Scroll wave drift
Due to Anisotropy Gradients
in the Cardiac Wall

Hans Dierckx

Snowbird DS19, 20 May 2019

Outline

Heart rhythm disorders: collective dynamics of non-linear waves

HEALTHY - PERTURBED - FAILING

3D dynamics in simulations of ventricular tachycardia

Cardiac excitation modeled as a reaction-diffusion process:

$$\partial_t \mathbf{u} = \partial_i \left(D^{ij}(\vec{r}) \partial_j \mathbf{P} \mathbf{u} \right) + \mathbf{F}(\mathbf{u}) \tag{1}$$

with $u_1 \equiv V$ transmembrane potential.

Questions

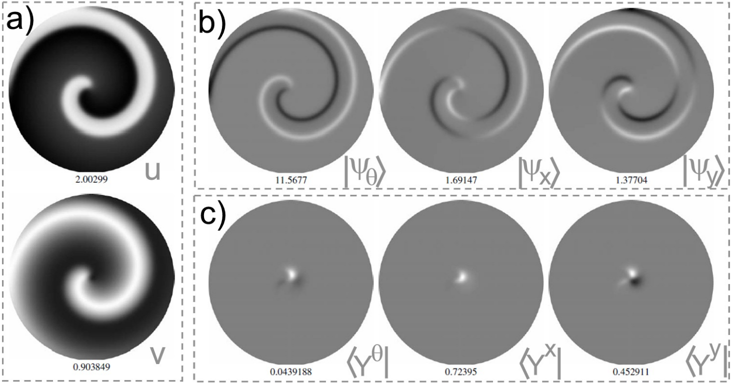
Can we predict the drift of a rotor in the 3D cardiac wall from wall thickness and intramural fiber orientation?

Outline

Preliminaries: Particle-wave duality of spiral waves

$$\partial_t \mathbf{u} = \Delta \mathbf{P} \mathbf{u} + \mathbf{F}(\mathbf{u}) + \mathbf{h}(\vec{r}, t)$$

$$\partial_t X^m = v_0^m(\Phi) + \langle \mathbf{Y}^m \mid \mathbf{h} \rangle, \quad m \in \{X, Y, \Phi\}, \quad \langle \mathbf{f} \mid \mathbf{g} \rangle = \iint_{\mathbb{R}^2} \mathbf{f}^H \mathbf{g} d^2 x$$



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1. Motivation
2. Methods
   - Response function framework
   - Curved-space viewpoint
   - Mean-field approach
3. Results
   - Drift in the surface approximation
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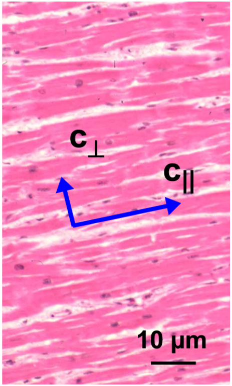
   - Finite thickness drift corrections
4. Conclusions

Preliminaries: Anisotropic wave propagation



If $det(\mathbf{D})$ constant and $D^{ij} \equiv g^{ij}$:

$$\partial_i \left(D^{ij}(\vec{r}) \partial_j V \right) = \frac{1}{\sqrt{g}} \partial_i (\sqrt{g} g^{ij} \partial_j V) = \mathcal{D}^2 V$$

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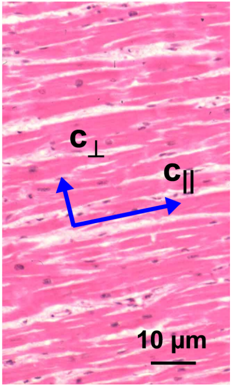

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The heart is a Riemannian manifold

Measuring distance in the heart using arrival time of traveling waves

$\Leftrightarrow$

Metric tensor $\mathbf{g} = \mathbf{D}^{-1}$

$$ds^2 = g_{xx} dx^2 + 2 g_{xy} dxdy + g_{yy} dy^2$$

Wellner et al. PNAS 2002;
Verschelde et al. PRL 2007;
Young et al. PNAS 2010

How to rescale the spiral wave in every cross-section of a scroll wave ?

1. Rescale axes according to in-plane conduction velocities?

$$x_1' = x_1/c_1, \qquad x_2' = x_2/c_2 \tag{2}$$

   Setayeshgar & Bernoff, PRL 2002; Verschelde et al. PRL 2007

2. Or, rescale according to the thickness-average of **D**?
   Chapelle et al. Math. Models & Meth. Appl. Sci. 2013

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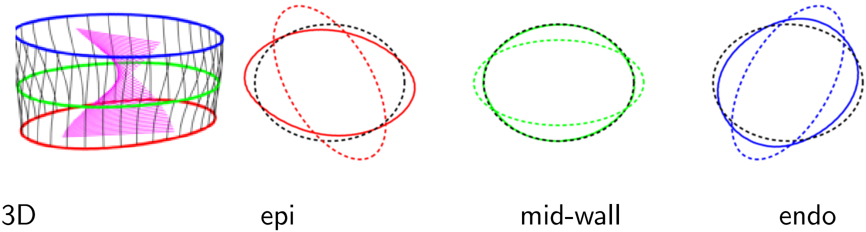
⇒ Numerical simulations in the Aliev-Panfilov model:



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A mean-field approximation to the diffusion tensor

- Define the thickness-average and its error:

$$\overline{f}(x,y) = \frac{1}{V}\int_0^L f(x,y,z)\sqrt{g}\,dz, \qquad V = \int_0^L \sqrt{g}\,dz \tag{3}$$

$$\widetilde{f}(x,y,z) = f - \overline{f} \tag{4}$$

where $\sqrt{g}dxdydz = |J|dxdydz$ is the infinitesimal volume element

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- We will need the **thickness-averaged diffusion tensor**

$$H^{ab}(x,y) = \overline{D^{ab}}, \qquad a,b \in \{x,y\} \tag{5}$$

$$H_{ab}H^{bc} = \delta_a^c, \qquad H = \det(H_{ab}) \tag{6}$$

$$D^{ab} = H^{ab} + \widetilde{D}^{ab} \tag{7}$$

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- Thickness-averaged state variables:

$$\mathbf{u} = \overline{\mathbf{u}} + \widetilde{\mathbf{u}} \tag{8}$$

Limit of vanishing thickness

- Say the spatial decay constant of the RFs is d
- If $\epsilon = (L/d)^2 \ll 1$, define relative depth $\sigma = z/L \in [0, 1]$ and let $\mathbf{u}(t, \tau)$ depend on time t and 'fast time' $\tau = t/\epsilon$:

$$\partial_t \mathbf{u} + \frac{1}{\epsilon}\partial_\tau \mathbf{u} = \partial_a(D^{ab}\partial_b \mathbf{P}\mathbf{u}) + \frac{1}{\epsilon}\mathbf{P}D^{zz}\partial_\sigma^2 \mathbf{u} + \mathbf{F}(\mathbf{u}). \tag{9}$$

- At the fast timescale ...

$$\partial_\tau \mathbf{u} = \mathbf{P}D^{zz}\partial_\sigma^2 \mathbf{u} \tag{10}$$

... there is only transmural diffusion!

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- In the limit of vanishing thickness, V is constant across the wall $\Rightarrow$ $\mathbf{u}$ is constant across the wall

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Averaging of the RDE (1/2)

1. Insert $\mathbf{u} = \overline{\mathbf{u}} + \tilde{\mathbf{u}}$ and into the RDE assuming $D^{xz} = D^{yz} = 0$:

$$\partial_t \bar{\mathbf{u}} + \partial_t \widetilde{\mathbf{u}} = \frac{1}{\sqrt{g}} \partial_a (\sqrt{g} D^{ab} \partial_b \bar{\mathbf{u}}) + \frac{1}{\sqrt{g}} \partial_z (\sqrt{g} D^{zz} \mathbf{P} \partial_z \widetilde{\mathbf{u}}) + \frac{1}{\sqrt{g}} \partial_a (\sqrt{g} D^{ab} \partial_b \widetilde{\mathbf{u}}) + \mathbf{F}(\bar{\mathbf{u}}) + \mathbf{F}'(\bar{\mathbf{u}}) \widetilde{\mathbf{u}} + \mathcal{O}(\epsilon^2) \qquad (11)$$

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2. Average over thickness:

$$\partial_t \bar{\mathbf{u}} = \frac{1}{V} \partial_a (V H^{ab} \partial_b \bar{\mathbf{u}}) + \mathbf{F}(\bar{\mathbf{u}}) + \mathcal{O}(\epsilon). \qquad (12)$$
$$= \frac{1}{\sqrt{H}} \partial_a (\sqrt{H} H^{ab} \partial_b \bar{\mathbf{u}}) + \partial_a \ln(V/\sqrt{H}) H^{ab} \partial_b \bar{\mathbf{u}} + \mathbf{F}(\bar{\mathbf{u}}) + \mathcal{O}(\epsilon)$$

$\Rightarrow$ Leading order: spiral ‘sees’ a curved surface with metric H^{ab}, with additional gradient term of the ‘potential’ $\ln(V/\sqrt{H})$.

Averaging of the RDE (2/2)

1. Infinitesimal volume in a wall portion is $Vdxdy = \sqrt{H}\mathcal{L}dxdy$, so call $\mathcal{L} = V/\sqrt{H}$ the 'effective filament length'.
   In simplest case: $\mathcal{L} = L/\sqrt{D^{zz}}$.

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2. Introduce local Euclidean coordinates around the tip such that $H^{ab} = \delta^{ab}$ and prescribe that $\bar{\mathbf{u}} = \mathbf{u}_0$ in these coordinates

$$v^M = -\langle \mathbf{W}^M \mid \partial_a \ln \mathcal{L} H^{ab} \partial_b \mathbf{u}_0 \rangle, \quad M \in \{x, y, \phi\}, \quad a, b \in \{x, y\}$$

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3. After averaging over one rotation:

$$v^a = -\gamma_1 D^{ab} \partial_b \ln \mathcal{L} - \gamma_2 \frac{\epsilon^{ab}}{\sqrt{H}} \partial_b \ln \mathcal{L} \tag{13}$$

where $\gamma_1 = \frac{1}{2}\langle \mathbf{W}^a \mid \mathbf{P}\partial_a \mathbf{u}_0 \rangle$: filament tension

Result for a filament in a wedge with opening angle β

- If $D^{ij} = \delta^{ij}$, then

$$
\begin{aligned}
V &= \int \sqrt{g} ds = \beta r = L \\
H^{ab} &= \frac{1}{V} \int \sqrt{g} \delta^{ab} ds = \delta^{ab} \\
\sqrt{H} &= 1 \\
\mathcal{L} &= L = \beta r
\end{aligned} \tag{14}
$$

so 'effective filament length' $\mathcal{L}$ here equals the usual filament length L

- Equation of motion becomes:

$$
\begin{aligned}
v^a &= -\frac{\gamma_1}{r} \vec{e_r} + \frac{\gamma_2}{r} \vec{e}_y \\
\Rightarrow \vec{v} &= \gamma_1 k \vec{N} + \gamma_2 k \vec{B}.
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- We recover the result from Biktashev, Holden & Zhang (1994)

Result for rotational anisotropy

- With myofiber direction $\vec{e}_f = \cos\alpha\vec{e}_x + \sin\alpha\vec{e}_y$,
  and total fiber rotation angle Θ over myocardial wall of thickness L:

$$\alpha(z) = \alpha_0 + \Theta.(z - L/2) \tag{16}$$

- From $D^{ij} = D_2\delta^{ij} + (D_1 - D_2)e_f^i e_f^j$, with $\alpha_0 = 0$, it follows that

$$(H^{ab}) = (\overline{D}^{ab}) = \begin{pmatrix} D_m + D_a\frac{\sin\Theta}{\Theta} & 0 \\ 0 & D_m - D_a\frac{\sin\Theta}{\Theta} \end{pmatrix} \tag{17}$$

$$1/H = \det(H^{ab}) = D_m^2 - D_a^2\frac{\sin^2\Theta}{\Theta^2} \tag{18}$$

where $D_m = (D_1 + D_2)/2$, $D_a = (D_1 - D_2)/2$.

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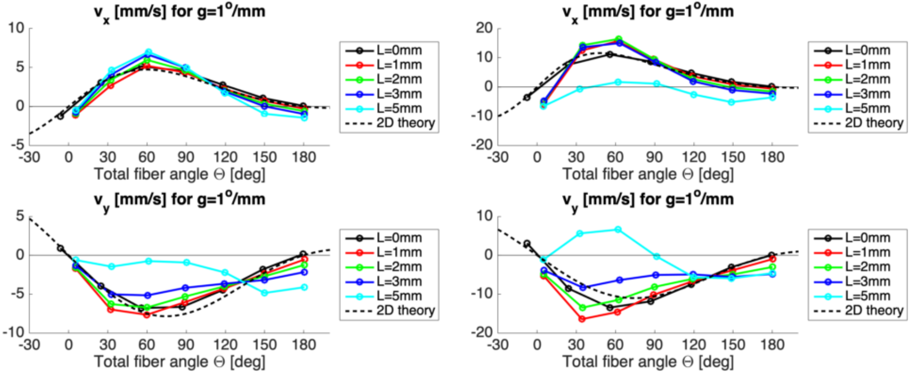
  where $D_m = (D_1 + D_2)/2$, $D_a = (D_1 - D_2)/2$.

- For $\gamma_1 > 0$, the scroll wants to minimize effective filament length:
  $\mathcal{L} \downarrow \Leftrightarrow\ 1/H \downarrow \Leftrightarrow\ \mathrm{sinc}^2\,\Theta \uparrow \Leftrightarrow\ |\Theta| \downarrow$ in $(0, \pi)$
  - For $\gamma_1 > 0$, spirals drift to region with smallest fiber rotation
  - For $\gamma_1 < 0$, spirals drift to region with largest fiber rotation

Comparison of 2D theory with 2D and 3D simulations

$(c_1/c_2)^2 = D_1/D_2 = 4$ $\qquad$ $(c_1/c_2)^2 = D_1/D_2 = 9$



- Aliev-Panfilov model $a = 0.15, k = 8, \epsilon = 0.002, \mu_1 = 0.2, \mu_2 = 0.3$
- Total fiber rotation angle $\Theta = \Theta(0) + gx$
- Good correspondence with theory for $L \leq 3$ mm, $g \leq 1^o$ /mm

What did we neglect?

- Recall that $D^{ab} = H^{ab} + \widetilde{D}^{ab}$; $\mathbf{u} = \bar{\mathbf{u}} + \widetilde{\mathbf{u}}$, so for constant V:

$$\overline{\partial_a(D^{ab}\partial_b \mathbf{u})} = \overline{\partial_a(H^{ab}\partial_b \bar{\mathbf{u}})} + \cancel{\overline{\partial_a(\widetilde{D}^{ab}\partial_b \bar{\mathbf{u}})}} + \cancel{\overline{\partial_a(H^{ab}\partial_b \widetilde{\mathbf{u}})}} + \color{red}{\overline{\partial_a(\widetilde{D}^{ab}\partial_b \widetilde{\mathbf{u}})}} \tag{19}$$

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- Varying anisotropy through the wall $\widetilde{D}^{ab}$ causes $\widetilde{\mathbf{u}}$ and interacts with it!
- Part of $\widetilde{\mathbf{u}}$ can be captured by dynamics of the scroll wave filament $[X(z,t), Y(z,t), \Phi(z,t)]$:

$$\widetilde{\mathbf{u}} = x^{\mu}\partial_{\mu}\mathbf{u}_0 + \widetilde{\mathbf{u}}_1 \tag{20}$$

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- What is the shape of the scroll wave core in a thin anisotropic slab?

Outline

Analytical solution for the scroll wave core (1/2)

For rotational anisotropy with fiber direction $\alpha(z)$ independent of x, y:

1. Rescale x,y such that $H^{ab} = \delta^{ab}$ such that

$$X^a = X_0^a(\Phi) + R_A^a(\Phi)x^A, \quad X^\phi = \Phi(t) + \phi(t), \quad \Phi(t) = \omega t \tag{21}$$

2. Take $\mathbf{u}(x, y, z, t) \approx \mathbf{u}_0(X^\mu(z, t), x, y) + \mathbf{u}_1 + \mathcal{O}(\epsilon^2)$
3. Keep leading order and project onto RFs to find:

$$\partial_t x^M - iM\omega x^M - P_N^M \partial_z^2 x^N = Q_{AB}^M \widetilde{D}^{AB}(\Phi, z) + \mathcal{O}(\epsilon^2) \tag{22}$$

where

$$P_N^M = \langle \mathbf{W}^M \mid \mathbf{P}\partial_N \mathbf{u}_0 \rangle, \qquad Q_{AB}^M = \langle \mathbf{W}^M \mid \mathbf{P}\partial_{AB}^2 \mathbf{u}_0 \rangle \tag{23}$$

4. Eq. (22) is a periodically driven linear PDE with known source

$$\widetilde{D}^{ab}(\Phi, z) = \sum_{k=1}^{\infty} \sum_{\ell=-2,0,2} D_{k,\ell}^{ab} \cos(kz) e^{i\ell\Phi} \tag{24}$$

Analytical solution for the scroll wave core (2/2)

5. Also write filament shape x^a in a double Fourier series:

$$x^a(\Phi, z) = \sum_{k=1}^{\infty} \sum_{\ell=-2,0,2} x^a_{k,\ell} \cos(kz) e^{i\ell\Phi} \tag{25}$$

6. Then, Fourier components for the shape of the scroll wave core are found from solving linear 3×3 systems, for $k \in \mathbb{N}$, $\ell \in \{-2, 0, 2\}$:

$$[i(\ell - M)\omega\delta^M_N + k^2 P^M_N] x^N_{k,\ell} = \sum_{\substack{a,b \in \{-1,1\} \\ a+b=\ell}} Q^M_{ab} D^{ab}_{k,\ell}. \tag{26}$$

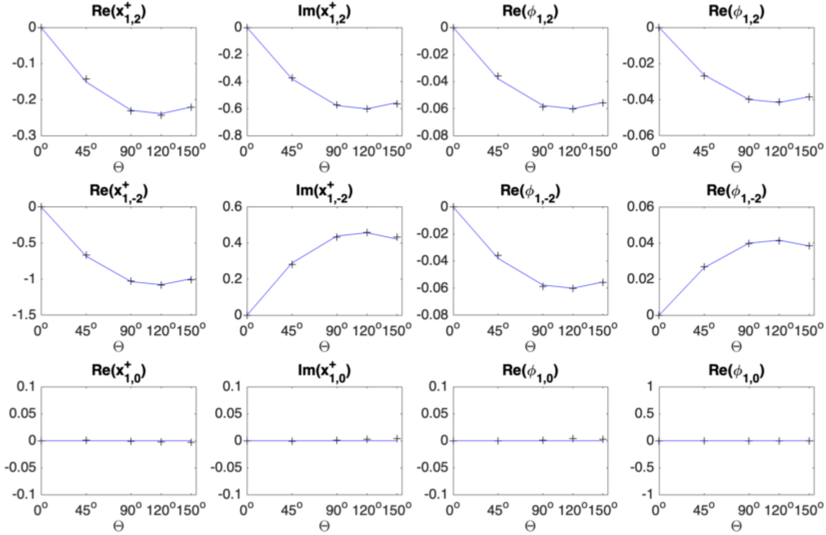
using the complex basis: if $Z^{\pm} = -(x \pm iy)$, then

$$\mathbf{W}^{\pm 1} = -(\mathbf{W}^x + i\mathbf{W}^y), \qquad \mathbf{V}_{\pm 1} = -\frac{1}{2}(\partial_x \mathbf{u}_0 - i\partial_y \mathbf{u}_0)$$

$$D^{++} = (D^{xx} - D^{yy}) + 2iD^{xy}, \qquad D^{+-} = D^{xx} + D^{yy}$$

Fit of core shape vs. anisotropy in Fourier space

We expect that $x^{\mu}_{k,a+b} \propto D^{ab}_k(\Theta)$ for given L:

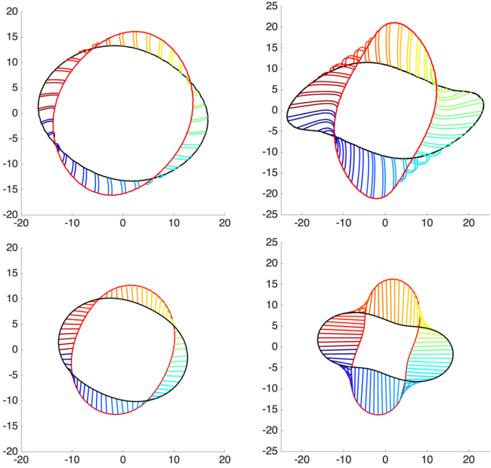


Fit of core shape vs. anisotropy

$L = 1cm$ $\quad D_1/D_2 = 4 \quad D_1/D_2 = 9$

Simulation

Theory



(theory includes only modes with $k = 0, 1$, $\ell = -2, 0, 2$)

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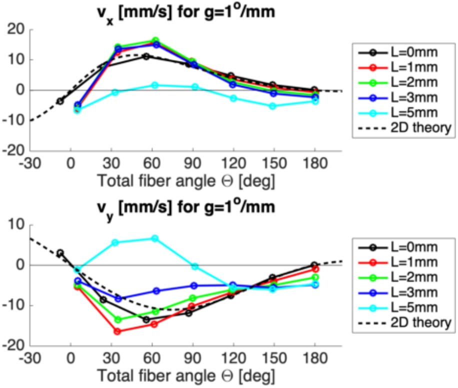
And finally: finite thickness corrections to rotor drift

Average the perturbation term over Φ and z:

$$
\begin{aligned}
V^c &= \frac{1}{2\pi}\oint d\Phi \langle \mathbf{W}^c \mid \mathbf{P}\overline{\partial_a(\widetilde{D}^{ab}\partial_b\widetilde{\mathbf{u}})}\rangle \\
&= \frac{1}{2\pi}\oint d\Phi \langle \mathbf{W}^c \mid \mathbf{P}\overline{\partial_a(\widetilde{D}^{ab}x^m\partial^2_{bm}\mathbf{u}_0)}\rangle \\
&= \frac{1}{2\pi}\oint d\Phi\, Q^c_{bm}(\Phi)\overline{F^b x^m}, \qquad\qquad \text{with } \partial_a D^{ab} = F^b \\
&= \sum_{k=1}^{\infty}\frac{1}{2\pi}\oint d\Phi\, Q^c_{bm}(\Phi)F^b_k x^m_k(\Phi) \\
&= \sum_{k=1}^{\infty}\sum_{b+m-c=\ell} Q^c_{bm}F^b_k x^m_{k,\ell} \\
&= \sum_{k=1}^{\infty}\sum_{b+m-c=\ell} Q^c_{bm}A^m_{nk}Q^n_{ad}D^{ad}_{k\ell}F^b_k \qquad \text{since } x^m_k = A^m_{kn}Q^n_{ad}D^{ad}_{kl}
\end{aligned}
$$

Finite thickness corrections to rotor drift in rotational anisotropy

$D_1/D_2 = 9$



Next steps:

- Predict cases from knowledge of P_n^m, Q_{nl}^m
- Quadratic theory to handle $L > 3$ mm
- Case of meander: $P_n^m(\Psi)$ where Ψ is phase of meander
- Detailed ionic models

Conclusions

If [decay length of spiral sensitivity] / [cardiac wall thickness] $\ll 1$:

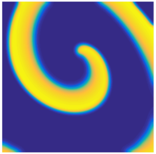
- Scroll wave 'sees' a surface with $H^{ab} = \overline{D}^{ab}$
- Leading order dynamics for circular-core spirals is

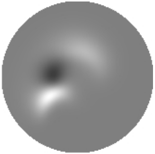
$$\dot{X}^a = - [\gamma_1 H^{ab} + \gamma_2 \frac{\epsilon^{ab}}{\sqrt{H}}]\partial_b \ln \mathcal{L} \qquad \text{Dierckx SIAM 2019}$$
$$- [q_1 H^{ab} + q_2 \frac{\epsilon^{ab}}{\sqrt{H}}]\partial_b \mathcal{R} \qquad \text{Dierckx et al. PRE 2013}$$

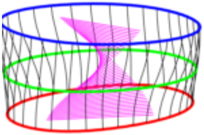
$\mathcal{R}$: Ricci scalar using metric H^{ab}

L: medium thickness or effective filament length, using metric D^{ab}

- Fourier series solution was found for the shape of the scroll wave core

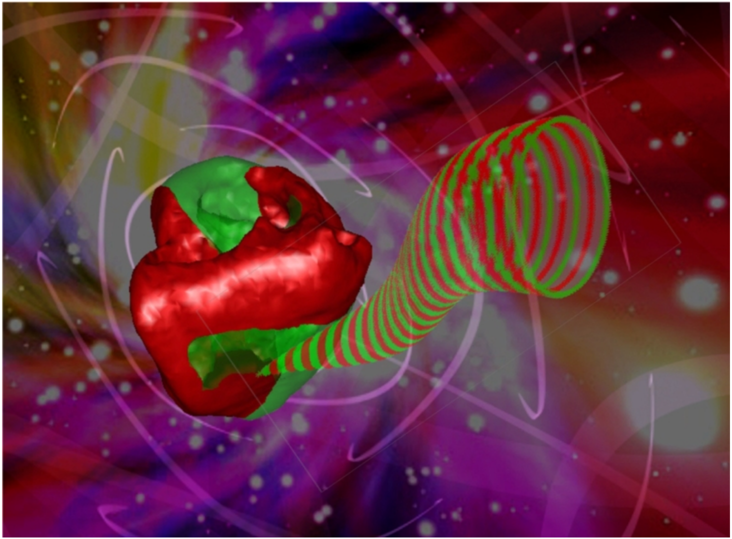




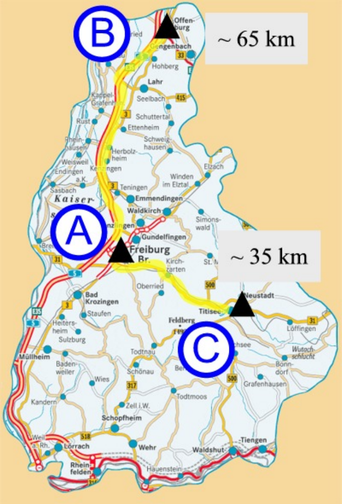


More talks from people in cardiac modeling:

- Tue 4pm, Superior A: Roman Grigoriev
  Discovery of High-order PDE models with latent variables
- Wed 9:15, Maybird: Shreya Segal
  Bifurcation Analysis of spiral waves
- Wed 5pm-6:40, Maybird: MS 156
  Lightning-fast interactive simulations of reaction-diffusion systems
  Abouzar Kaboudian, Shahriar Iravanian, Yanyan Ji, Hector Velasco Perez
- Thu 8:55am, Ballroom 2: Laura Munoz
  Prediction of Abnormal Cardiac Rhythms with a 1D Dynamical Model
- Thu 3:35pm, Ballroom 3: Philipp Kuegler
  Multiple Time Scale Analysis of Early Afterdepolarizations in Cardiac Action Potentials

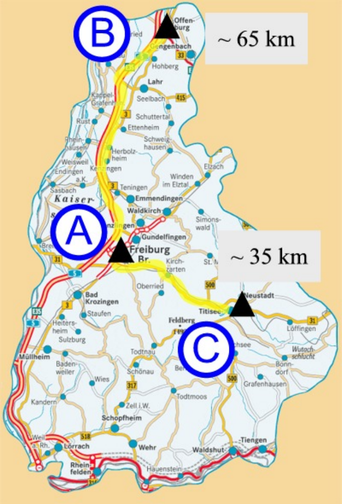


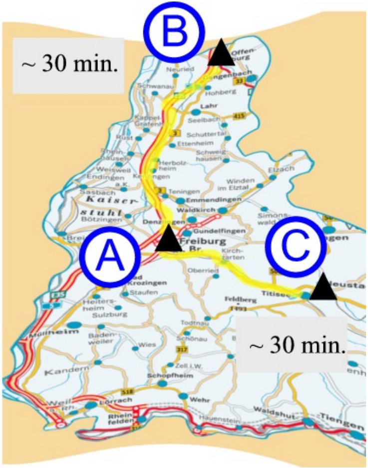
Is place C closer to A than B?



The road map analogy

Is place C closer to A than B?





Both B and C have the same travel time from A!