Modelling of thermally induced electrical instabilities in intestine using COMSOL Multiphysics

A. Gizzi, C. Cherubini, S. Migliori and S. Filippi
University "Campus Bio-Medico" of Rome.
Nonlinear Physics and Mathematical Modelling Lab.

Overview

Biological Problem
 Mathematical Model
 COMSOL Multiphysics Implementation
 Results

1.1 Paralytic lleus

Temporary intestine destabilization:

- impairment of the peristaltic motion
- 24 48 h following main abdominal surgeries
- Multyfactorial disorder:
 - mechanical stresses
 - anaesthesia drugs

steep temperature changes

1.1 Paralytic lleus

Temporary intestine destabilization:

- impairment of the peristaltic motion
- 24 48 h following main abdominal surgeries
- Multyfactorial disorder:
 - mechanical stresses
 - anaesthetic drugs
 - steep temperature changes

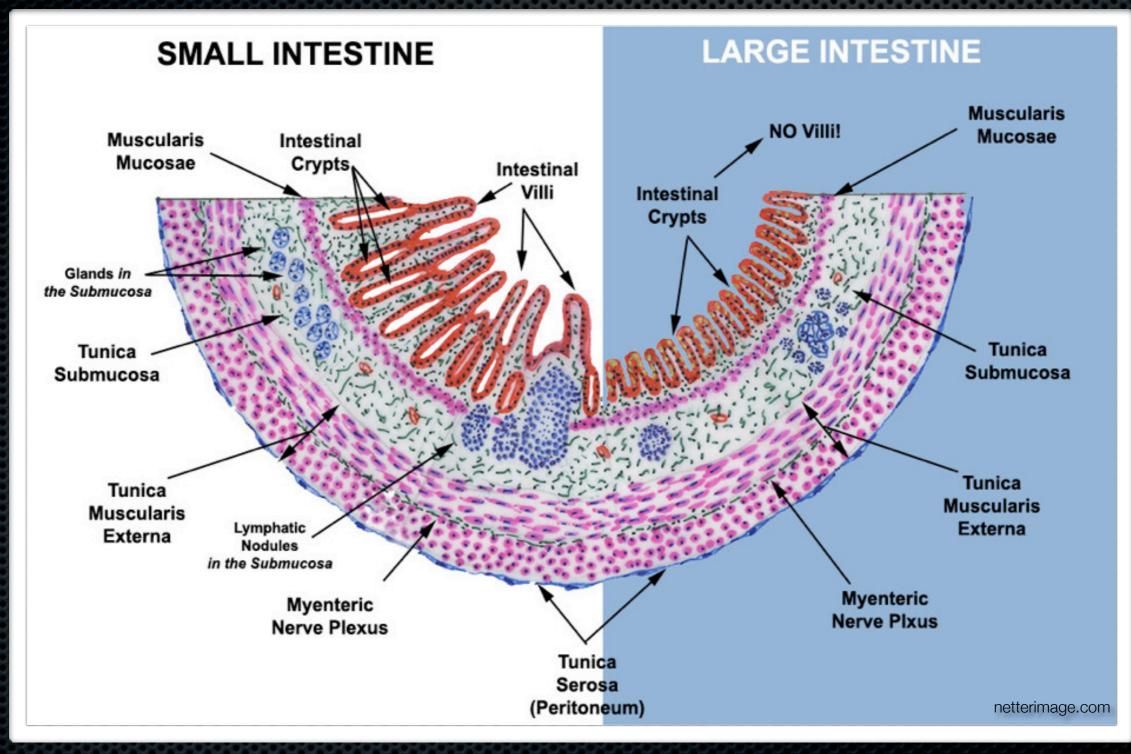
1.1 Paralytic lleus

Temporary intestine destabilization:

- impairment of the peristaltic motion
- 24 48 h following main abdominal surgeries
- Multyfactorial disorder:
 - mechanical stresses
 - anaesthesia drugs

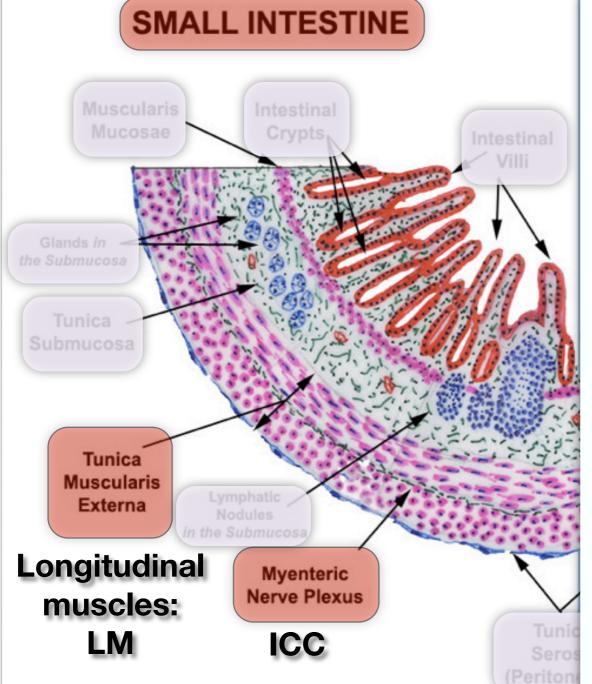
steep temperature changes

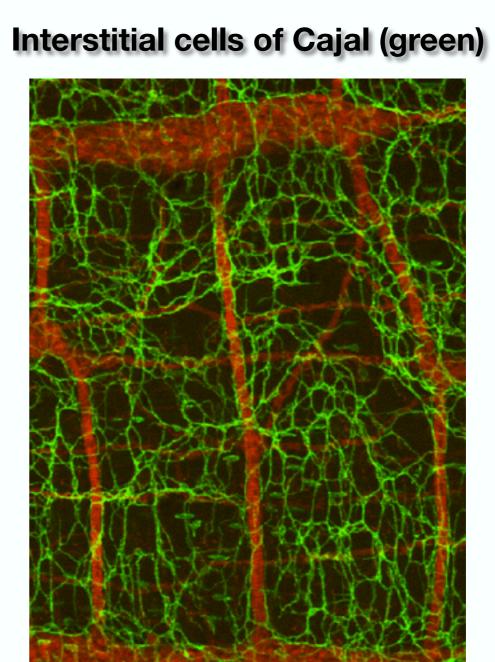
1.2 Intestine Tissue



Multilayered structure

1.3 Tissues Modelled





The Journal of Physiology October 1, 2009, 587 (19)

Multilayered structure

2.1 Math. Modelling

- **Excitable double layered structure: LM, ICC**
 - Physical distinct but Mathematical <u>coincident</u>
- Electric Aliev-Richards-Wikswo model
 - Pair of PDEs (4 eqs.)
 - FitzHugh-Nagumo scheme
 - Reaction-diffusion system
 - Homogeneous and Isotropic
- Multiphysical Bio-Thermal transport
 - thermo-ionic <u>feedback</u>

2.1 Math. Modelling

- Excitable <u>double</u> layered structure: LM, ICC
 - Physical distinct but Mathematical <u>coincident</u>
- Electric Aliev-Richards-Wikswo model
 - Pair of PDEs (4 eqs.)
 - FitzHugh-Nagumo scheme
 - Reaction-diffusion system
 - Homogeneous and Isotropic
- Multiphysical Bio-Thermal transport
 - thermo-ionic <u>feedback</u>

2.1 Math. Modelling

- **•** Excitable <u>double</u> layered structure: LM, ICC
 - Physical distinct but Mathematical <u>coincident</u>
- Electric Aliev-Richards-Wikswo model
 - Pair of PDEs (4 eqs.)
 - FitzHugh-Nagumo scheme
 - Reaction-diffusion system
 - Homogeneous and Isotropic
- Multiphysical Bio-Thermal transport (Pennes)
 - thermo-ionic <u>feedback</u>

2.2 Equations ARW-model

 $\begin{aligned} \partial_t U_l &= f\left(U_l\right) + D_l \Delta U_l - V_l + F_l\left(U_l, U_i\right) \\ \partial_t V_l &= Q_{10}\left(T\right)\zeta_l [\delta_l\left(U_l - \alpha_l\right) - V_l] \\ \partial_t U_i &= g\left(U_i\right) + D_i \Delta U_i - V_i + F_i\left(U_l, U_i\right) \\ \partial_t V_i &= Q_{10}\left(T\right)\zeta_i\left(z\right) [\delta_i\left(U_i - \alpha_i\right) - V_i] \end{aligned}$



ARW-model

 $\begin{aligned} \partial_t U_l &= f\left(U_l\right) + D_l \Delta U_l - V_l + F_l\left(U_l, U_i\right) \\ \partial_t V_l &= Q_{10}\left(T\right) \zeta_l [\delta_l \left(U_l - \alpha_l\right) - V_l] \\ \partial_t U_i &= g\left(U_i\right) + D_i \Delta U_i - V_i + F_i\left(U_l, U_i\right) \\ \partial_t V_i &= Q_{10}\left(T\right) \zeta_i\left(z\right) [\delta_i \left(U_i - \alpha_i\right) - V_i] \end{aligned}$



Transmembrane potentials

Slow currents

ARW-model

$$\begin{aligned} \partial_t U_l &= f\left(U_l\right) + D_l \Delta U_l - V_l + F_l\left(U_l, U_i\right) \\ \partial_t V_l &= Q_{10}\left(T\right) \zeta_l [\delta_l \left(U_l - \alpha_l\right) - V_l] \\ \partial_t U_i &= g\left(U_i\right) + D_i \Delta U_i - V_i + F_i\left(U_l, U_i\right) \\ \partial_t V_i &= Q_{10}\left(T\right) \zeta_i\left(z\right) [\delta_i \left(U_i - \alpha_i\right) - V_i] \end{aligned}$$

/: LM /: ICC

Nonlinear reaction functions

$$\begin{cases} f(U_l) = \gamma_l U_l (U_l - b_l) (1 - U_l) \\ F_l (U_l, U_i) = \mu_l D_{li} (U_l - U_i) \\ g(U_i) = \gamma_i U_i (U_i - b_i) (1 - U_i) \\ F_i (U_l, U_i) = \mu_i D_{il} (U_l - U_i). \end{cases}$$

ARW-model

$$\begin{aligned} \partial_t U_l &= f\left(U_l\right) + D_l \Delta U_l - V_l + F_l\left(U_l, U_i\right) \\ \partial_t V_l &= Q_{10}\left(T\right) \zeta_l [\delta_l \left(U_l - \alpha_l\right) - V_l] \\ \partial_t U_i &= g\left(U_i\right) + D_i \Delta U_i - V_i + F_i\left(U_l, U_i\right) \\ \partial_t V_i &= Q_{10}\left(T\right) \zeta_i\left(z\right) [\delta_i \left(U_i - \alpha_i\right) - V_i] \end{aligned}$$



Excitability parameter

 $\zeta_i(z) = 0.032 + 0.05 \exp\left(-\frac{z}{68}\right)$

/: LM

i: ICC

2.2 Equations

ARW-model

$$\begin{aligned} \partial_{t} U_{l} &= f\left(U_{l}\right) + D_{l} \Delta U_{l} - V_{l} + F_{l}\left(U_{l}, U_{i}\right) \\ \partial_{t} V_{l} &= Q_{10}\left(T\right) \zeta_{l} [\delta_{l}\left(U_{l} - \alpha_{l}\right) - V_{l}] \\ \partial_{t} U_{i} &= g\left(U_{i}\right) + D_{i} \Delta U_{i} - V_{i} + F_{i}\left(U_{l}, U_{i}\right) \\ \partial_{t} V_{i} &= Q_{10}\left(T\right) \zeta_{i}\left(z\right) [\delta_{i}\left(U_{i} - \alpha_{i}\right) - V_{i}] \end{aligned}$$

Pennes **bio-heat** equation

$$\partial_t T = \Gamma \Delta T + \Omega \left(T_a - T \right)$$

ARW-model

$$\begin{aligned} \partial_{t}U_{l} &= f\left(U_{l}\right) + D_{l}\Delta U_{l} - V_{l} + F_{l}\left(U_{l}, U_{i}\right) \\ \partial_{t}V_{l} &= Q_{10}\left(T\right)\zeta_{l}[\delta_{l}\left(U_{l} - \alpha_{l}\right) - V_{l}] \\ \partial_{t}U_{i} &= g\left(U_{i}\right) + D_{i}\Delta U_{i} - V_{i} + F_{i}\left(U_{l}, U_{i}\right) \\ \partial_{t}V_{i} &= Q_{10}\left(T\right)\zeta_{i}\left(z\right)\left[\delta_{i}\left(U_{i} - \alpha_{i}\right) - V_{i}\right] \end{aligned}$$

/: LM /: ICC

Pennes **bio-heat** equation

$$\partial_t T = \Gamma \Delta T + \Omega \left(T_a - T \right)$$

Isotropic thermal diffusion

Homogeneous perfusion

/: LM

i: ICC

2.2 Equations

$$\begin{aligned} \partial_{t}U_{l} &= f\left(U_{l}\right) + D_{l}\Delta U_{l} - V_{l} + F_{l}\left(U_{l}, U_{i}\right) \\ \partial_{t}V_{l} &= Q_{10}\left(T\right)\zeta_{l}[\delta_{l}\left(U_{l} - \alpha_{l}\right) - V_{l}] \\ \partial_{t}U_{i} &= g\left(U_{i}\right) + D_{i}\Delta U_{i} - V_{i} + F_{i}\left(U_{l}, U_{i}\right) \\ \partial_{t}V_{i} &= Q_{10}\left(T\right)\zeta_{i}\left(z\right)\left[\delta_{i}\left(U_{i} - \alpha_{i}\right) - V_{i}\right] \end{aligned}$$

Pennes **bio-heat** equation

> Thermo-ionic feedback

 $\partial_t T = \Gamma \Delta T + \Omega \left(T_a - T \right)$

 $P_{10} = B \exp\left[\left(T - T_a\right)/10^\circ C\right]$

3.0 Geometry Model

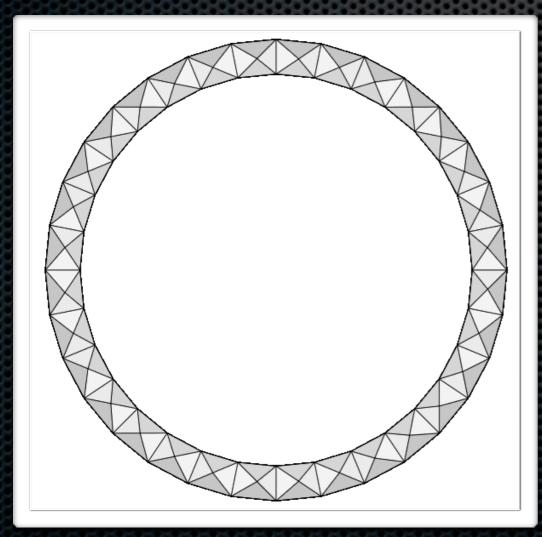
Cylindrical shape:

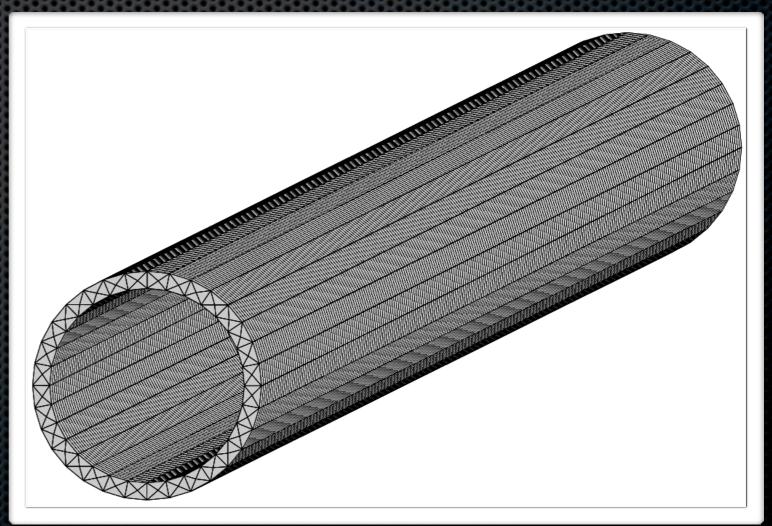
Ri = 1.7 cm Re= 2.0 cm L = 240.0 cm

Rectified small intestine geometry

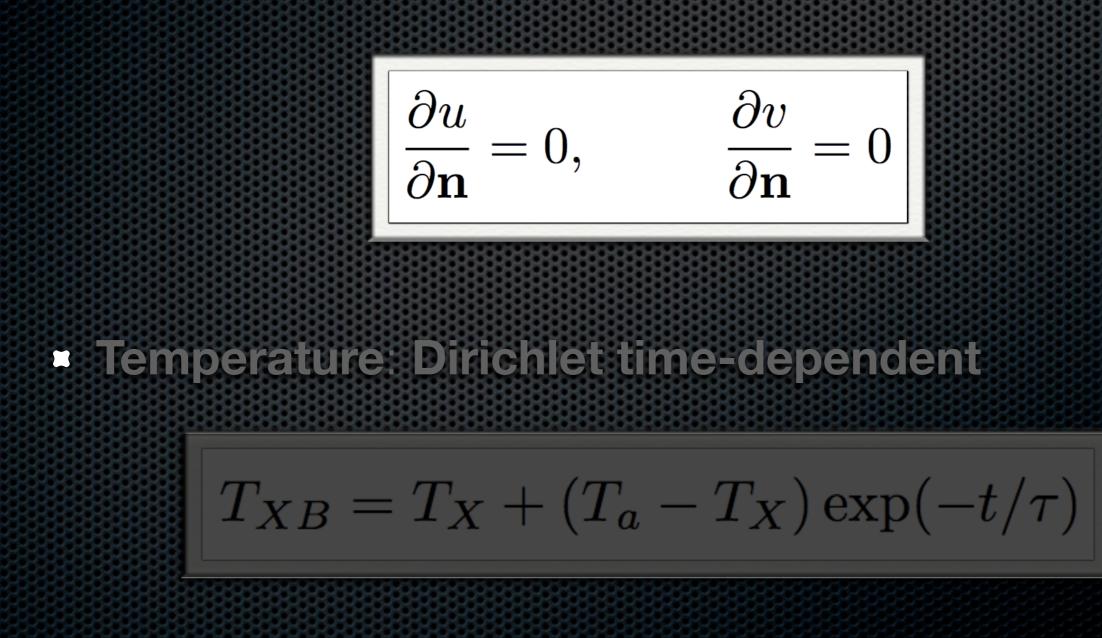
3.0 Geometry Model

Tetrahedral swept mesh: 3e4 Lagrange Quadratic El. - 8e5 d.o.f.





Electric variables: Neumann zero flux



Electric variables: Neumann zero flux

$$\frac{\partial u}{\partial \mathbf{n}} = 0, \qquad \frac{\partial v}{\partial \mathbf{n}} = 0$$

Temperature: Dirichlet time-dependent

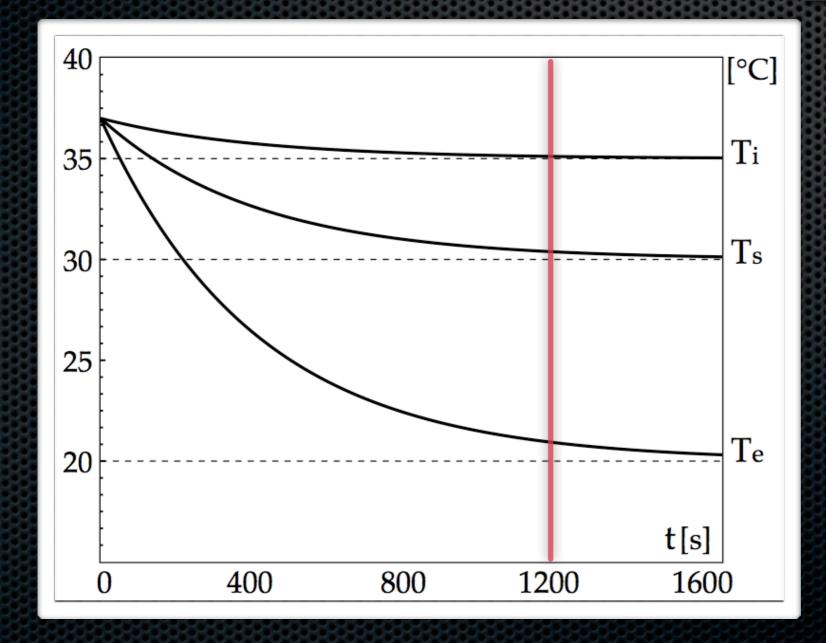
$$T_{XB} = T_X + (T_a - T_X) \exp(-t/\tau)$$

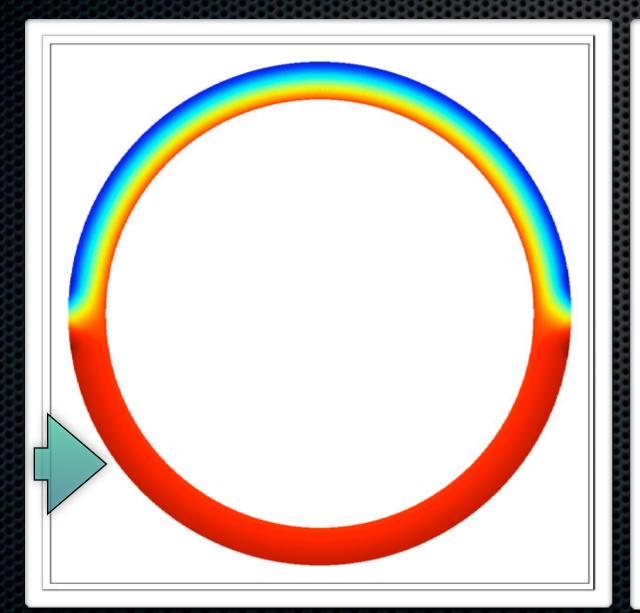
Three thermal punctual regions

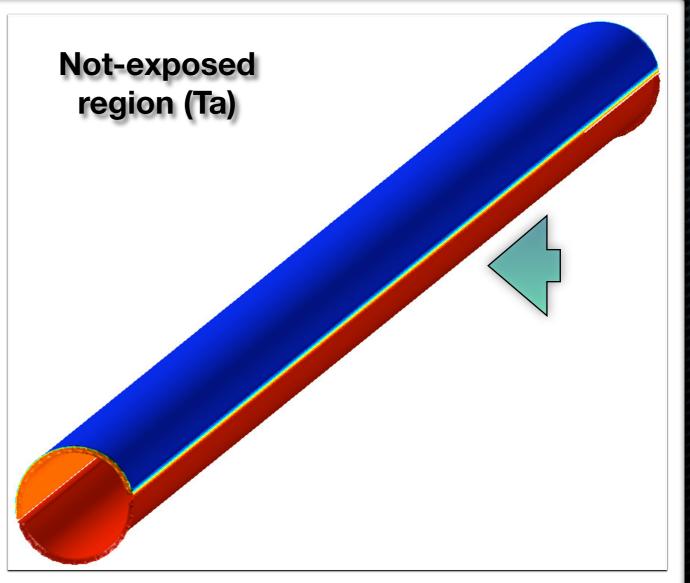
$$T_{XB} = T_X + (T_a - T_X) \exp(-t/\tau)$$

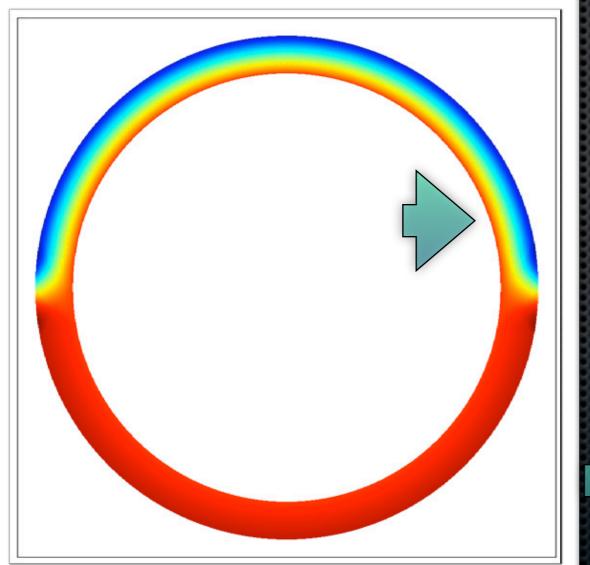
au

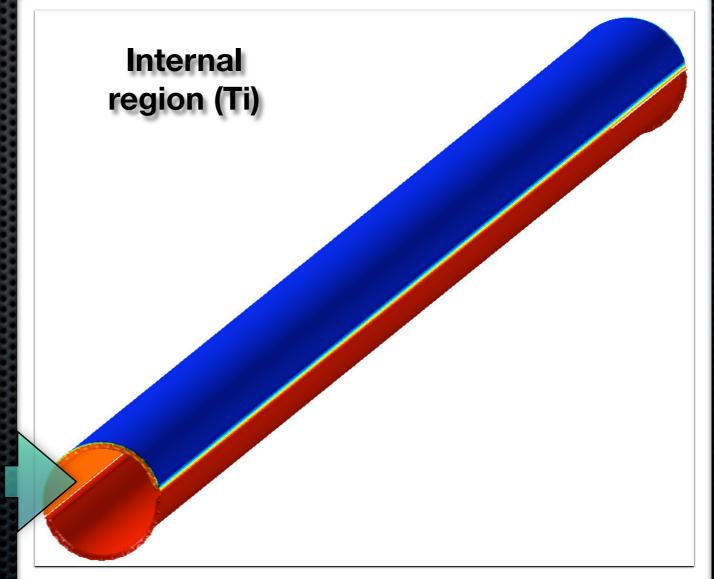
 $400 \, s$

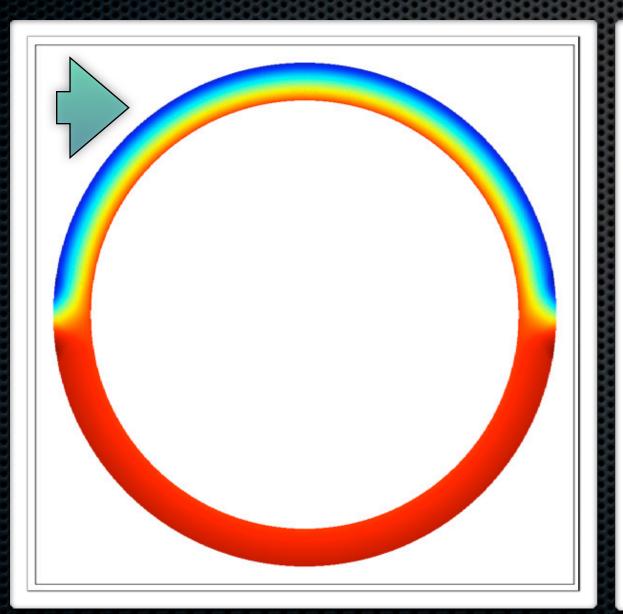


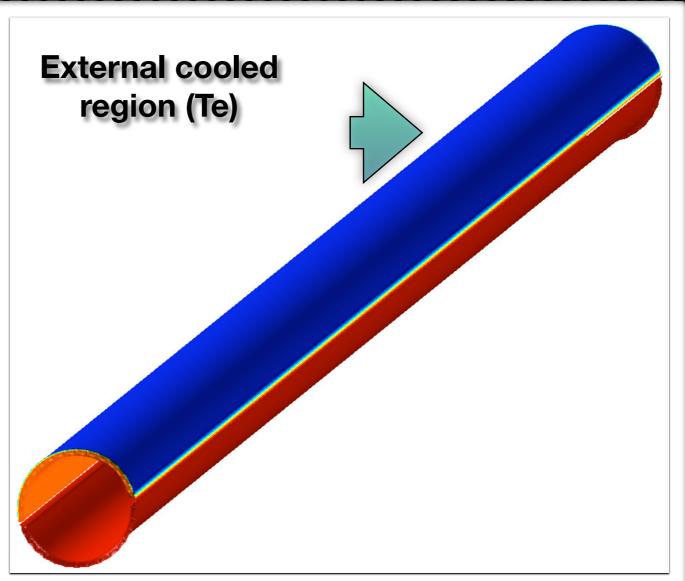


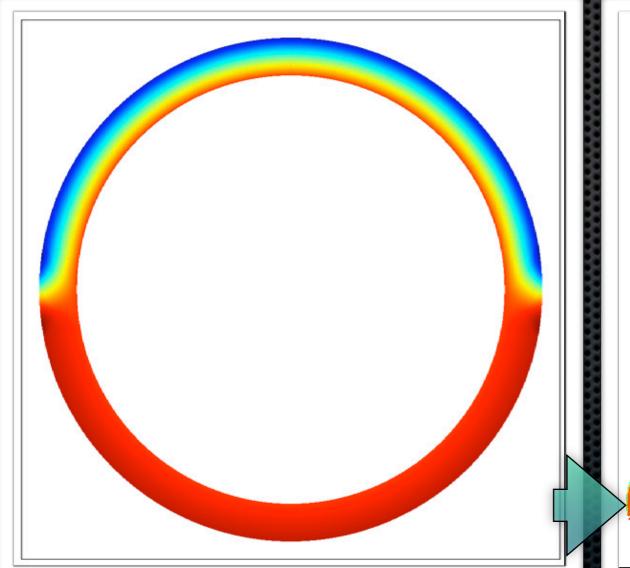


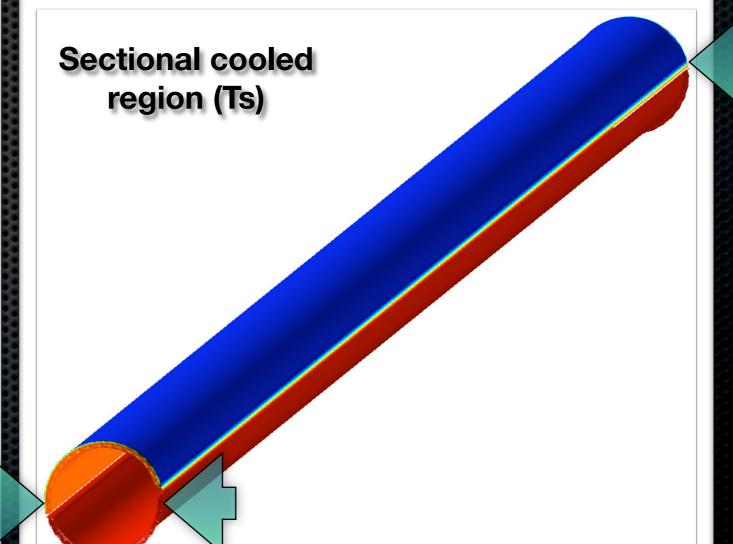












3.2 Initial Conditions

Constant-homogeneous conditions:

- auto-excitatory electric model
- boundary time-dependent thermal conditions
- Simulations
 - T = $3^{*}\tau$ = 1200 s (after electric stabilization)
 - Rel. Err. = 1e-4, Abs. Err. = 1e-5, Direct PARDISO

Electrical activity on normothermal tissue

Spikes

- Longitudinal propagation
- Phase break (space-dep excitability)

Nondimensional action potential map

Electrical activity on normothermal tissue

- Spikes
- Longitudinal propagation
- Phase break (space-dep excitability)

Nondimensional action potential map

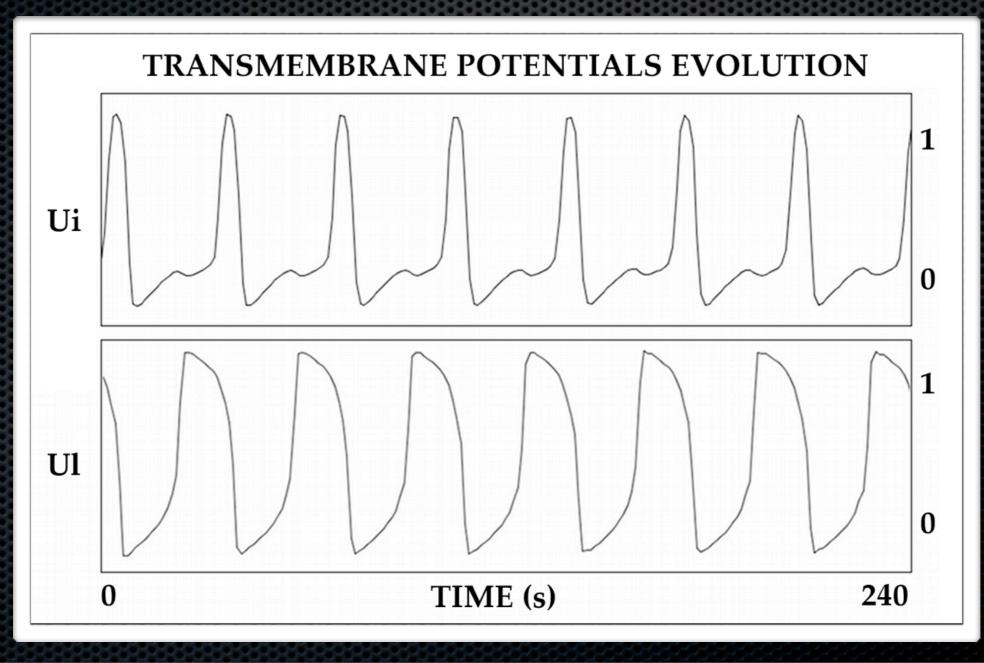
.....

Electrical activity on normothermal tissue

- Spikes
- Longitudinal propagation
- Phase break (space-dep excitability)

Nondimensional action potential map

Electrical action potential time evolution

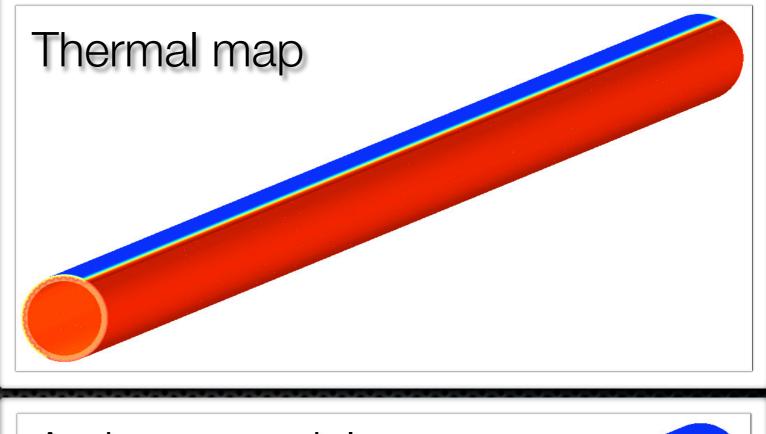


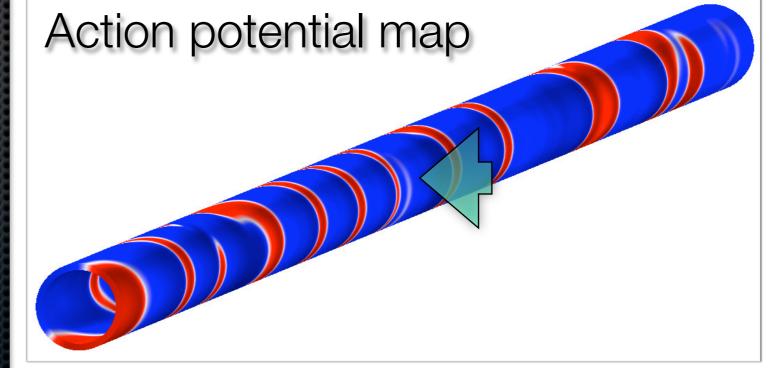
Thermal inhomogeneities induce electrical pertubations

Electrical instabilities

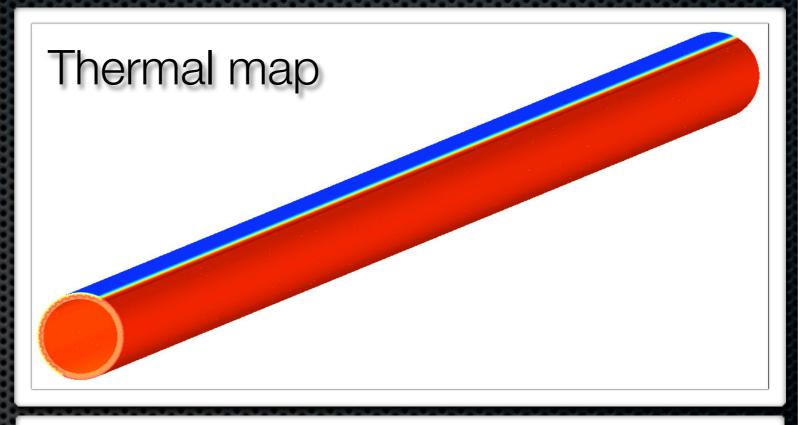
Distorted action potentials

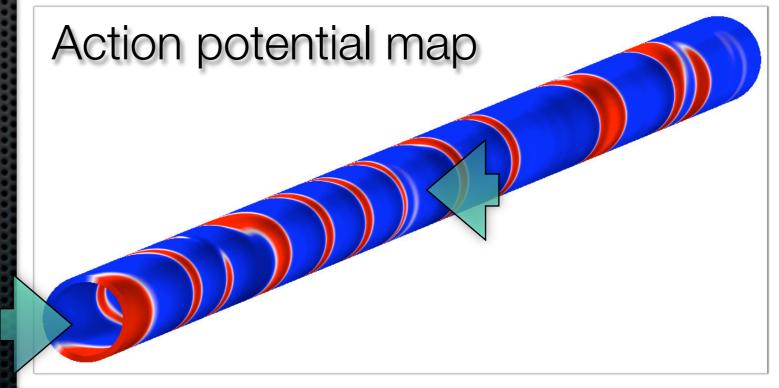
 Turbulent patterns and Spiralling behaviours



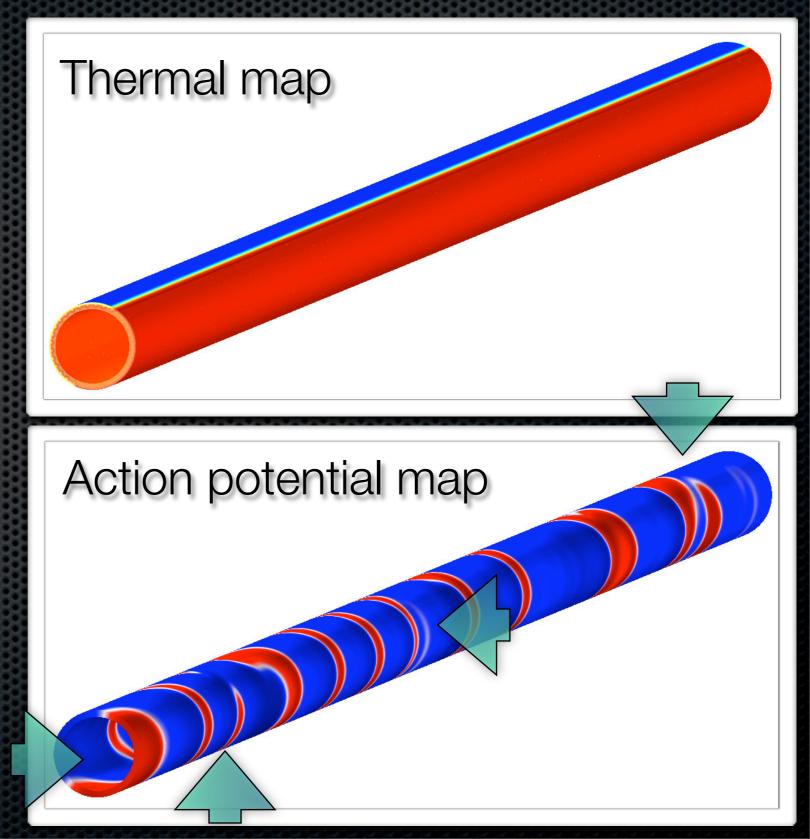


- Electrical instabilities
- Distorted action potentials
- Turbulent
 patterns
 and
 Spiralling
 behaviours



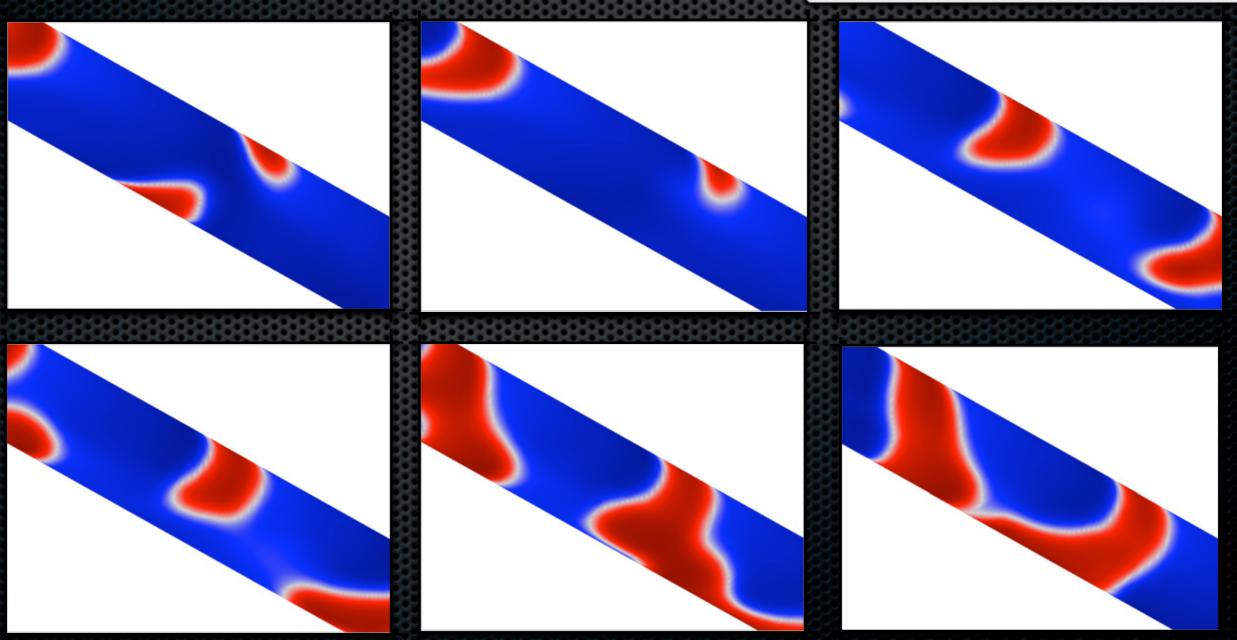


- Electrical instabilities
- Distorted action potentials
- Turbulent patterns and Spiralling behaviours



4.2 Results

Zoom...time series



Remark

Multiphysical implementation

New insight into biological problems

Thank you for your attention