Scroll Waves in Anisotropic Excitable Media with Application to the Heart

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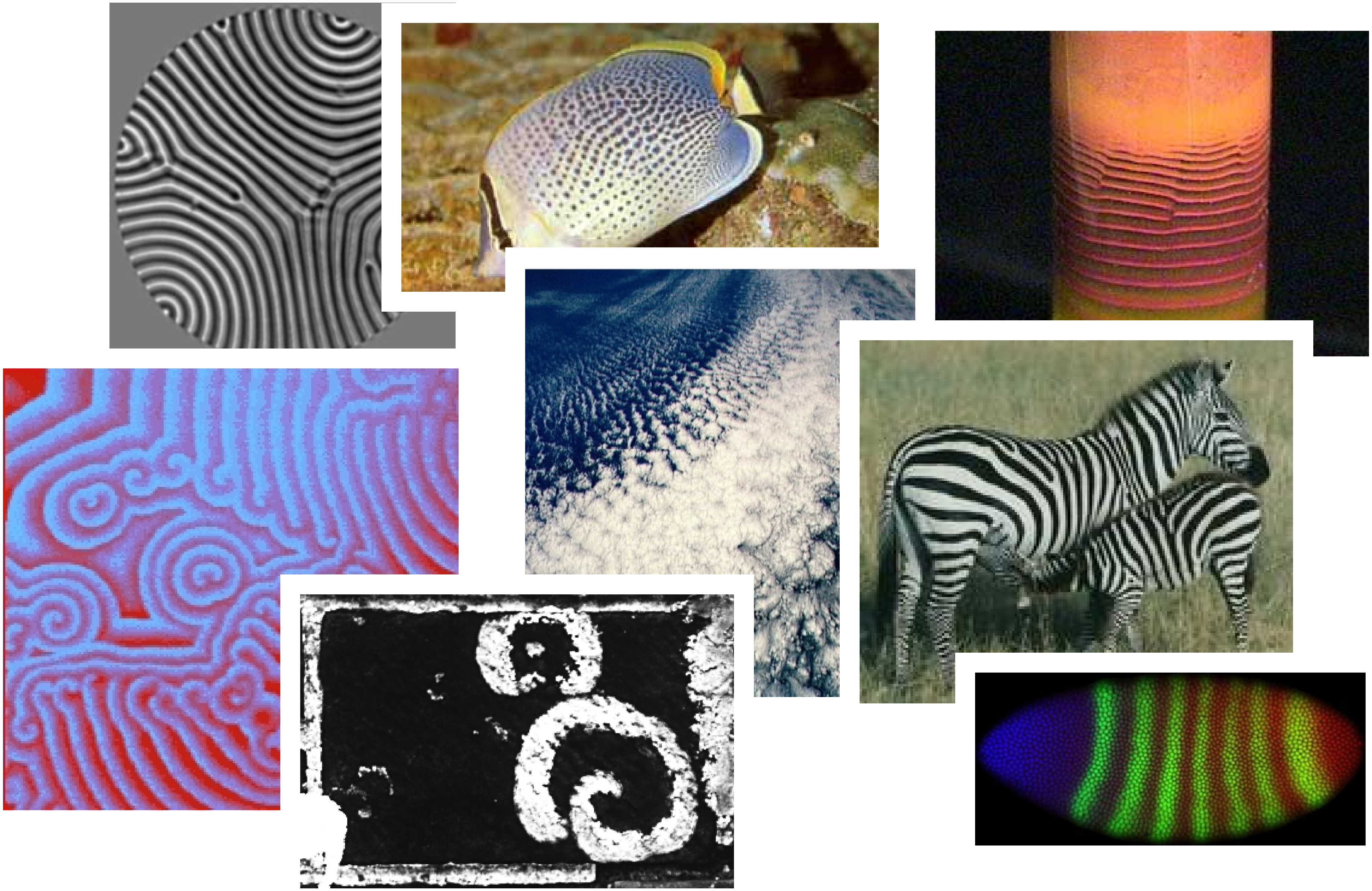
Stripes, Spots and Scrolls

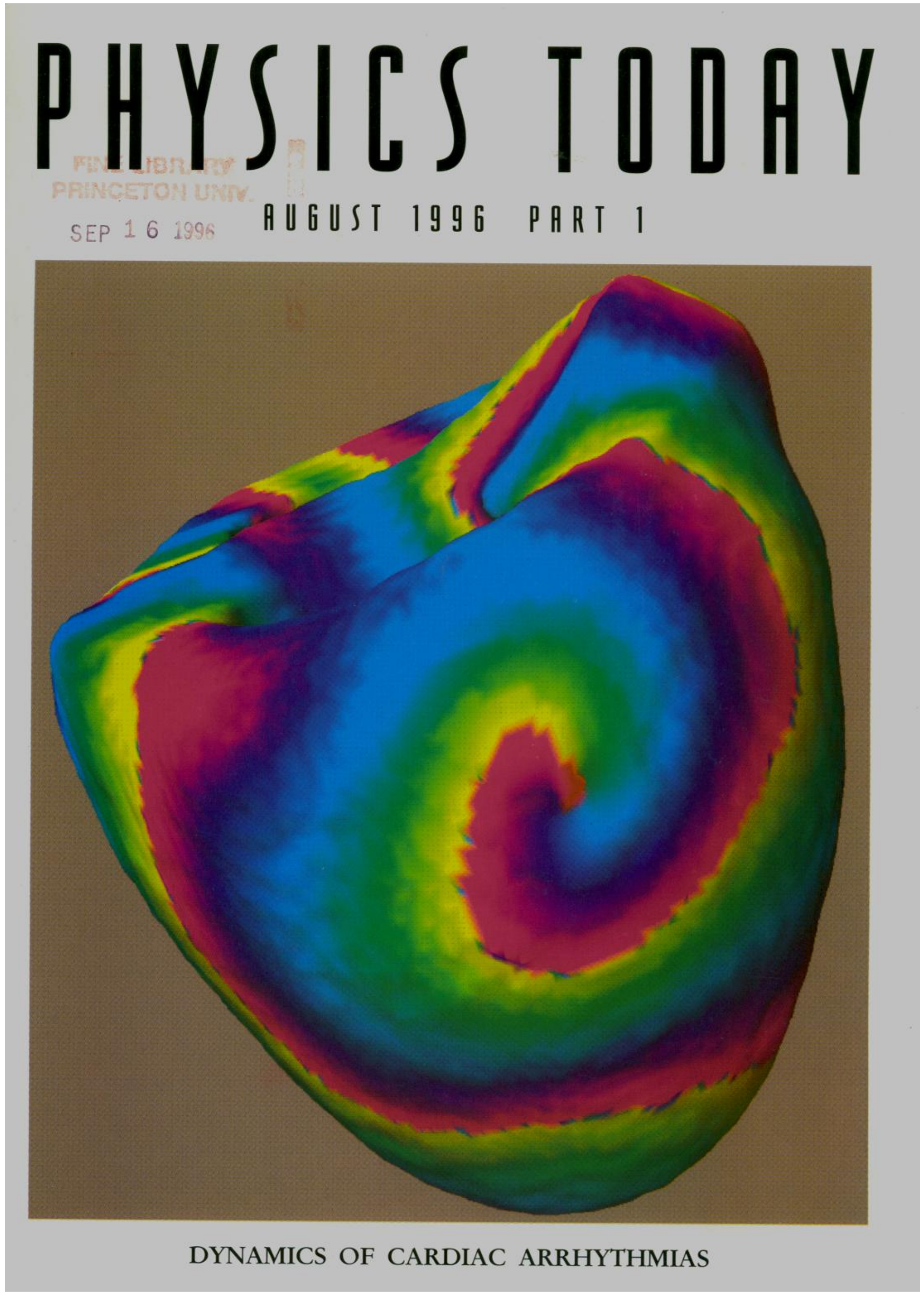


Overview

- Common processes underlying natural patterns give rise to model equations capturing generic features of pattern-forming systems

- Theoretical approaches accessible near onset, but must resort to numerical tools and experiments far from onset

- Need for high-fidelity scientific computation to describe realistic physical systems as a bridge between theory and experiment


PHYSICS TODAY
PRINCETON UNIV.
SEP 16 1996
AUGUST 1996 PART 1
DYNAMICS OF CARDIAC ARRHYTHMIAS

The Heart as a Physical System

- Sudden cardiac failure is the leading cause of death in industrialized nations.

1000 deaths/day in North America

- Growing experimental evidence that self-sustained patterns of electrical activity in cardiac tissue are related to fatal arrhythmias.
- Goal is to use analytical and numerical tools to study the dynamics of reentrant waves in the heart on physiologically realistic domains.

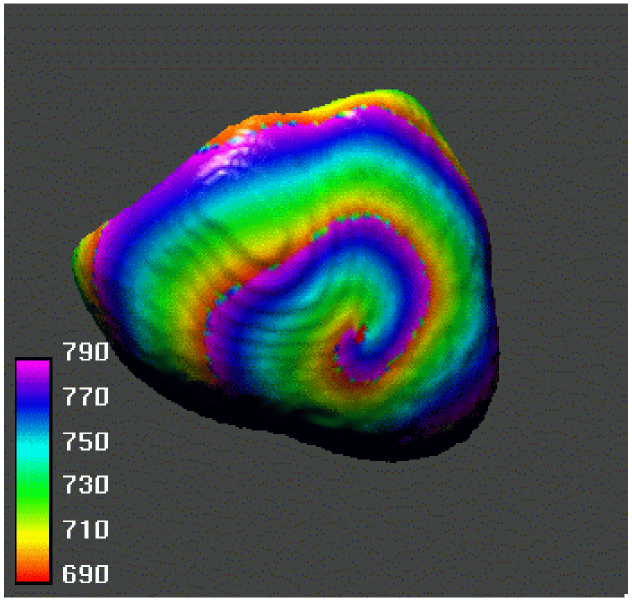
And ...

- The heart is an interesting arena for applying the ideas of pattern formation.

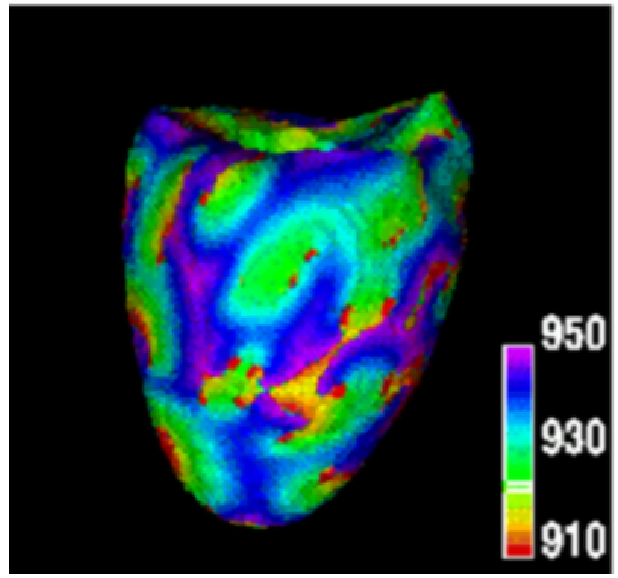
Big Picture

What are the mechanisms for transition from ventricular *tachychardia* to *fibrillation*? How can we control it?

Tachycardia:



Fibrillation:



Courtesy of Sasha Panfilov, University of Utrecht

Click for animation.

Paradigm: Breakdown of single spiral to disordered state resulting from various mechanisms of spiral instability.

Focus

What is the role of the anisotropy inherent in the fiber architecture of the heart on scroll wave dynamics?

Motivated by:

A. T. Winfree, in *Progress in Biophysics and Molecular Biology, D. Noble et al. eds., (1997).*

Numerical "experiments"

In rectangular slab geometries:

- Panfilov, A. V. and Keener, J. P., Physica D **84**, 545 (1995): *Scroll wave breakup due to rotating anisotropy.*
- *Fenton, F. and Karma, A., Chaos* **8***, 20 (1998): Rotating anisotropy leading to "twistons", eventually destabilizing scroll filament.*

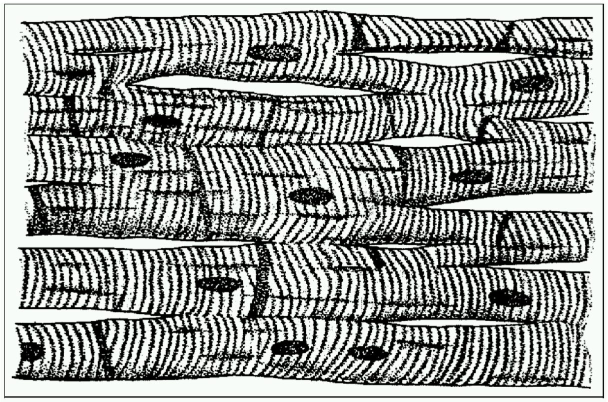
Analytical work

Dynamics of scroll waves in isotropic excitable media, beginning with:

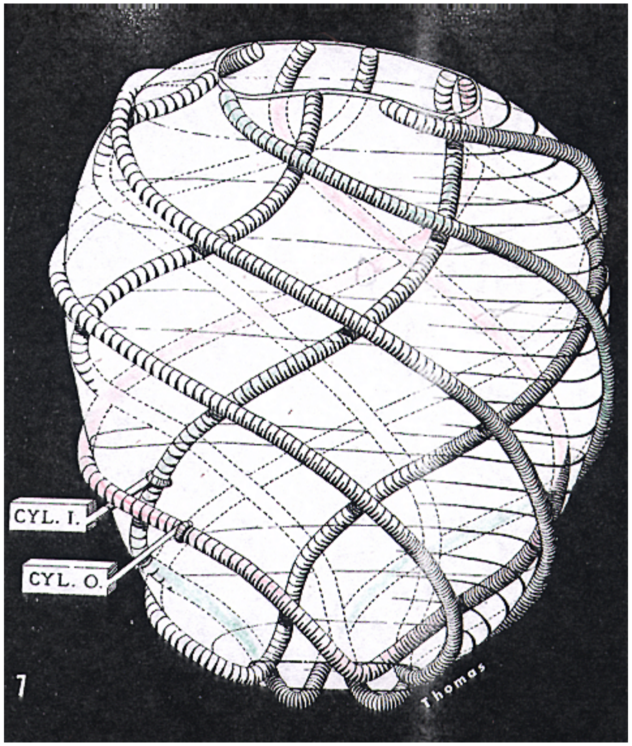
- Keener, J. P., Physica D **31**, 269 (1988).
- Biktashev, V. N., Physica D **36**, 167 (1989).

Tissue Structure

- $3d$ conduction pathway with uniaxial anisotropy
- Propagation speeds:
  $c_{\parallel} = 0.5$ m/s,
  $c_{\perp} = 0.17$ m/s



From *Textbook of Medical Physiology*, by Guyton and Hall



From Thomas, Am. J. Anatomy (1957).

Credits

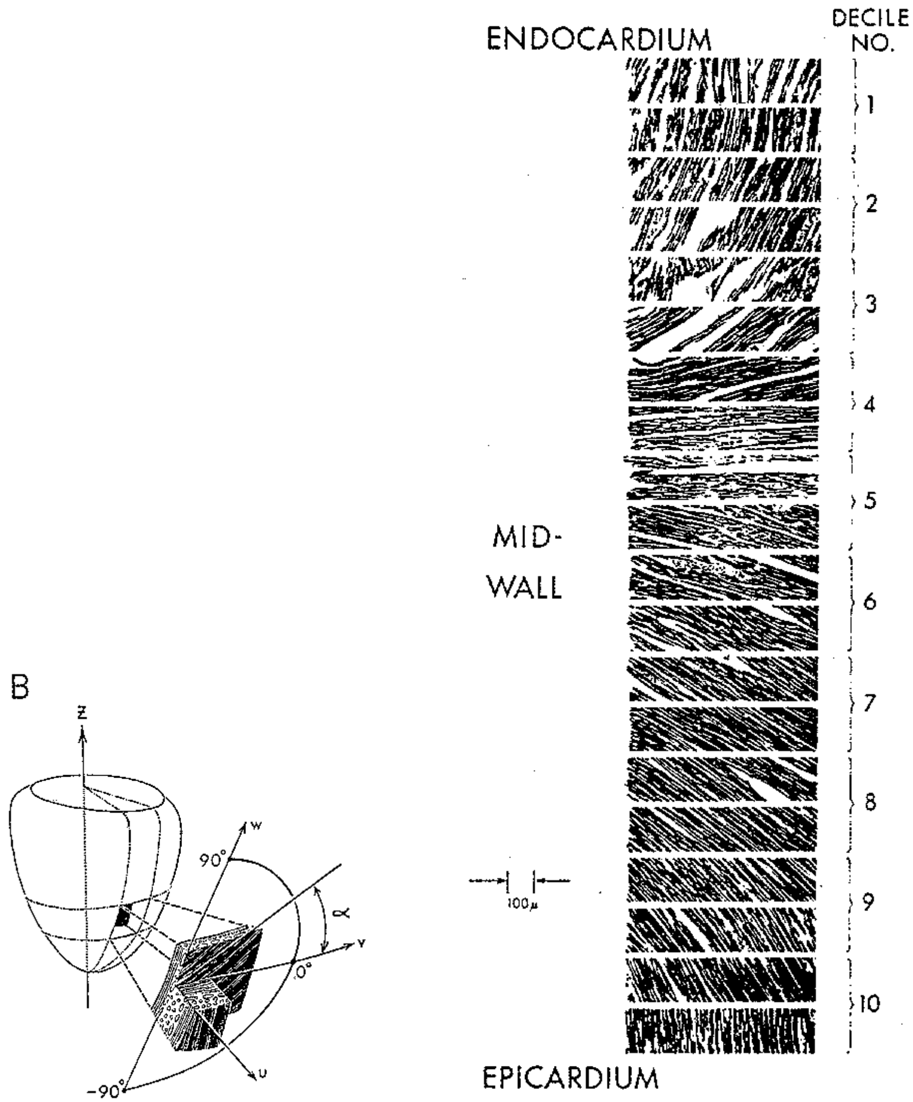
Collaborator

- *Andrew Bernoff*,
  Mathematics Department, Harvey Mudd College

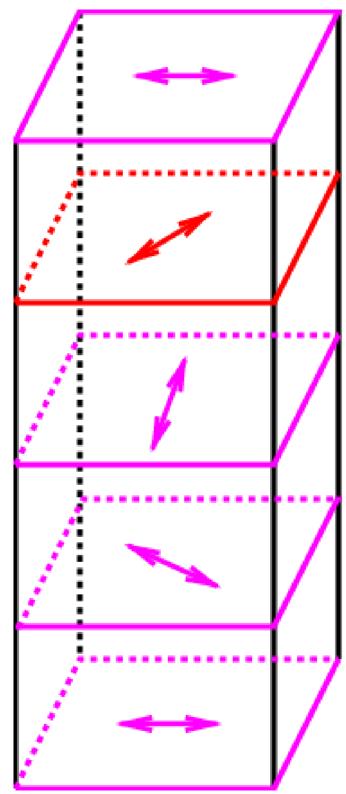
Acknowledgements

- *Alain Karma*,
  Physics Department, Northeastern University
- *Herb Keller*,
  Applied Mathematics Department, Caltech

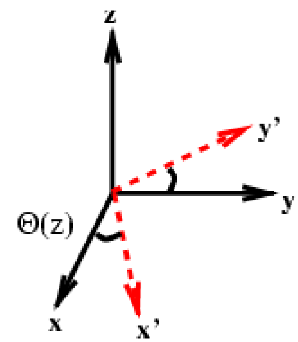
Rotating anisotropy



from Streeter, *et al.*, Circ. Res. **24**, p. 339 (1969).



$$\begin{pmatrix} D_{\perp_1} & 0 & 0 \\ 0 & D_{||} & 0 \\ 0 & 0 & D_{\perp_2} \end{pmatrix}$$



$$\begin{pmatrix} D_{||} & 0 & 0 \\ 0 & D_{\perp_1} & 0 \\ 0 & 0 & D_{\perp_2} \end{pmatrix}$$

Diffusion constants:

$$D_{||} > D_{\perp_1} \sim D_{\perp_2}$$

Coordinate System

Natural coordinate system defined by fiber direction:

$$\underbrace{\begin{pmatrix} \tilde{x} \\ \tilde{y} \\ \tilde{z} \end{pmatrix}}_{\text{'new'}} = \underbrace{\begin{pmatrix} 1 & 0 & 0 \\ 0 & \alpha & 0 \\ 0 & 0 & 1 \end{pmatrix}}_{S} \underbrace{\begin{pmatrix} \cos\Theta(z) & \sin\Theta(z) & 0 \\ -\sin\Theta(z) & \cos\Theta(z) & 0 \\ 0 & 0 & 1 \end{pmatrix}}_{R} \underbrace{\begin{pmatrix} x \\ y \\ z \end{pmatrix}}_{\text{'old'}}$$

S : **rescaling, according to 2d anisotropy** $\alpha \equiv (D_{\perp_1}/D_{\parallel})^{1/2}$

R : **rotation, according to fiber direction** $\Theta(z)$

Governing Equations

Governing reaction-diffusion equation in new coordinates:

$$
\begin{aligned}
\vec{u}_t \quad = \quad & \vec{f}(\vec{u}) + \boldsymbol{D}_{\|} \cdot \Delta_2 \vec{u} + \boldsymbol{D}_{\perp_2} \cdot \vec{u}_{zz} \\
& + \boldsymbol{D}_{\perp_2} \cdot \left\{ \Theta'^2 \left[\frac{\partial^2}{\partial \theta^2} + (\alpha^2 - 1) x^2 \frac{\partial^2}{\partial y^2} + \left(\frac{1}{\alpha^2} - 1 \right) y^2 \frac{\partial^2}{\partial x^2} \right] \vec{u} \right. \\
& \quad - 2\Theta' \left[\frac{\partial}{\partial \theta} + (\alpha - 1) x \frac{\partial}{\partial y} - \left(\frac{1}{\alpha} - 1 \right) y \frac{\partial}{\partial x} \right] \frac{\partial \vec{u}}{\partial z} \\
& \quad \left. - \Theta'' \left[\frac{\partial}{\partial \theta} + (\alpha - 1) x \frac{\partial}{\partial y} - \left(\frac{1}{\alpha} - 1 \right) y \frac{\partial}{\partial x} \right] \vec{u} \right\},
\end{aligned}
$$

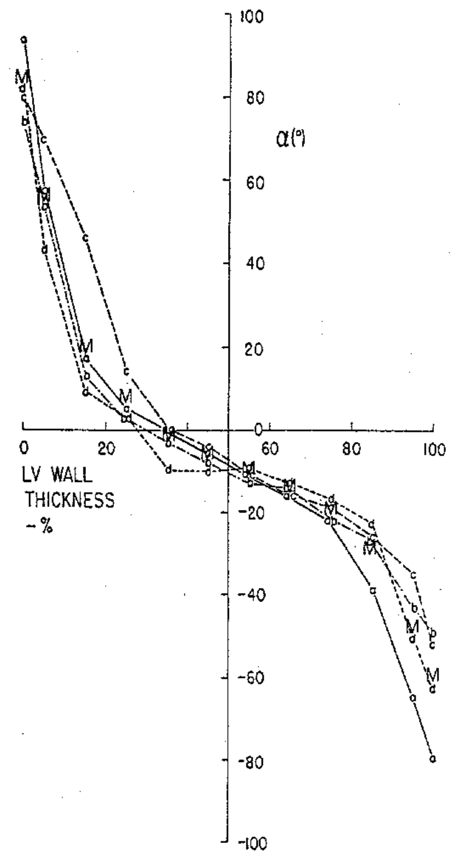
Only depends on fiber rotation rate, Θ' (no explicit dependence on $\Theta(z)$).

For FitzHugh-Naguomo (FHN) kinetics:

$$
\vec{u} = \begin{pmatrix} u \\ v \end{pmatrix}, \qquad \vec{f} = \begin{pmatrix} -u^3 + 3u - v \\ \epsilon(u - \delta) \end{pmatrix}, \qquad \boldsymbol{D}_{\|} = \begin{pmatrix} D_{\|} & 0 \\ 0 & 0 \end{pmatrix}, \qquad etc \ldots
$$

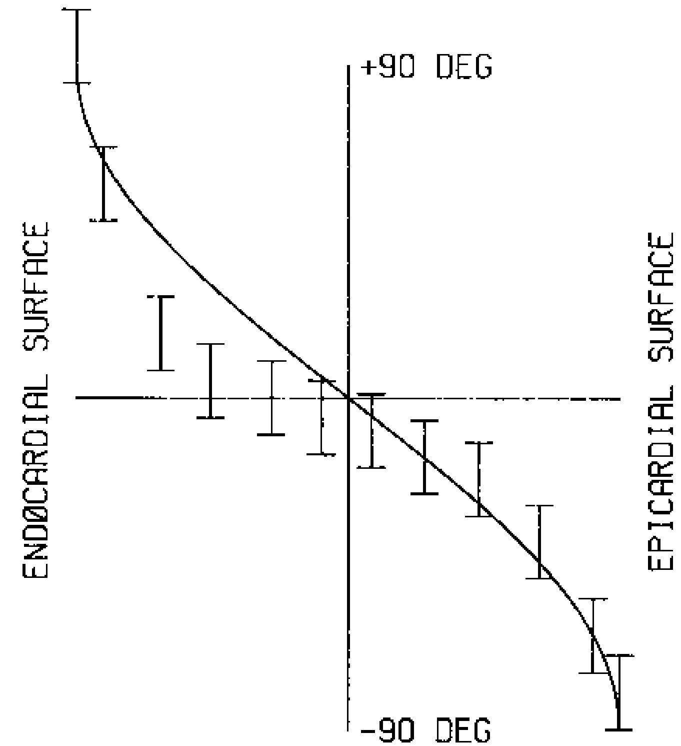
Peskin Fiber Distribution Profile

Measured



from Streeter, *et al.*, Circ. Res. **24**, p. 339 (1969)

Derived



from Peskin, *et al.*, Comm. on Pure and Appl. Math **42**, p. 79 (1989)

$$\Theta(z) = \sin^{-1}(z/rL)$$

$r =$ cutoff parameter
$2L =$ thickness of ventricular wall

Perturbation Analysis

Consider the limit of 'small rotating anisotropy' :

- **Non-dimensional small parameter:**

$$\epsilon^2 = \frac{D_{\perp 2}}{\omega_0 L^2} \frac{1}{r^2 - 1} \left(\frac{\gamma^2}{4} - 1 \right)$$

$\left(\frac{D_{\perp 2}}{\omega_0}\right)^{1/2}$	**: transverse diffusion length,** ℓ
$2L$	**: thickness of ventricular wall**
r	**: cutoff parameter**
$\gamma = \alpha + 1/\alpha$	**: 'anisotropy'**

- **Seek a solution in the form of:**

$$\vec{u} = \vec{U}_0(r, \theta - \omega_0 t + \Theta(z) + \phi(z,t)) + \epsilon^2 \vec{u}_2,$$

where $\vec{U}_0(r, \theta - \omega_0 t)$ **satisfies:**

$$\mathcal{O}(1): \quad \frac{\partial \vec{U}_0}{\partial t} = \vec{f}(\vec{U}_0) + D_{\parallel} \cdot \Delta_2 \vec{U}_0$$

- **Scaling assumptions:** $\vec{u}_2 \sim \mathcal{O}(1), \quad \phi_z \sim \mathcal{O}(\epsilon), \quad \phi_t \sim \mathcal{O}(\epsilon^2).$

Validity of Perturbation Analysis?

What is the value of the small parameter for the human ventricle?

Parameter	Value
$D_{\parallel}$	$1.0\ cm^2\, s^{-1}$
$D_{\perp}$	$0.1\ cm^2\, s^{-1}$
ω_0	$12.6\ s^{-1}$
$\Delta\Theta$	180°
$2L$	$1.0\ cm$
r	1.5

$$\epsilon^2 \sim 0.45$$

Phase Equation

At $\mathcal{O}(\epsilon^2)$, introducing $\Phi(z,t) \equiv \left(\frac{c_1}{c_2}\right) \left[\phi(z,t) - \left(\frac{\gamma}{2} - 1\right)\Theta(z)\right]$:

$$\boxed{\Phi_t - \Phi_z^2 - \Phi_{zz} = A(\gamma, r)\, F(z; r), \qquad -1 < z < 1}$$

Burgers' equation, with forcing given by fiber rotation:

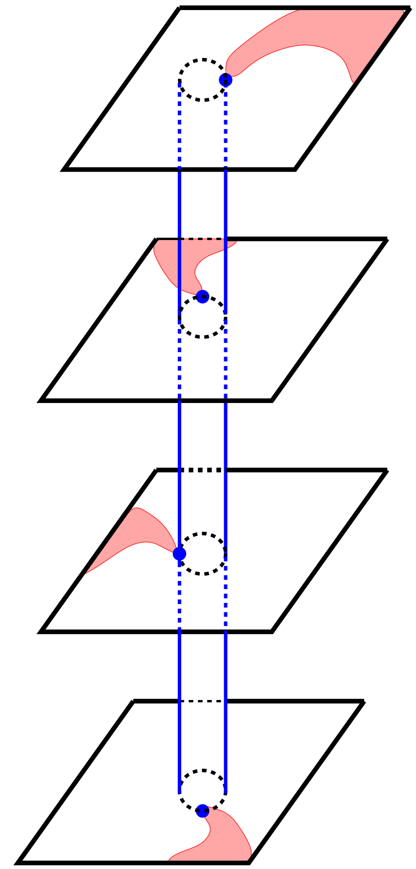
- $F(z;r) = \frac{1-1/r^2}{1-(z/r)^2}, \qquad A(\gamma, r) = \tilde{A}\left(\frac{\gamma^2}{4} - 1\right)\frac{1}{r^2-1}, \qquad \tilde{A} = \left(\frac{c_1}{c_2}\right)^2 \left(\frac{4a_1}{c_1} - 1\right)$
- (a_i, c_i) given by inner products from the solvability condition, e.g.,

$$a_1 = \left\langle \vec{\tilde{Y}}_\theta,\ \boldsymbol{D}_{\perp_2} \cdot \vec{U}_{0_{\theta\theta}} \right\rangle$$

Seek asymptotic and numerical solutions, using constant frequency-shift ansatz:

$$\Phi(z,t) = \int_{-1}^{z} \underbrace{k(z')}_{\text{twist}}\, dz' + \lambda t + \Phi_0$$

Scroll Twist



For a straight scroll:

$$k(z,t) = \left(\frac{\partial \hat{N}}{\partial z} \times \hat{N} \right) \cdot \hat{z}$$

$\hat{N} = \vec{\nabla} u / |\vec{\nabla} u|$
normal to tip trajectory

In new coordinates:

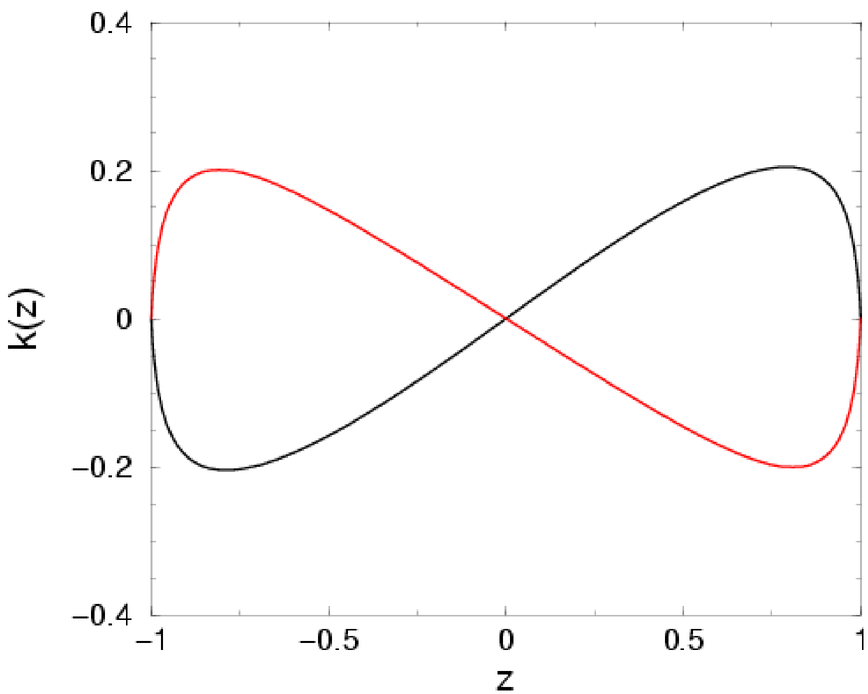
$$k(z,t) = \phi_z(z,t) + \Theta'(z).$$

In old coordinates:

$$k(\tilde{z},t) = \Theta'(\tilde{z}) - \frac{2\alpha \left(\phi_{\tilde{z}}(\tilde{z},t) + \Theta'(\tilde{z}) \right)}{(\alpha^2 - 1)\ \cos\left[2\ (\omega_0 t - \phi(\tilde{z},t) - \Theta(\tilde{z}))\right] + (1+\alpha^2)}.$$

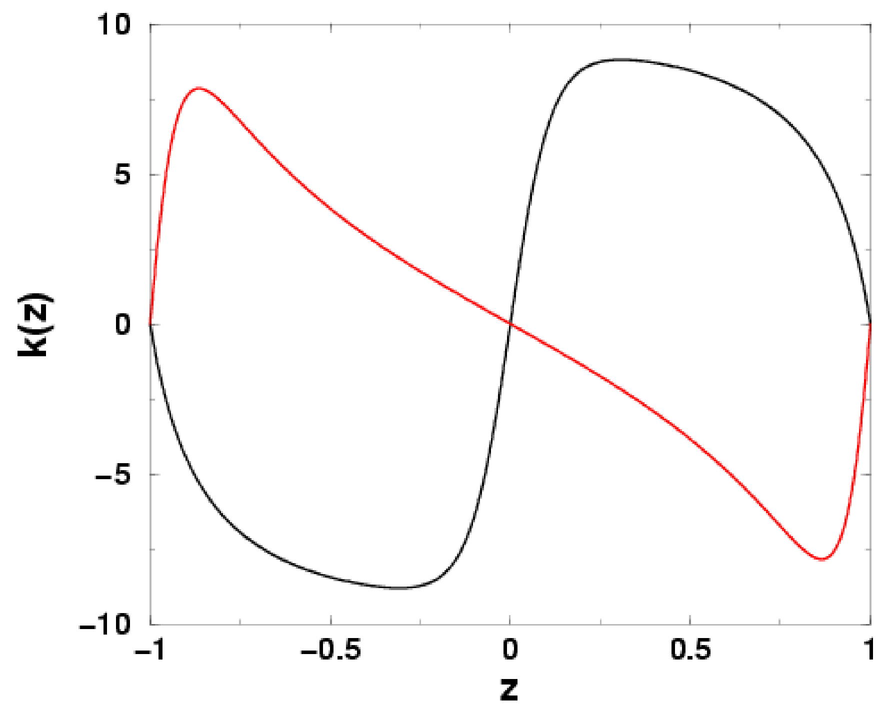
Twist Solutions

Diffusive Regime: $\Phi_{zz} \gg \Phi_z^2$



$A > 0$, $A < 0$: Maximum twist at boundary

Twist-dominated Regime: $\Phi_{zz} \ll \Phi_z^2$



$A > 0$: Formation of large twist in boundary layer in bulk

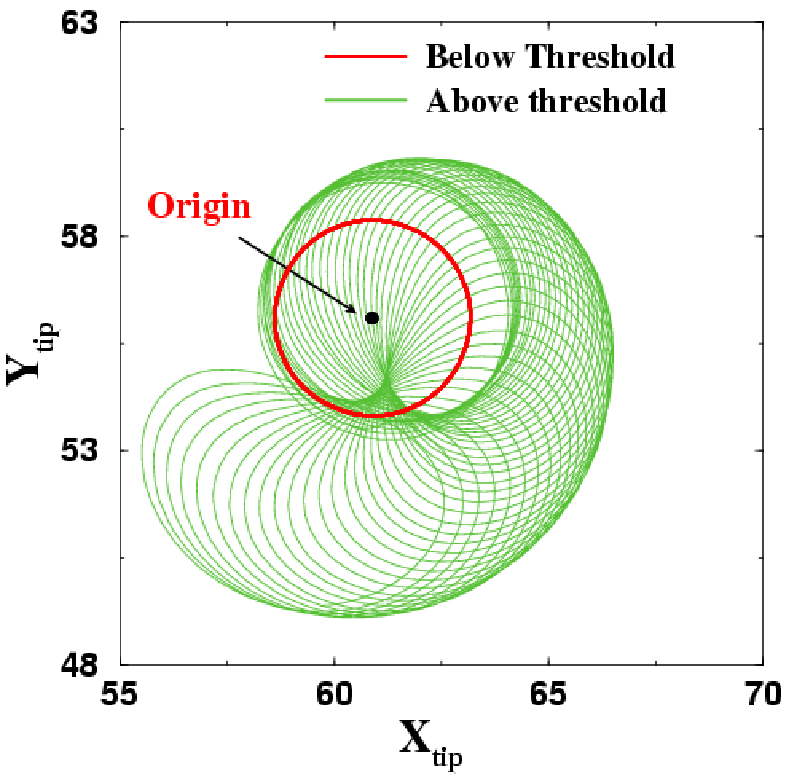
$A < 0$: Expulsion of large twist from bulk to boundaries

Relevance?

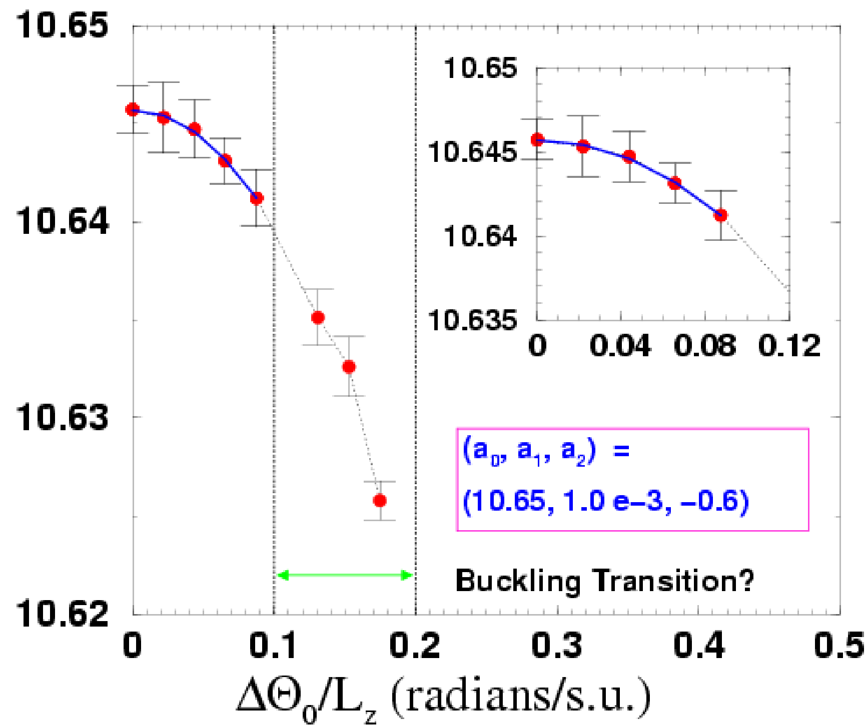
Henzi, Lugosi, Winfree, Can. J. Phys. **68**, 683 (1990): $\alpha = 1$

Helical buckling ("sproing instability") for $twist > twist^*$

Tip Trajectory



Scroll Period vs. Scroll Twist



With rotating anisotropy, $\alpha \neq 1, \Theta_z \neq 0$???

Summary

What has been done:

Extension of asymptotics of scroll waves in isotropic media to include rotating anisotropy of cardiac tissue

- ▷ **Phase dynamics (forced Burgers equation):**
  nonconstant fiber rotation rate generates twist [a]

Extensions:

- Coupling between twist and filament dynamics
- Extension to biodomain description of cardiac tissue

a : Setayeshgar and Bernoff, Phys. Rev. Lett. (2002).

Summary (cont'd)

- Numerical sproing bifurcation diagram with rotating anisotropy