On the identification of cavities in a nonlinear model arising from cardiac electrophysiology

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4. The stationary monodomain model
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Motivation

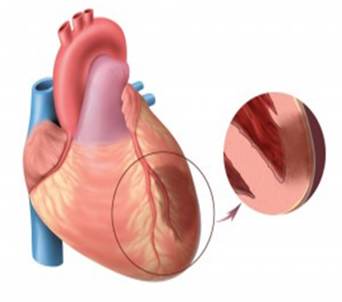
Main goal

Detecting heart ischemia, *at early stages* of their development from noninvasive measurements such as *body surface* (ECG) or unknown shape and/or position of ischemic areas from *intracardiac* (iECG) *measurements*

- Applications to medical imaging
- New and challenging inverse problems for nonlinear partial differential equations

Ischemic regions

- Ischemia: a region of the tissue not properly supplied with blood
- Effects: alterated electric properties of the cardiac tissue
- Outcomes: myocardial infarction, muscle damages, ventricular arrhythmia and fibrillation



Modelling heart ischemia

- The ischemic region is a non-excitable tissue that can be modeled as a conductivity inclusion with low conductivity
- The cardiac electrical activity can be described in terms of the monodomain model, consisting of a boundary value problem for a semilinear reaction-diffusion equation.

- Sundes-Lines-Cai-Nielsen-Mardal-Tveito, Computing the Electrical Activity in the Heart, Springer 2006
- Colli Franzone-Pavarino-Scacchi, Mathematical Cardiac Electrophysiology, Springer 2014

The monodomain model

$$\begin{aligned} u_t - \mathrm{div}(A_0 \nabla u) + I_{ion}(u) = 0 &\quad \text{in } \Omega \times (0,T) \\ (A_0 \nabla u) \cdot \mathbf{n} = 0 &\quad \text{on } \partial\Omega \times (0,T) \\ u(\cdot, 0) = u_0 &\quad \text{in } \Omega \end{aligned}$$

u *transmembrane potential*

$I_{ion} = Ku(u - u_1)(u - u_2)$ *ionic current* at a cellular level

A_0 is a Lipschitz continuous anisotropic tensor (conductivity)

u_0 *electrical stimulus*

In the presence of an ischemic region: $D \subset \Omega$

Altered conductivity tensor

$$A_0(x) \leftarrow A_1(x)\chi_{\Omega \setminus D}(x) + A_0(x)\chi_D(x), \quad I_{ion}(u) \leftarrow I_{ion}(u)(1 - \chi_D)$$

Related work

Inverse problem

Assume that the transmembrane potential $u(D)$ can be measured on $\partial\Omega$ or on a part $\Gamma \subset \partial\Omega$. Can we then determine D?

- E.B., C. Cerutti, A. Manzoni, D. Pierotti "On a semilinear elliptic boundary value problem arising in cardiac electrophysiology" *M3AS*, 26 (2016) no 4, 645-670
- E. B., A. Manzoni and L. Ratti "A reconstruction algorithm based on topological gradient for an inverse problem related to a semilinear elliptic boundary value problem" *Inv. Probl.*, Vol 33 No. 3, (2017)
- E. B., C. Cavaterra, C. Cerutti, A. Manzoni, L. Ratti "On the inverse problem of locating small dimensions ischemias for the monodomain equation of cardiac electrophysiology: theoretical analysis and numerical reconstruction, *Inv. Probl.* 33 (2017)
- E. B., L. Ratti, M. Verani "A phase field approach for the interface reconstruction in a nonlinear elliptic problem arising from cardiac electrophysiology" *Comm. Math. Sci.*, 16 no. 7 (2018)
- E. B., C. Cavaterra, L. Ratti "On the determination of ischemic regions in the monodomain model of cardiac electrophysiology from boundary measurements" *Nonlinearity*, (2020)

Modelling an ischemic region as a cavity

- The ischemic region is a non-excitable tissue that can be modeled as an electrical insulator

  Lopez-Perez, Sebastian, Izquierdo, Ruiz, Bishop and Ferrero, Frontiers in Physiology, (2019)

- The cardiac electrical activity can be described in terms of the monodomain model, consisting of a boundary value problem for a semilinear reaction-diffusion equation.

A simplified model to start

We consider the steady-state monodomain problem

$$\begin{cases} -\text{div}(A_0(x)\nabla u) + I_{ion}(u) = f, & \text{in } \Omega \setminus D \\ \dfrac{\partial^{A_0} u}{\partial \mathbf{n}} = 0, & \text{on } \partial\Omega \cup \partial D \end{cases} \tag{1}$$

$I_{ion}(u) = u^3$

f initial electrical stimulus

Main a-priori assumptions

1. *On the reference medium*: $\partial\Omega \in C^{0,1}$ (of Lipschitz class),
2. *On the unknown cavity*: $D \in \mathcal{D}$ where

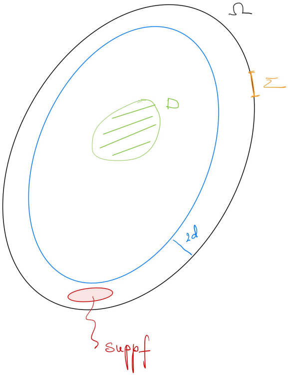
   $$\mathcal{D} = \{D \subset \overline{\Omega} : \text{compact, simply conn.}, D \in C^{0,1}, \text{dist}(D, \partial\Omega) \geq 2d_0\},$$

3. *On the data*:

   $$f \in L^\infty(\Omega),\ f \geq 0,\ \text{supp}(f) \subset \Omega_{d_0} = \{x \in \Omega : dist(x, \partial\Omega) \leq d_0\},$$

4. *On the conductivity tensor*: $A_0(x)$ uniformly elliptic, with Lipschitz entries.

Geometrical setting



Well-posedness of the forward problem

B.-Cerutti- Pierotti (2022)

Theorem (Existence and uniqueness for the forward problem)

For $f \in (H^1)'$ and $\Omega \setminus D$ Lipschitz the Neumann problem

$$\begin{cases} -\mathrm{div}(A_0(x)\nabla u) + u^3 = f, & \text{in } \Omega \setminus D \\ \dfrac{\partial^{A_0} u}{\partial \mathbf{n}} = 0, & \text{on } \partial\Omega \cup \partial D. \end{cases} \tag{2}$$

has a unique solution $u \in H^1(\Omega \setminus D)$ satisfying

$$\|u\|_{H^1(\Omega\setminus D)} \leq C(\|f\|_{(H^1)'} + \|f\|_{(H^1)'}^{1/3}) \tag{3}$$

where the constant $C = \max\{\frac{1}{\lambda}, |\Omega \setminus D|^{1/3}\}$ and $(H^1)' = H^1(\Omega \setminus D)'$.

A key estimate

Theorem

Let $f \in L^2(\Omega \setminus D)$. Then the solution u of the Neumann problem satisfies

$$\left(ess\ \inf f\right)^{1/3} \leq u(x) \leq \left(ess\ \sup f\right)^{1/3} \qquad \text{a.e.} \quad x \in \Omega \setminus D\,.$$

Remark

This estimate allows to extend the well-posedness of the direct problem to a more general class of cavities with finite perimeter by an approximation procedure and to prove continuity of solutions with respect to perturbations of the domain D.

The inverse problem

Assume we have a single measurement of the potential u on some open arc $\Sigma \subset \partial\Omega$, Σ is it possible to uniquely determine D?

Theorem (B., Cerutti, Pierotti, 2021)

Let f $D_1, D_2 \in \mathcal{D}$ satisfy the previous a-priori assumptions and let u_1 and u_2 be solutions to the above problem respectively with $D = D_1$ and $D = D_2$. Moreover let $u_1\big|_\Sigma = u_2\big|_\Sigma$. Then $D_1 \equiv D_2$.

Proof of uniqueness

Let us argue by contradiction. Assume $D_1 \neq D_2$ and let $w = u_1 - u_2$. Then

$$w\big|_{\Sigma} = 0 \qquad \text{and} \qquad \frac{\partial^{A_0} w}{\partial \mathbf{n}}\bigg|_{\Sigma} = 0$$

Moreover, w is a solution to

$$-\operatorname{div}\left(A_0(x)\nabla w\right) + q(x)\, w = 0 \qquad \text{in } \Omega \setminus (D_1 \cup D_2)$$

where $q(x) = u_1^2 + u_1 u_2 + u_2^2$. From uniqueness for the Cauchy problem and the weak unique continuation property

$$w \equiv 0 \qquad \text{in} \qquad G$$

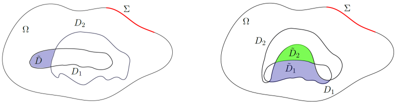
where G is the connected component of $\overline{\Omega} \setminus \big(D_1 \cup D_2\big)$ that contains Σ.

Proof of uniqueness cont.

Let $\tilde{G} = \Omega \setminus G$ and observe that:

$$\tilde{G} \supseteq D_1 \cup D_2, \quad \partial\tilde{G} = (\partial D_1 \cup \partial D_2) \cap \partial G.$$

Let $\tilde{D}$ be a connected component of $\tilde{G} \setminus D_2$.



We may assume that $\tilde{D}$ contains a subset of D_1 with nonempty interior, (if not just exchange the roles of D_1 and D_2). Then we have

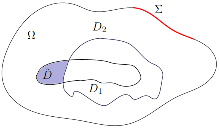
$$\partial\tilde{D} \subseteq \partial(\tilde{G} \setminus D_2) \subseteq \partial\tilde{G} \cup \partial D_2 \,. \tag{4}$$

Let us now define

Proof of uniqueness cont.

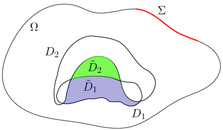
We have $\dfrac{\partial^{A_0} u_2}{\partial \mathbf{n}} = 0$ on $\partial\tilde{D}$ and $-\mathrm{div}\,(A_0(x)\nabla u_2) + u_2^3 = 0 \quad$ in $\tilde{D}$

$$\Downarrow$$



$u_2 \equiv 0$ on $\tilde{D}$ (uniqueness in the Neumann problem) and, by unique continuation, $u_2 \equiv 0$ in $G \setminus \overline{\mathrm{supp}\, f}$. Moreover if v solves the Schrödinger equation

$$-\mathrm{div}\,(A_0(x)\nabla v) + u_2^2 v = 0 \text{ in } K \supset \overline{\mathrm{supp} f}$$



$\Rightarrow \int_K f\, v = 0$. If v is such that $v\big|_{\partial K} = \alpha < 0$: then maximum principle implies that $v < 0$ in K and from $\displaystyle\int_K f\, v = 0$ with $f \geq 0$ we conclude that $f \equiv 0$ in K which contradicts the initial hypotheses.

Uniqueness

Remark

Uniqueness from one measurement extends also to the case where $D = \cup_{i=1}^{N} D_i$ *where* $D_i, i = 1, \ldots N$ *are separated simply connected compact Lipschitz sets.*

Conditional stability

- Under smoothness constraints on the unknown cavities we expect to derive the same weak rate of stability as for the linear conductivity equation

Alessandrini, B., Rosset, Vessella (2000)

$$d_H(\partial D_1, \partial D_2) \leq C \left| \log \left(\|u_1 - u_2\|_{L^2(\Sigma)} \right) \right|^{-\eta}, \; \eta \in (0,1)$$

$$d_H(C, D) = \max \left\{ \max_{x \in C} dist(x, D), \max_{x \in D} dist(x, C) \right\}$$

- For special geometries of D (e.g. circles, ellipses, polygons) Lipschitz stability should hold.

Reconstruction

B.-Cerutti-Pierotti-Ratti, 2022

Tikhonov regularization of the functional via a *perimeter penalization* term:

Regularization

$$\min_{D \in \mathcal{D}} J(D) : \; J(D) = \frac{1}{2} \int_{\Sigma} (u(D) - u_{meas})^2 d\sigma + \alpha \mathrm{Per(D)}$$

where

Continuity properties of solutions with respect to perturbations of D in the Hausdorff metric

$$\Downarrow$$

A minimum exists and is stable with respect to perturbations in the data.

Reconstruction algorithm

Bourdin and Chambolle, 2003 topological optimization

First step

We fill the cavity with a ficticious material of small conductivity

$$\min_{v \in X_{0,1}} J_\delta(v) : \; J_\delta(v) = \frac{1}{2}\int_\Sigma (u_\delta(v) - u_{meas})^2 d\sigma + \alpha \mathrm{TV}(v)$$

$$X_{0,1} = \{v \in BV(\Omega) : v(x) \equiv \chi_{\Omega \setminus D} \text{ a.e. in } \Omega \;, D \in \mathcal{D}\}$$

$u = u_\delta(v)$ is the variational solution to

$$\begin{cases} -\mathrm{div}(a_\delta(v)\nabla u) + vu^3 = f & \text{in } \Omega \\ \dfrac{\partial u}{\partial \mathbf{n}} = 0, \qquad \text{on } \partial\Omega, & \end{cases}$$

where $a_\delta(v) = \delta + (1-\delta)v$, $\delta << 1$.

Reconstruction algorithm

Second step

Introduce the *Modica-Mortola type functional* phase field approximation of the total variation

Proposed by several authors in the context of inverse problems:

- Rondi (2011) EIT detection of cracks and cavities
- Deckelnick-Elliott-Styles (2016) EIT: detection of conducitvity inclusions
- B.-Ratti-Verani, (2019) stationary monodomain model detection of conductivity inclusions
- Lam-Yousept (2020) nonlinear Maxwell equations
- Aspri-B.-Cavaterra-Rocca-Verani (2022) linear elasticity

Reconstruction algorithm

Phase field relaxation

$$\min_{v\in\mathcal{K}} J_{\delta,\varepsilon}(v)$$

$$\mathrm{J}_{\delta,\varepsilon}(v) = \frac{1}{2}\int_\Sigma (u_\delta(v) - u_{meas})^2 d\sigma + \alpha\int_\Omega \left(\gamma\varepsilon|\nabla v|^2 + \frac{\gamma}{\varepsilon}v(1-v)\right)$$

where $\mathcal{K} = \{v \in H^1(\Omega):\ 0 \leq v \leq 1,\ v = 1 \text{ a.e in } \Omega_{d_0}\}$.

Approximate solutions to the original minimization problem for J with minimizers for $J_{\delta,\varepsilon}$ with δ, ε small enough via Γ convergence arguments

Rigorous justification

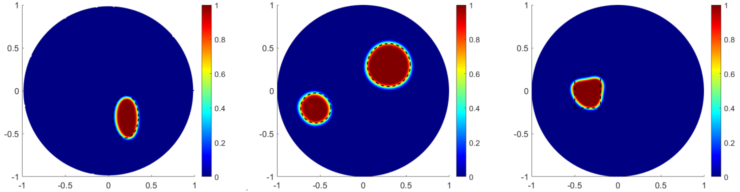
We can prove Γ-convergence restricting the minimization of $J_{\delta,\varepsilon}$ to a weakly closed, non-convex subset $\mathcal{K}_\eta$ of $\mathcal{K}$

$$\mathcal{K}_\eta = \{v \in \mathcal{K} : \{v \geq \eta\} = \Omega_D \text{ a. e. for some } D \in \mathcal{D}, \text{ for } \eta \in (0,1)\}$$

Γ convergence B., Cerutti, Pierotti, Ratti, 2022

1. $J_{\delta,\varepsilon} \xrightarrow{\Gamma} J_\delta$ as $\varepsilon \to 0$ for any $\delta > 0 \Rightarrow$ minima of $J_{\delta,\varepsilon}$ $v_{\delta,\varepsilon}$ converge in $L^1(\Omega)$ to a minimum v_δ of J_δ
2. $J_\delta \xrightarrow{\Gamma} J$ as $\delta \to 0 \Rightarrow$ minima v_δ converge in $L^1(\Omega)$ to a minimum $v = \chi_{\Omega\setminus D}$ of J for some $D \in \mathcal{D}$

Numerical results at a glimpse



Numerical evidence shows that it is possible to perform such a minimization on the whole convex set $\mathcal{K}$ and still have convergence to a conductivity satisfying the desired additional regularity.

Final remarks

- Fill the gap between the theoretical results and the numerical implementation
- Extension of the analysis of the inverse problem to time dependent monodomain model (work in progress in collaboration with Aspri, Francini, Pierotti, Vessella)

Final remarks

Extend the analysis of the inverse problem to the monodomain model possibly in dimension 3

$$
\begin{aligned}
u_t - \operatorname{div}(A_0 \nabla u) + f(u,w) = 0 &\quad \text{in } \Omega \times (0,T) \\
w_t + g(u,w) = 0 &\quad \text{in } \Omega \backslash D \times (0,T) \\
(A_0 \nabla u) \cdot \mathbf{n} = 0 &\quad \text{on } \partial\Omega \cup \partial D \times (0,T) \\
u(\cdot,0) = u_0 \quad w(\cdot,0) = w_0 &\quad \text{in } \Omega \backslash D
\end{aligned}
$$

where

$$
f(u,w) = Au(u-a)(u-1) + uw \qquad g(u,w) = \epsilon(Au(u-1-a) + w)
$$

w *concentration of ionic species*

u *transmembrane potential*

Thank you for your attention!

Numerical results

Extension of the algorithm allowing for the minimization of J:

1. generate synthetic data
   - create a domain Ω with a cavity D;
   - select N_f source functions $\{f_i\}_{i=1}^{N_f}$;
   - solve the forward problem to get $\{u_i|_\Sigma\}_{i=1}^{N_f}$;
   - add some random noise (noise level 2%);
2. select suitable values of $\alpha, \delta, \varepsilon$
3. minimize $J_{\delta,\varepsilon}$
   - choose an initial guess $v^{(0)} \in H^1(\Omega; [0,1])$ (e.g. $v^{(0)} = 0$);
   - update it by means of the gradient of $J_{\delta,\varepsilon}$ (requires the solution of the forward problem and an adjoint one for each iteration)
4. once a minimizer of $J_{\delta,\varepsilon}$ is reached, reduce the value of ε and δ

The numerical approximation of the forward and adjoint problems is performed by means of a Finite Element solver.