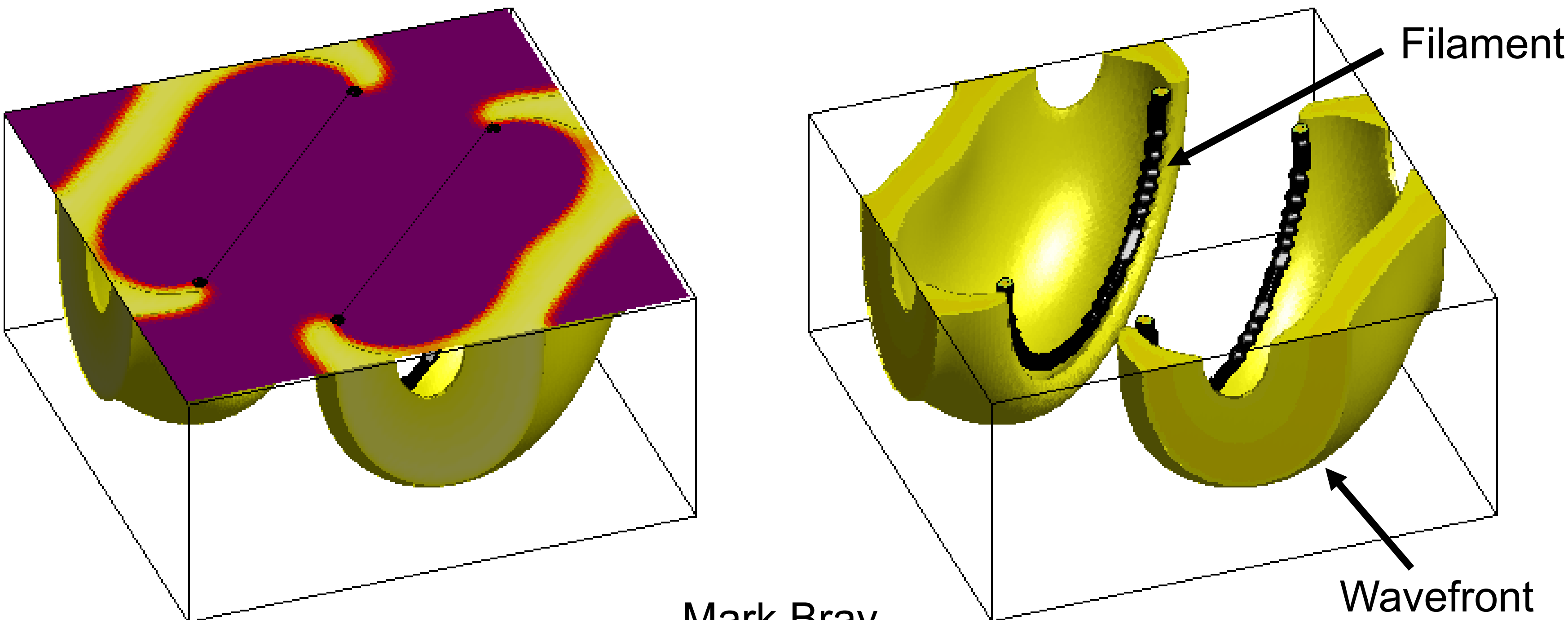
Quatrefoil Reentry



MA Bray, SF Lin, RR Aliev, BJ Roth, and JP Wikswo, J.P., "Experimental and theoretical analysis of phase singularity dynamics in cardiac tissue.," *J Cardiovasc Electrophys*, vol. 12, no. 6, pp. 716-722, 2001.

Quatrefoil Reentry

- We replicate the experimentally observed quatrefoil reentry configuration using a simulated pair of adjacent circular filaments (scroll rings) oriented along their symmetry axes with varying initial radii and separation distances



Mark Bray

Reaction-Diffusion System

- We use a two-variable model of the Belousov-Zhabotinsky (BZ) reaction using the Field-Koros-Noyes formulation

$$\frac{dv}{d\tau} = \frac{1}{\varepsilon}\left[v(1-v) - \left(2q\alpha\frac{w}{1-w} + \beta\right)\frac{v-\mu}{v+\mu}\right] + \nabla^2 v$$

$$\frac{dw}{d\tau} = x - \alpha\frac{w}{1-w} + \delta\nabla^2 w$$

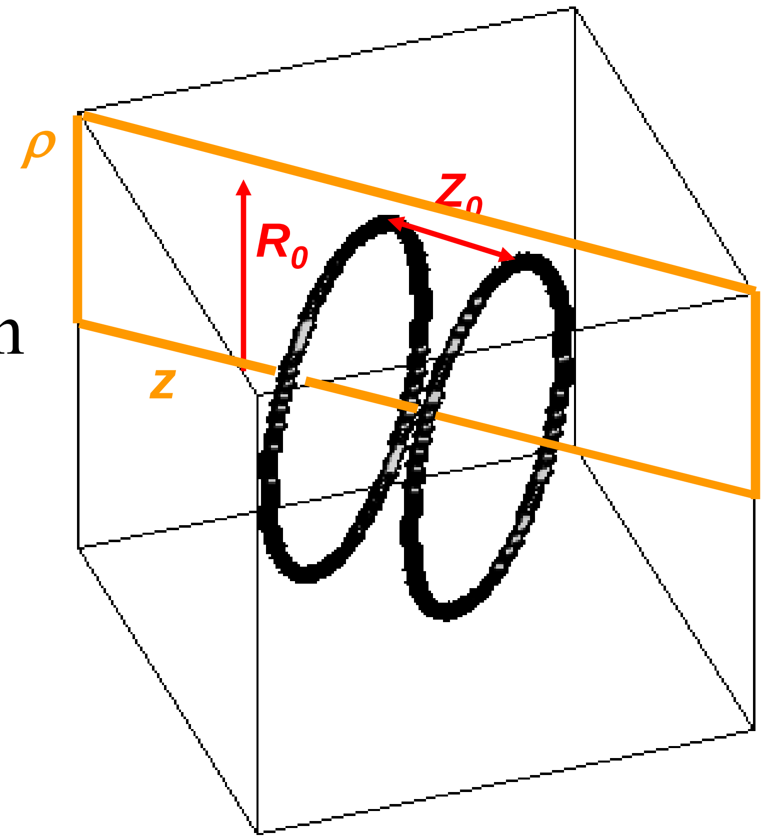
where v is the bromous acid concentration, w is the relative ferroin concentration, and $\delta = D_w/D_v$ ($\delta = 1$ in this case)

- For $\delta = 1$, $\frac{d(R^2)}{dt}$ = -2D

- With this BZ formulation, a single ring shrinks with a relative absence of translational drift; permits us to observe interaction without large single ring dynamics

Methodology

- Modeled 3-D system using an axisymmetric cylindrical coordinate system (z,ρ,θ), such that all results are independent of angle $\theta \rightarrow$ Need only to examine 2-D (z,ρ) plane
- Started rings at initial separation (Z_0) and initial radius (R_0) and examined life-time (T_L) and motion in (z,ρ) plane
- Simulated cathode and anode break with appropriate initial conditions



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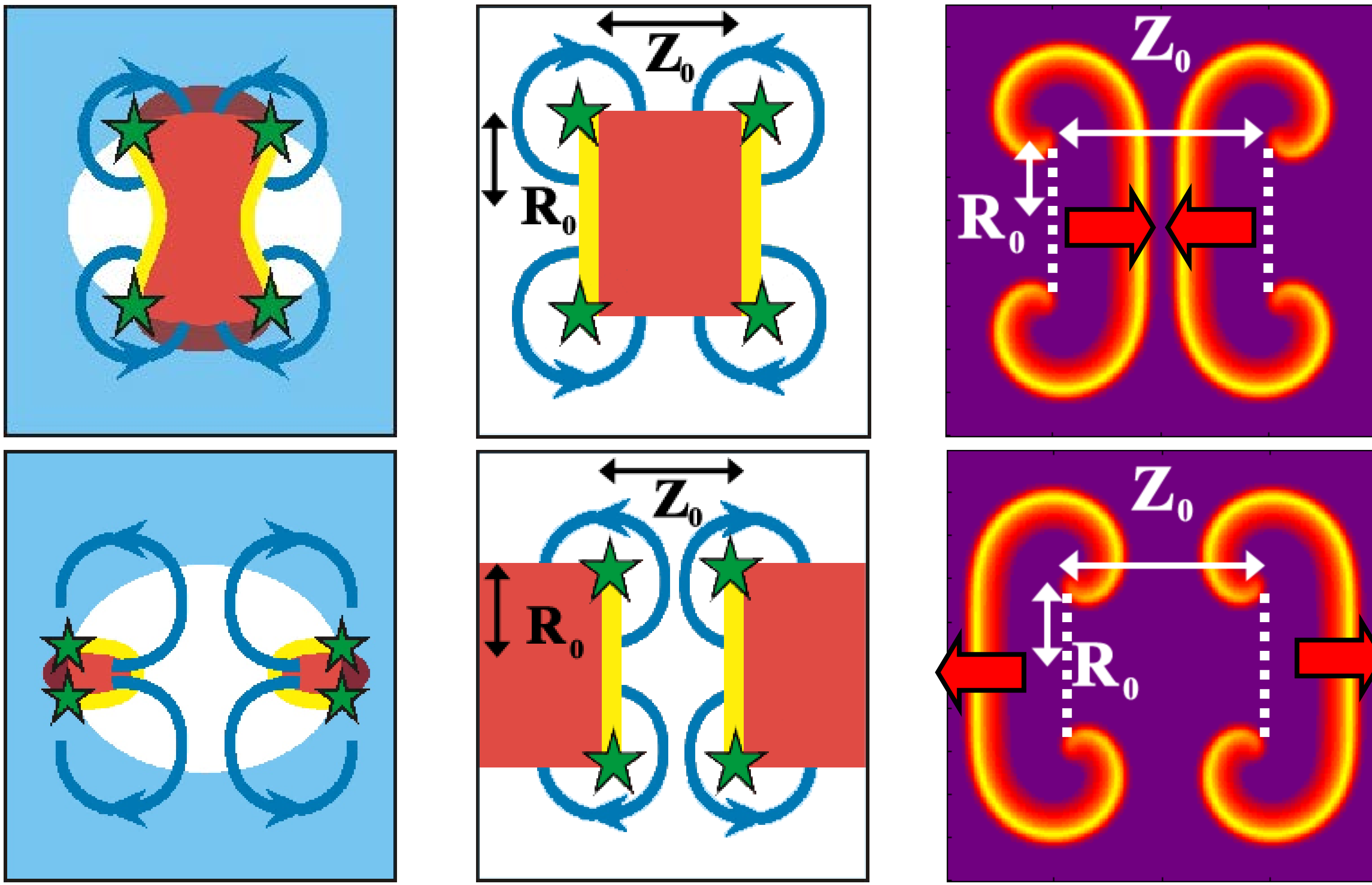
Initial Conditions

Experimental | Numerical | Numerical – Wave Fronts

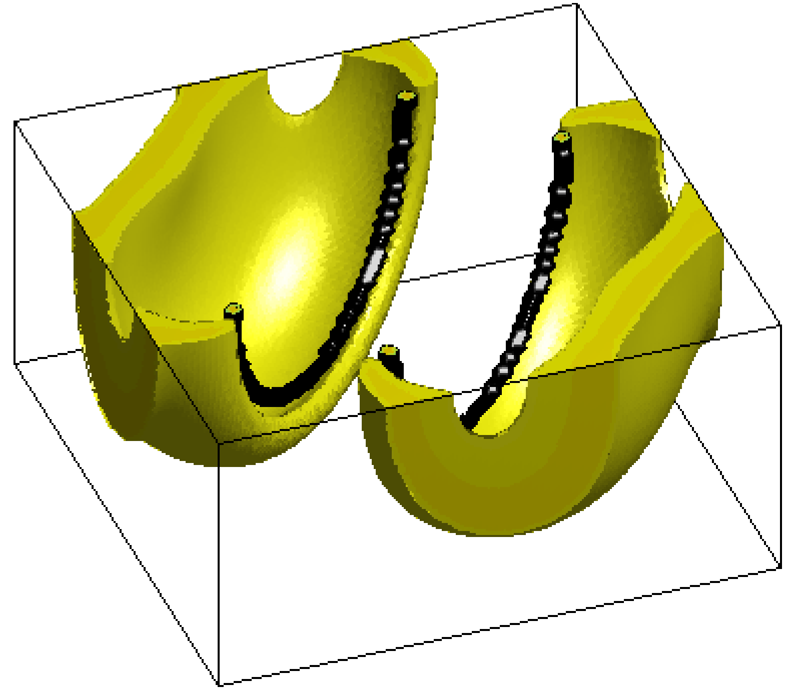
Cathode break

Anode break

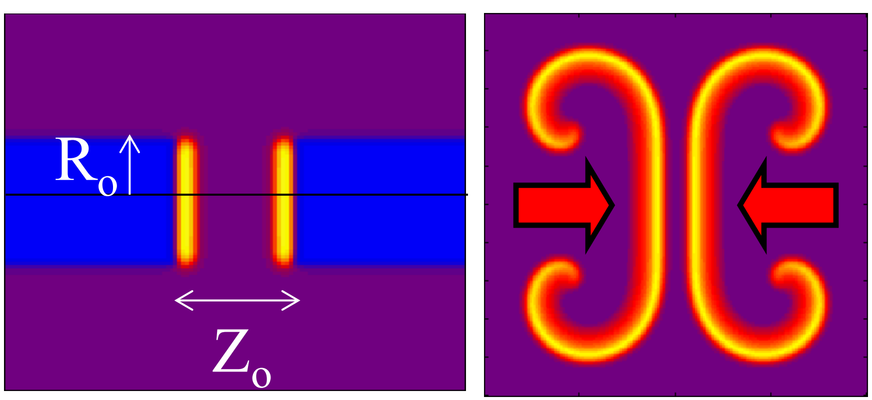


Simulated Singularity Interactions

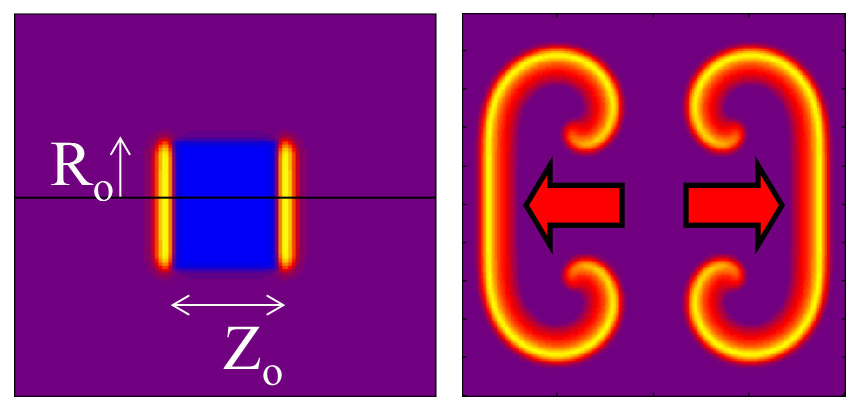
- Start with a pair of vortex rings of fixed diameter and positive line tension
- Measure decay time as a function of separation and initial size



BZ: Anode break

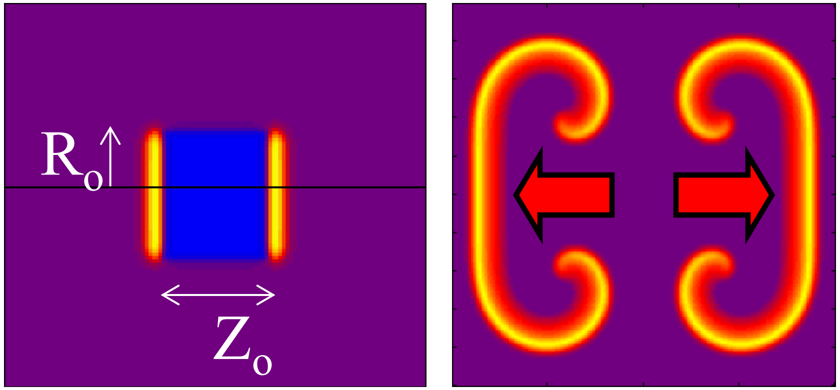


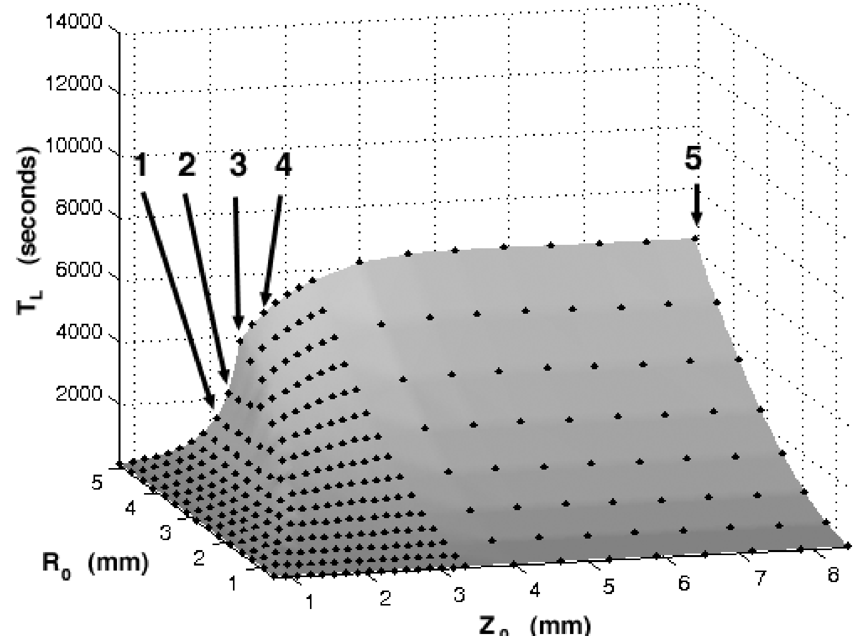
BZ: Cathode break



Mark Bray

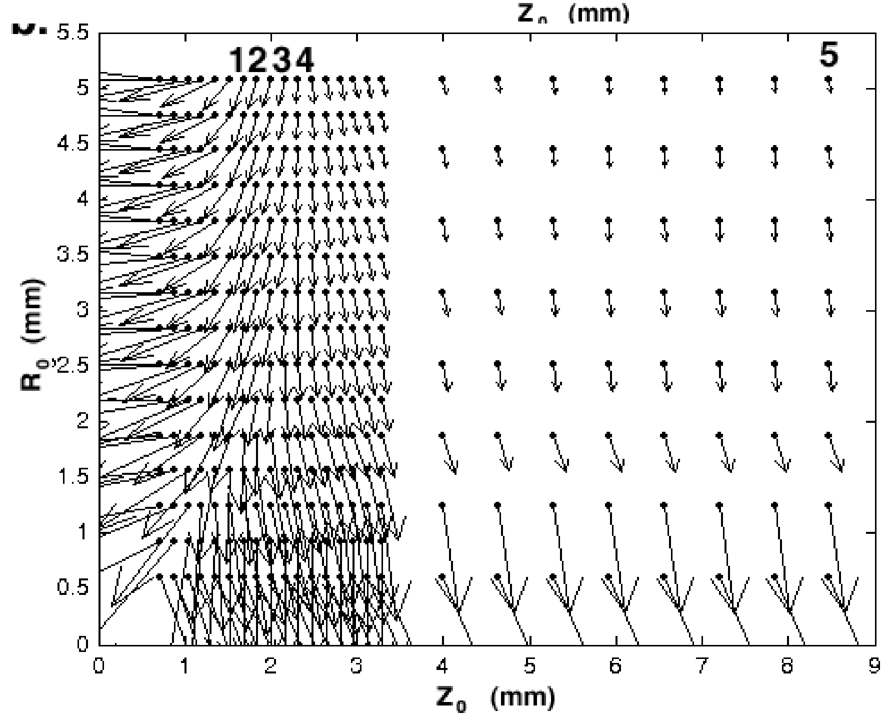
Cathodal Break





- 5: Free decay and self-annihilation per Paniflov, Rudenko and Krinsky, Biophysics, 31: 926 (1986)
- 4: Repulsion per Elphick and Meron, Physica D, 53: 385 (1991)
- 1: Enhanced decay, attraction, and mutual annihilation per Elphick and Meron, Physica D, 53: 385 (1991)

Mutual annihilation by collision

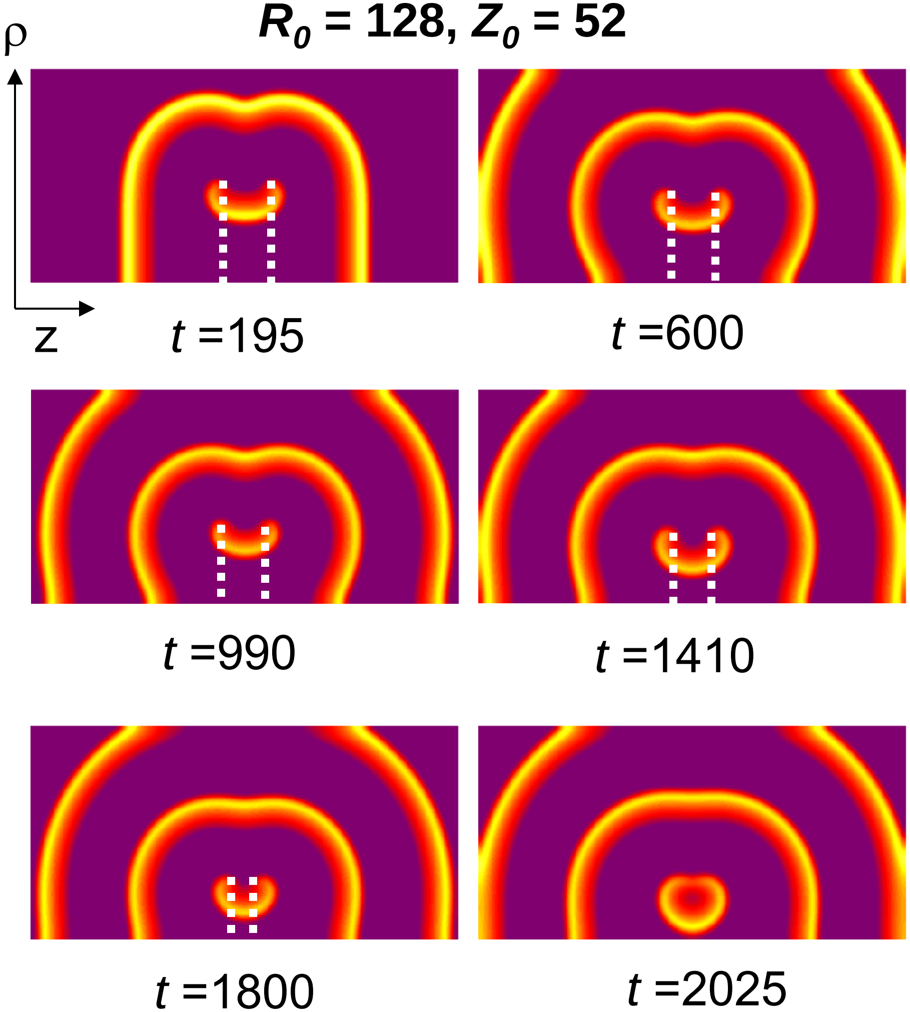


Self-annihilation by shrinkage

M Bray and J. Wikswo, in preparation

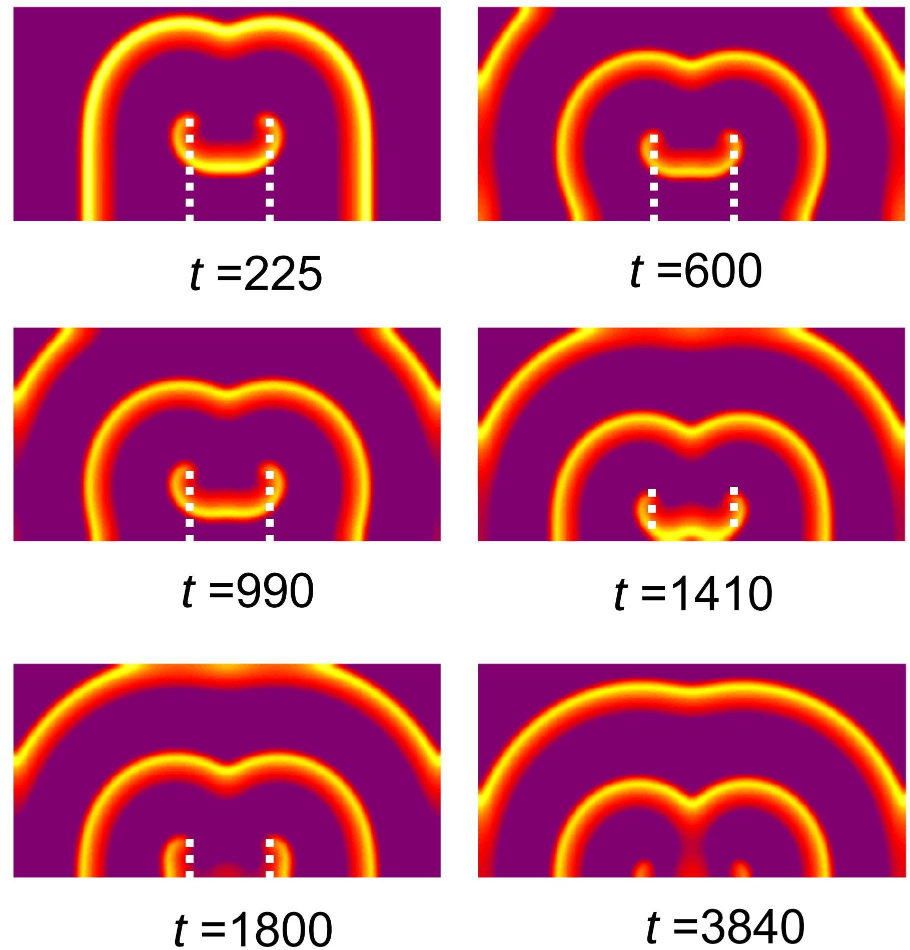
Cathode break movie

R_0 = 128, Z_0 = 52



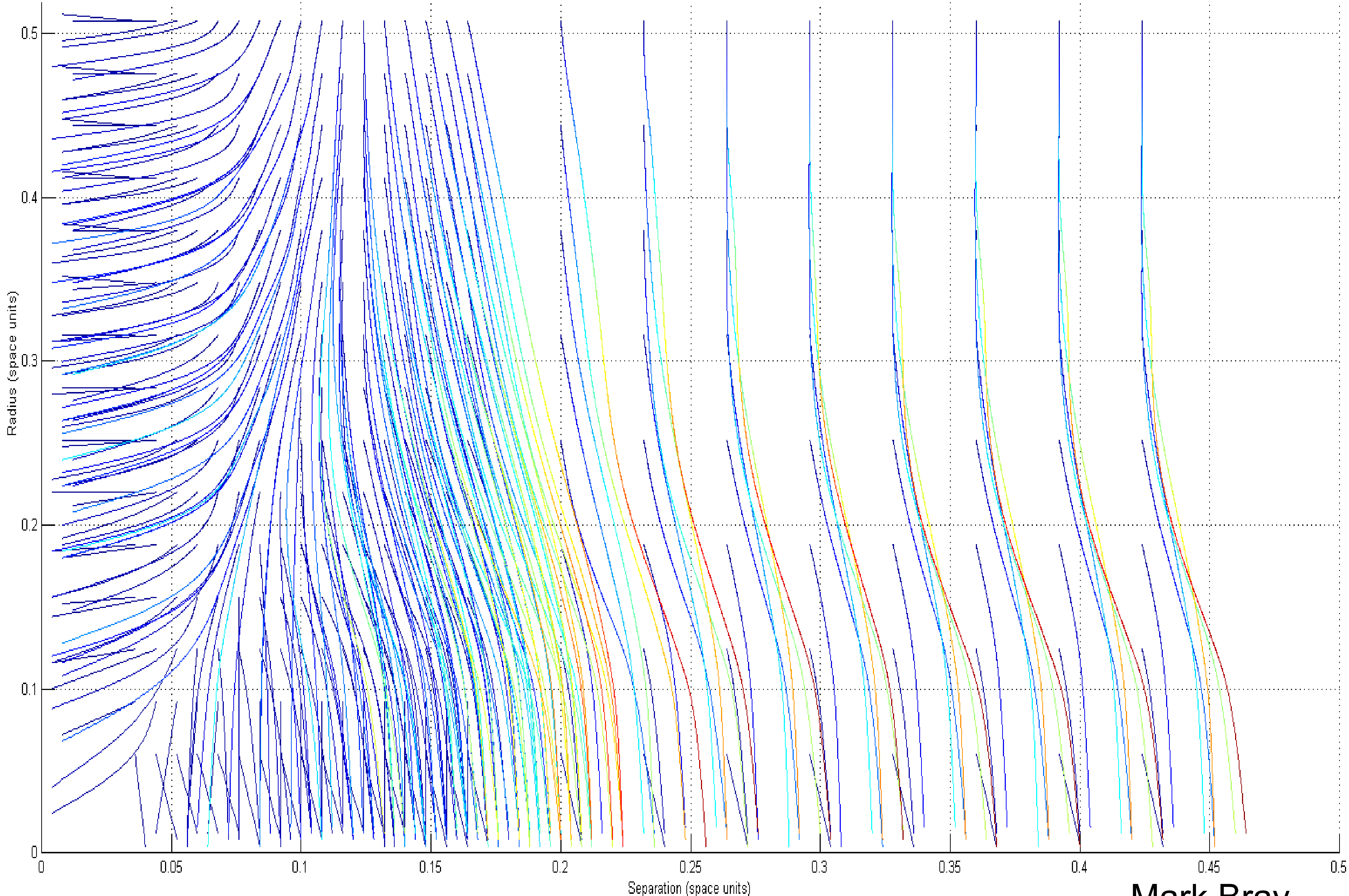
Filament annihilation by collision

R_0 = 128, Z_0 = 60



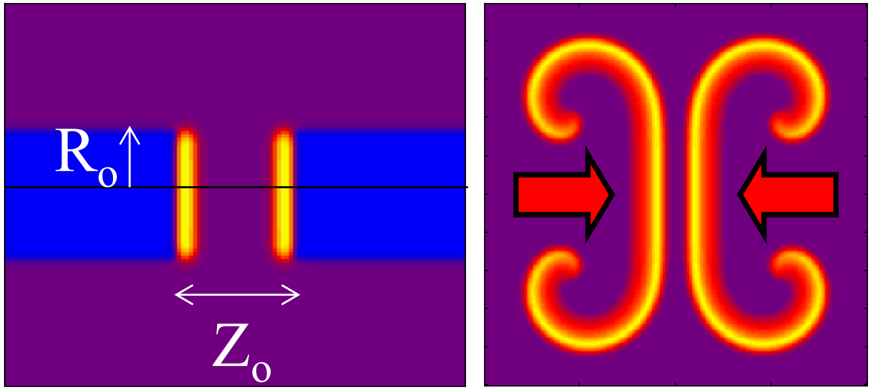
Self-annihilation by shrinkage

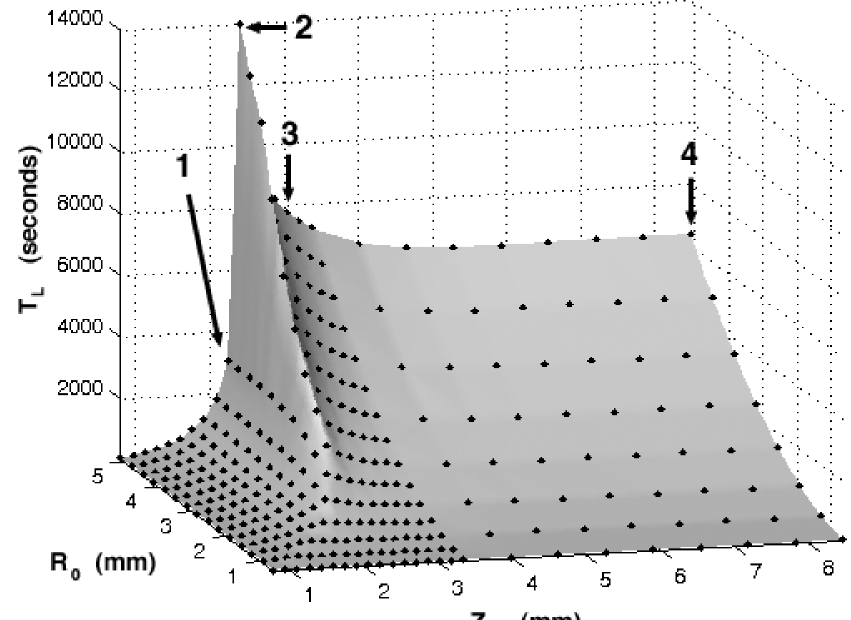
Cathodal Break Trajectories



Mark Bray

Anodal Break





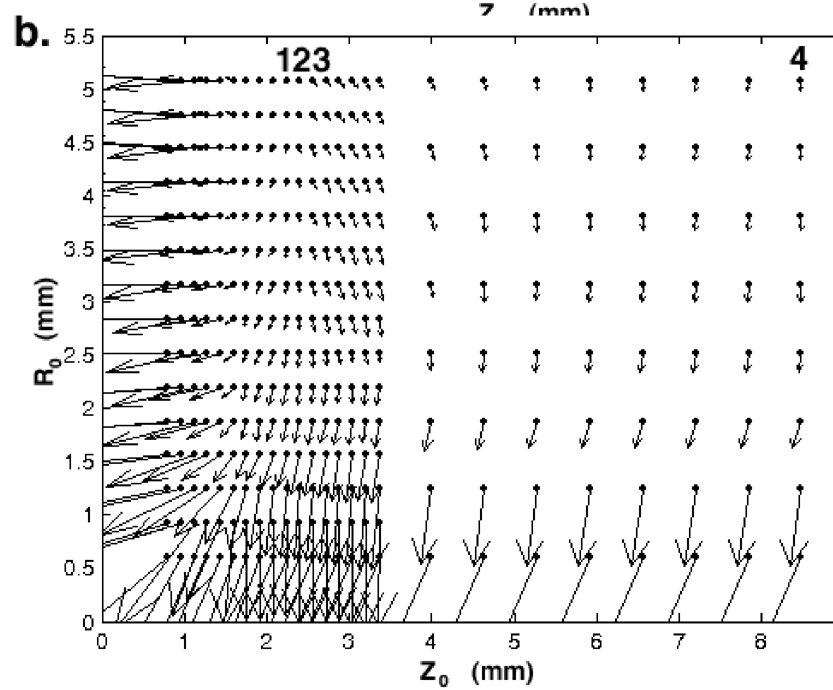
4: Free decay and self-annihilation Paniflov, Rudenko and Krinsky, Biophysics, 31: 926 (1986)

1: Enhanced decay, attraction, and mutual annihilation per per Elphick and Meron, Physica D, 53: 385 (1991)

2: Extended lifetime

3: Repulsion per per Elphick and Meron, Physica D, 53: 385 (1991)

Mutual annihilation by collision

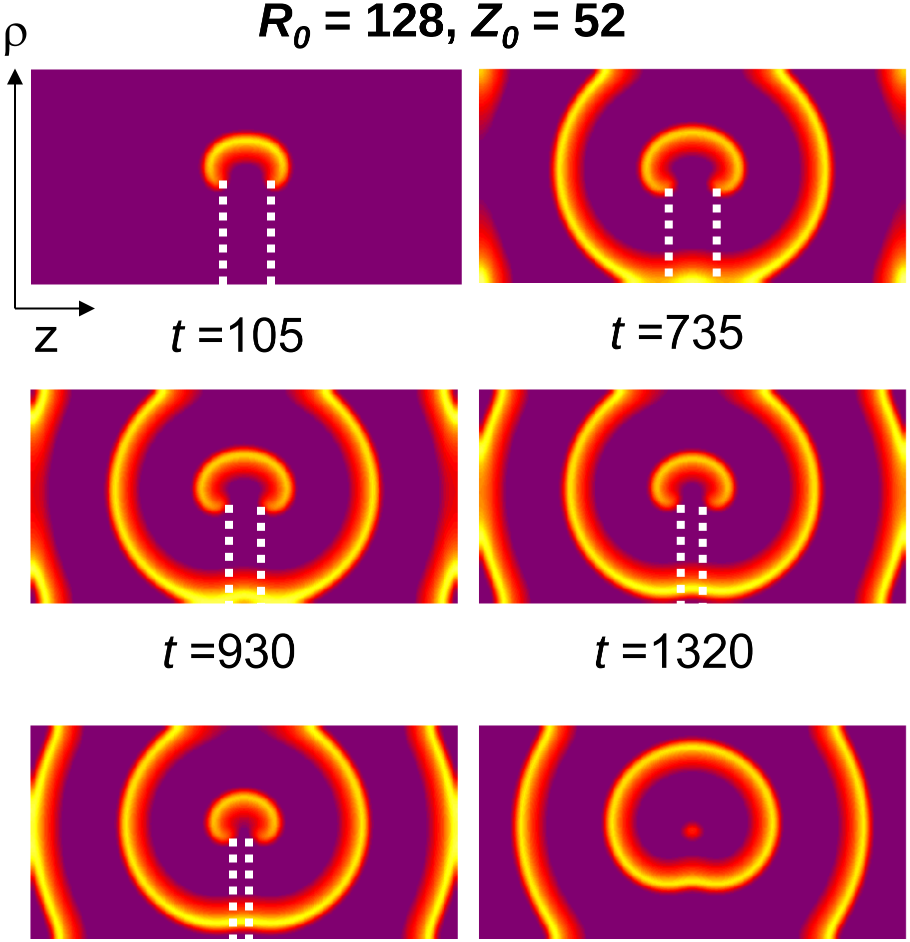


Self-annihilation by shrinkagec

Mark Bray

Anode break movie

$R_0 = 128$, $Z_0 = 52$



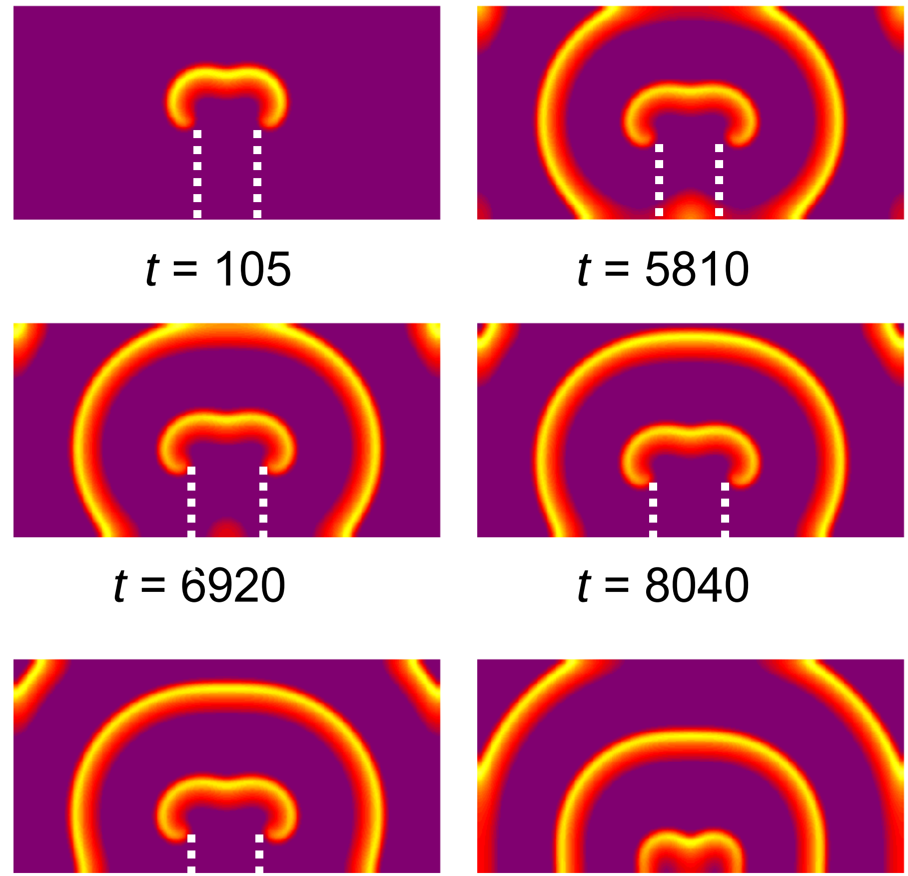
t =105 t =735

t =930 t =1320

t =1515 t =1635

Filament annihilation by collision

$R_0 = 128$, $Z_0 = 60$



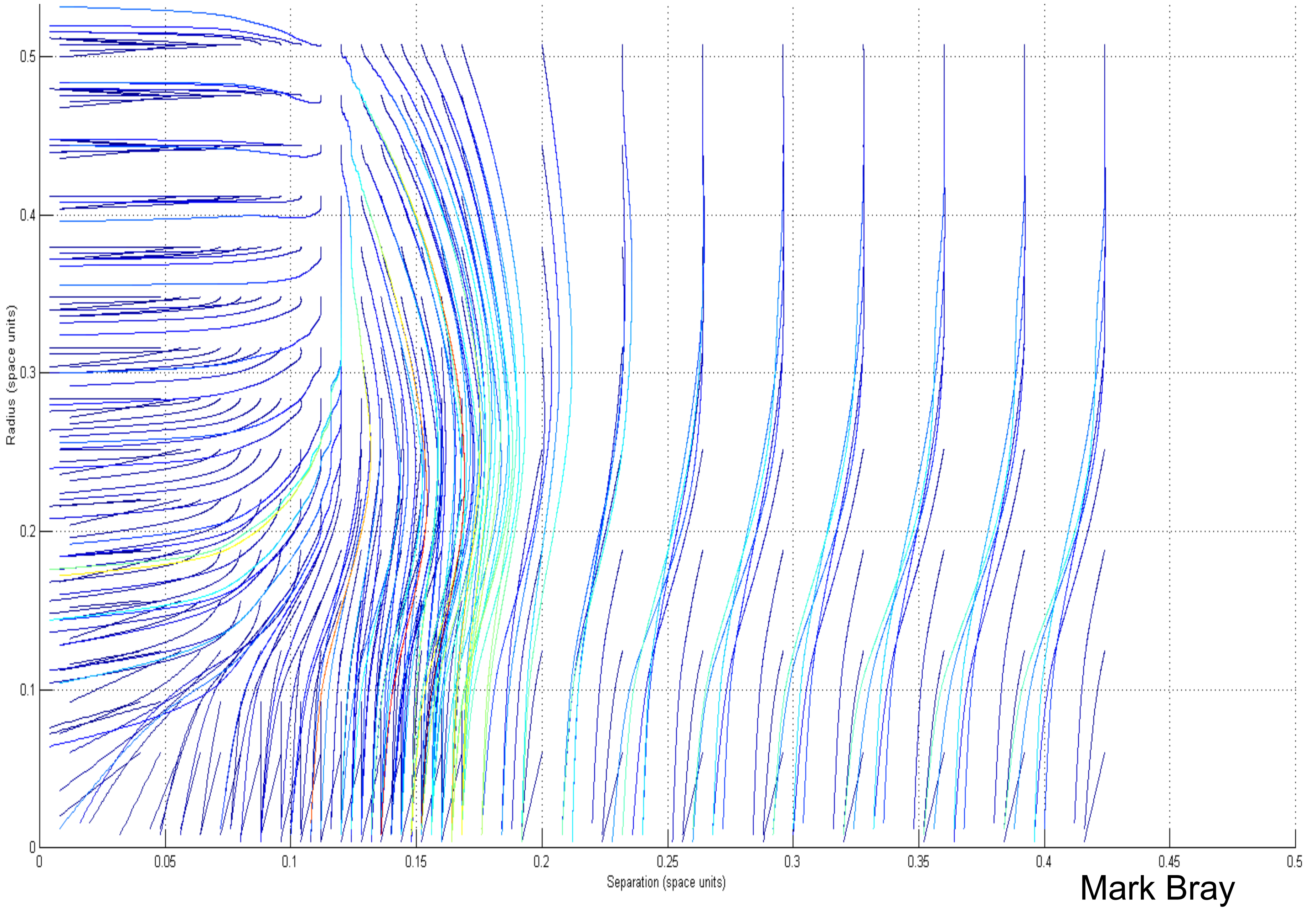
t = 105 t = 5810

t = 6920 t = 8040

t = 9160 t = 11390

Delayed self-annihilation by shrinkage

Anodal Break Trajectories



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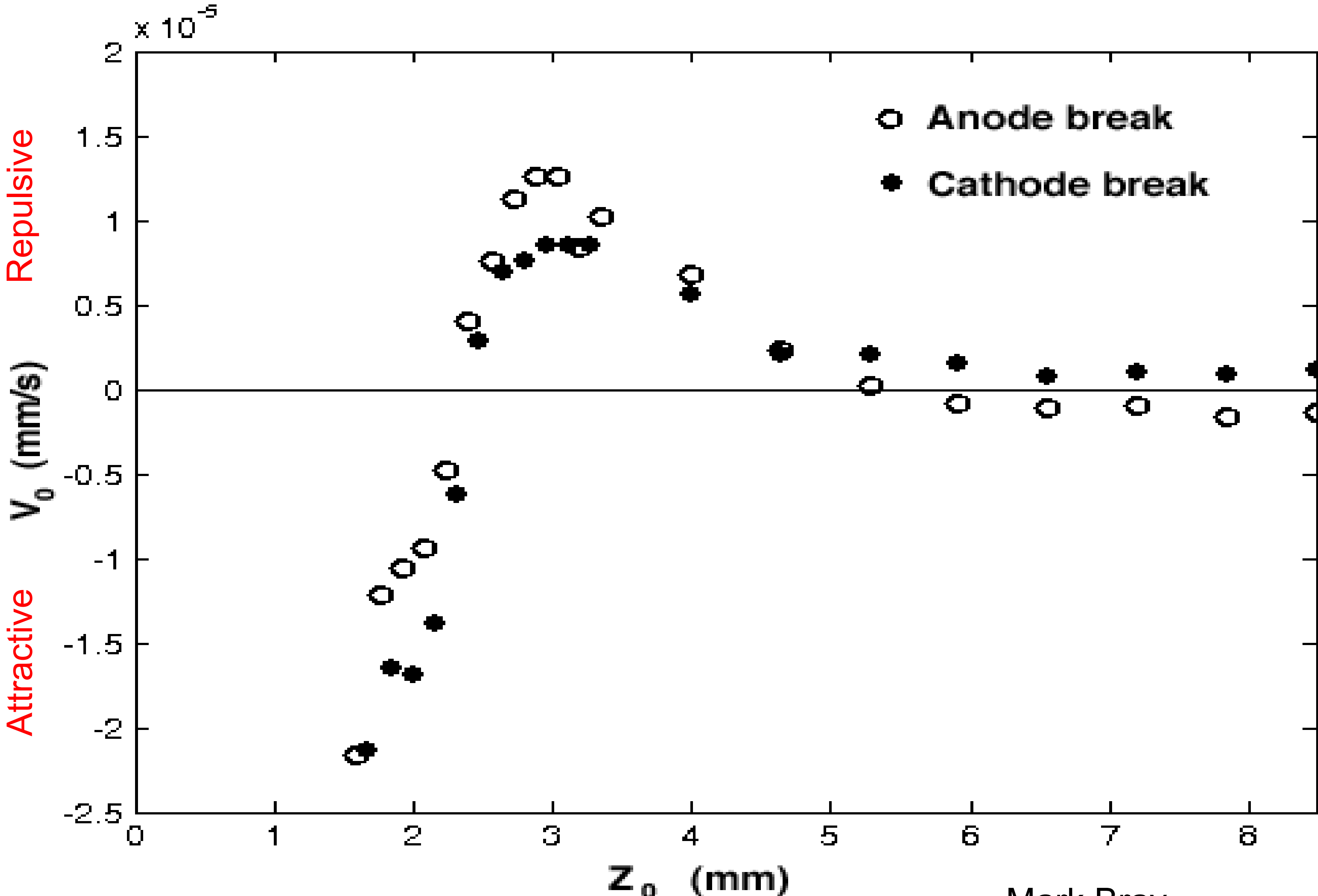
Initial Velocity = Force



Mark Bray

Outline

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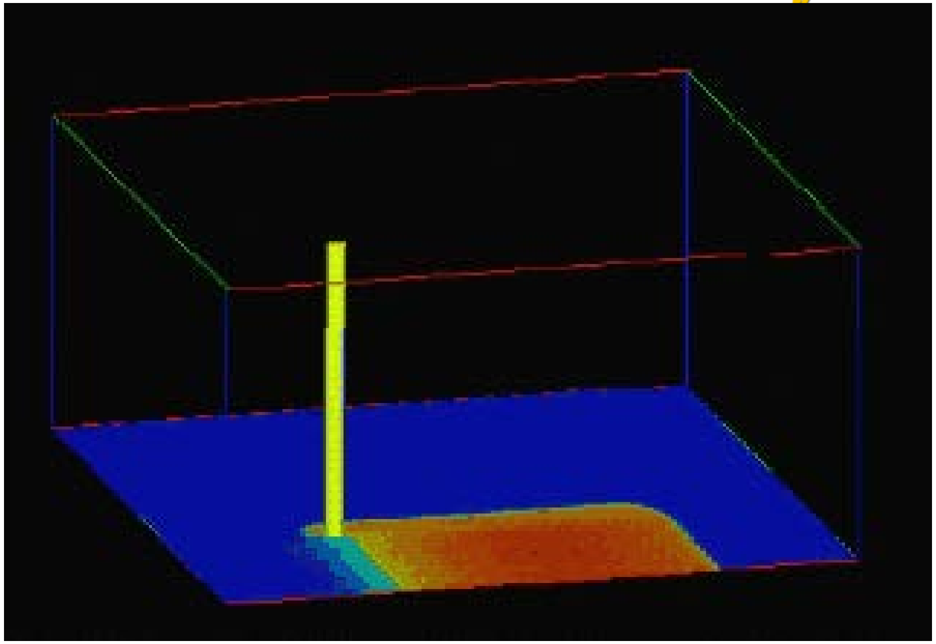
- What is needed?
  - Interaction potential
  - String creation operator

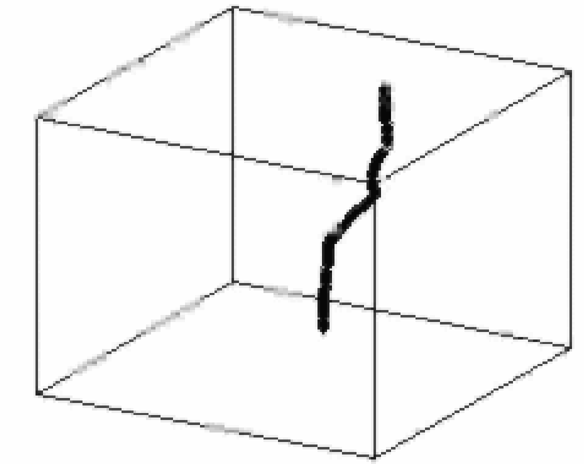
Courtesy of Jim Weiss

Movies Courtesy of Flavio Fenton

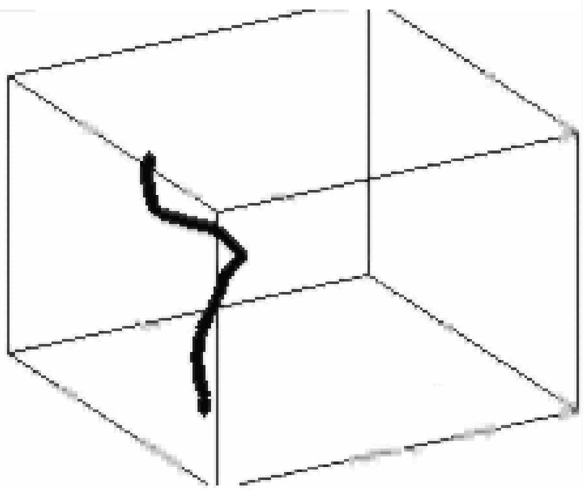
String Creation and Annihilation: Positive Line Tension with Fiber Rotation



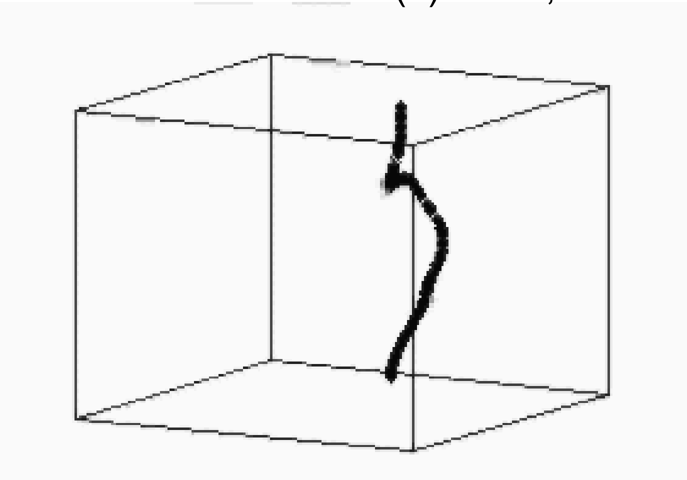
F. Fenton and A. Karma *Chaos* 8 (1):20-47, 1998



Vacuum loop creation/annihilation

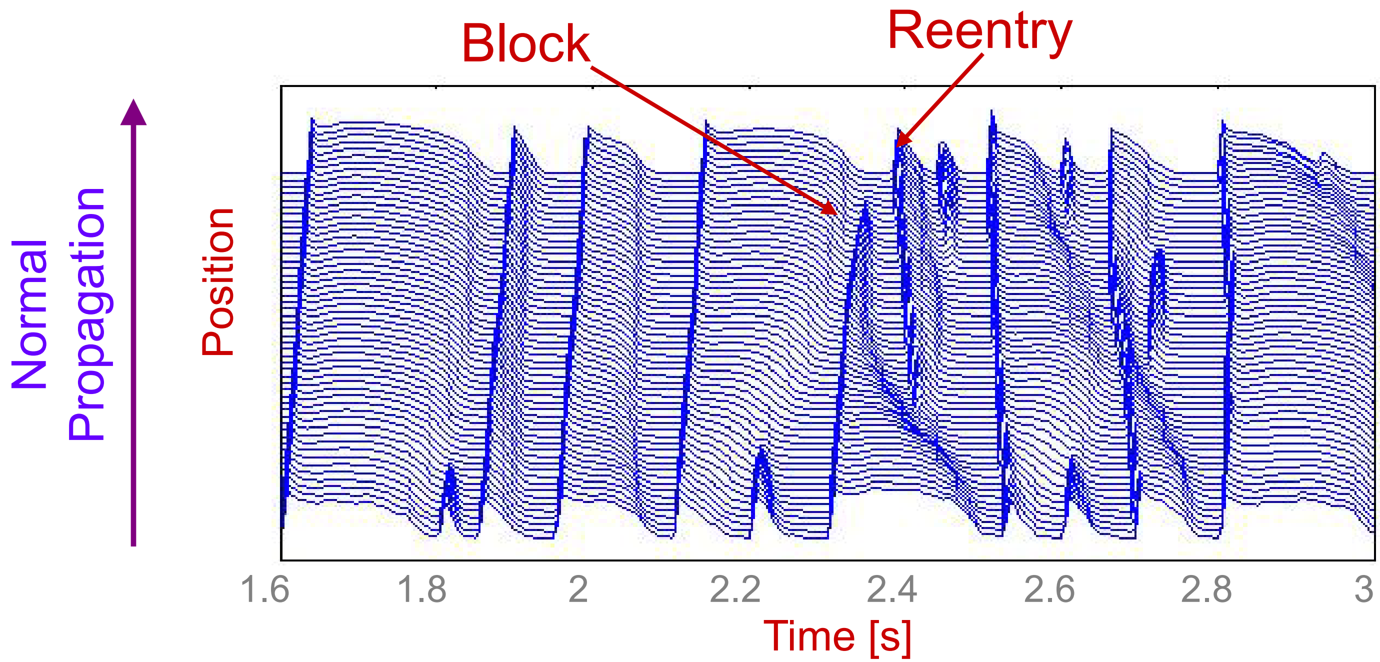


Loop pinch-off



Vacuum loop creation and coupling

Wavebreak = Vacuum Creation



Courtesy of Nathalie Virag, Medtronic

- Wave break occurs when the leading edge of a wave runs into the tail of a preceding wave
- Wavebreaks create filaments which create reentrant activation

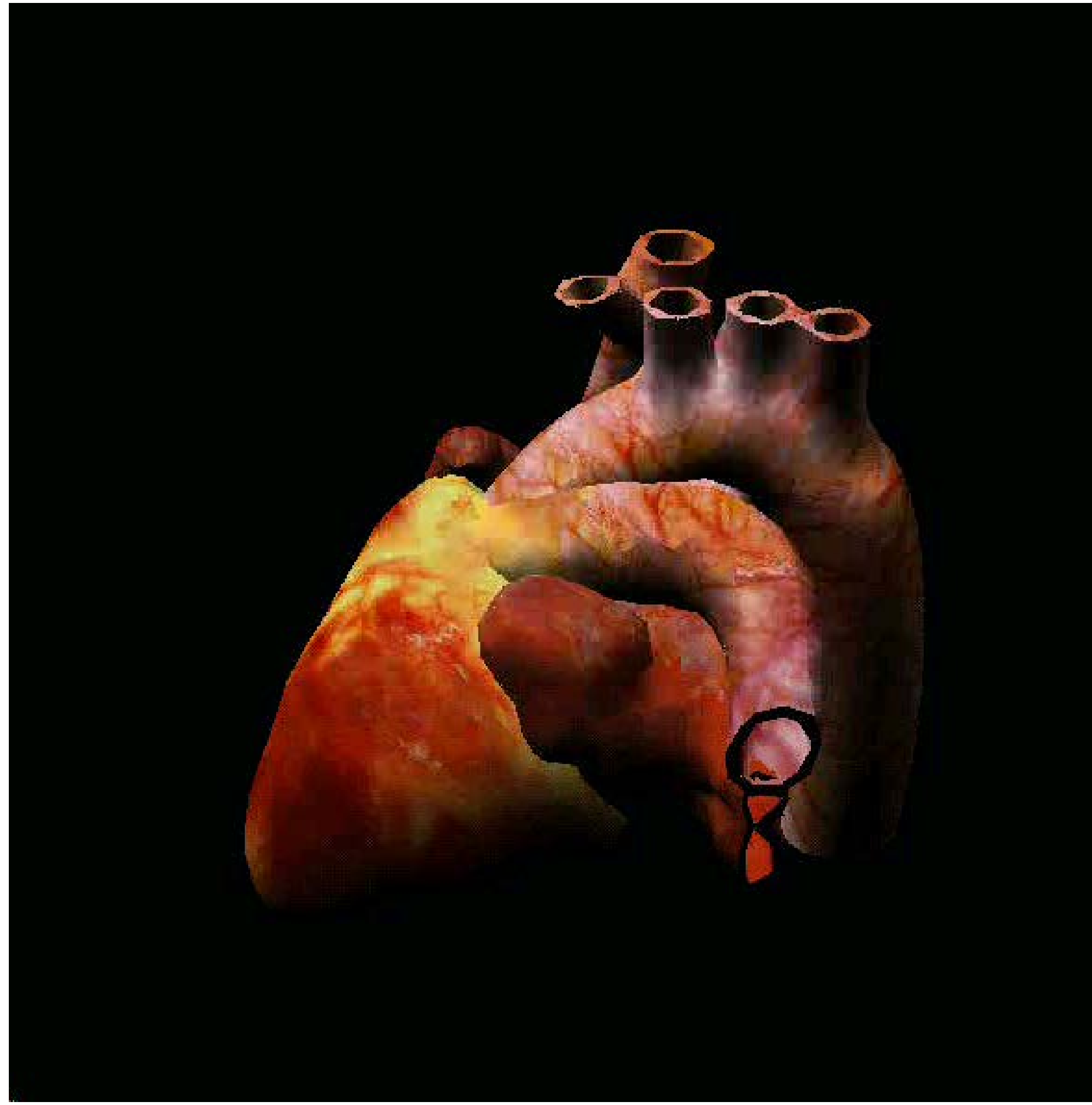
Jim Weiss, The Wedge, Newport Beach, CA

Future Questions

- For both cases, what parameters determine attractive versus repulsive behavior? Parameter gradients?
- Can a kinematic relationship be derived for the scroll ring interactions?
  - Is the effective mass constant or not, since it is a dissipative system?
  - Can the ring interaction be described by a point-to-point potential, and if so, are there obvious centers of action?
- In a field model, how do you introduce string creation from the vacuum?

Acknowledgements

- Rubin Aliev
- **Mark Bray**
- Elizabeth Cherry
- Deborah Echt
- **Flavio Fenton**
- **Rick Gray**
- Peter Hunter
- Alain Karma
- Mark Lin
- Neils Otani
- Arkardy Pertsov
- Nathalie Virag
- Jim Weiss
- And many others

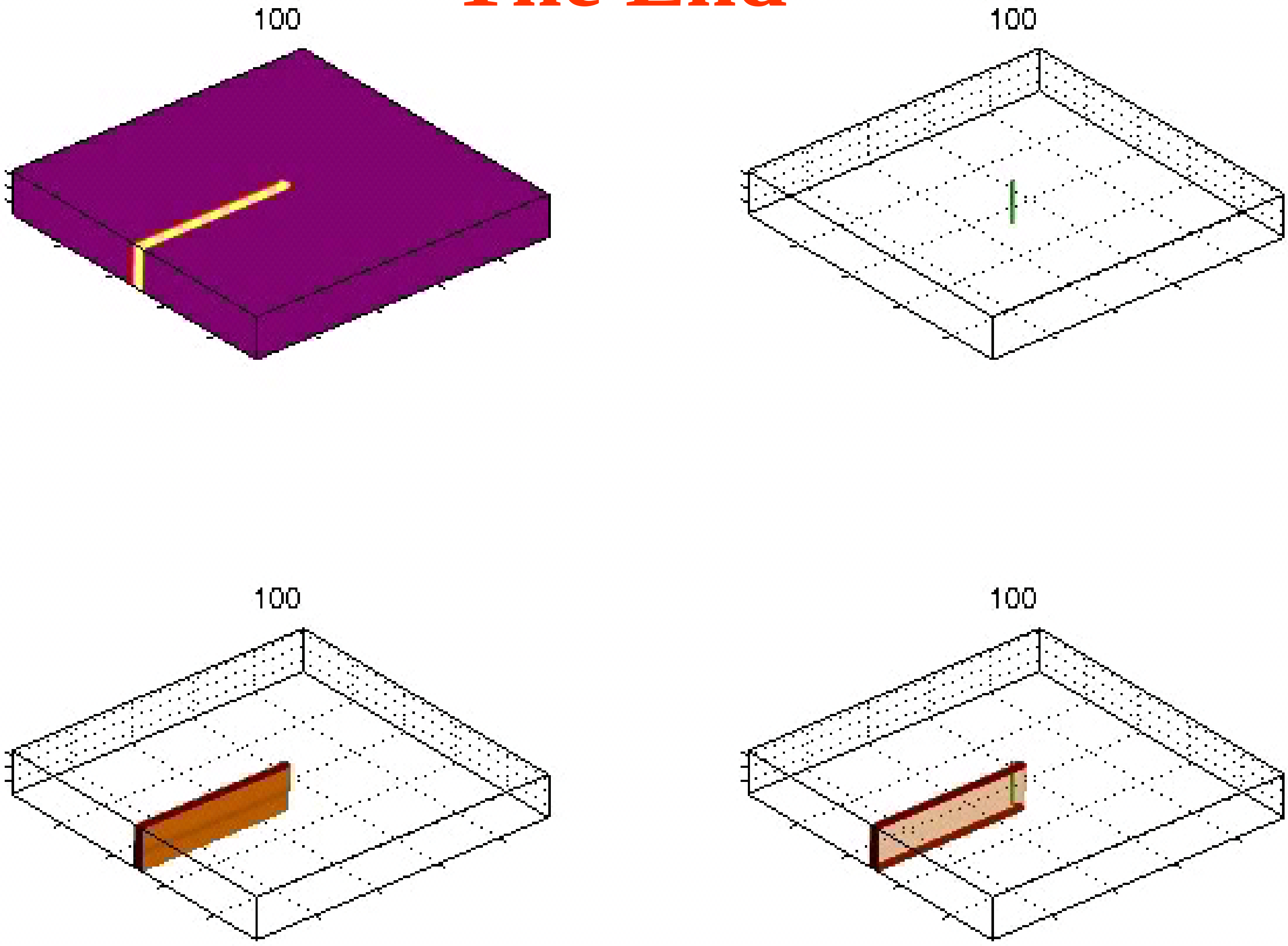


Courtesy of Peter Hunter, Auckland

fhnplus_scroll_wave_break_4panel.avi

textured-heart-spin.mpg

The End



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