Estimating Local Apparent Conductivity with a 2-D Electrophysiological Model of the Heart

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Abstract. In this article we study the problem of estimating the parameters of a 2-D electrophysiological model of the heart from a set of temporal recordings of extracellular potentials. The chosen model is the reaction-diffusion model on the action potential proposed by Aliev and Panfilov. The strategy consists in building an error criterion based upon a comparison of depolarization times between the model and the measures. This error criterion is minimized in two steps : first a global and then a local adjustment of the model parameters. The feasibility of the approach is demonstrated on real measures on canine hearts, showing also the necessity to introduce anisotropy and probably a third spatial dimension in the model.

1 Introduction

Direct models of the electrical activity of the heart are numerous ([12,3,8]). Since *in vivo* measures are available([10,4,14]), a new challenge is to solve the inverse problem, that is to find the parameters of a model that best fit the measures obtained from a specific patient. Fitting a model on real measures is necessary for building a patient specific model suitable for diagnosis of electrical pathologies as well as for intervention planning.

When inspecting electrophysiological data, cardiologists often base their analysis on the depolarization and repolarization maps of the epicardium or endocardium ([14]). From those maps, expert eyes can detect different electrophysiological pathologies ranging from the presence of low conduction zones caused by infarcted tissue, to the occurrence of fibrillation caused by scrolling waves.

The aim of the research effort presented in this paper is to provide cardiologists with additional information for a better diagnosis and a better planning of therapies by finding the parameters of a cardiac electrophysiology model that can best explain electrophysiological observations (isochrones).

By inverting such a model, we can expect two important outcomes. First, we aim at estimating "hidden" physical parameters which help to better understand and quantify the heart physiology (conductivity for instance) from an original set of physical measurements (depolarization times). Second, with this set of

parameters, we can use the direct model to study pathologies, to plan and even simulate some therapeutic protocols.

In vivo electric measures on the endocardium or epicardium ([10,4]) consist in measuring of the extracellular potential, from which the depolarization times are computed. Very accurate models such as bidomain models ([6]) or Luo-Rudy models ([9]) provide excellent insight into the physiological phenomena provoking the electrical activity of the heart but are probably too sophisticated for our inverse problem. Indeed, these models are designed to capture very subtle modifications in the shape of the action potential whereas we only measure here the depolarization times. For this type of measures, a phenomenological model describing the action potential propagation is probably sufficient, such as the FitzHugh-Nagumo [5] model. Aliev and Panfilov developed a modified version suited to the cardiac action potential [1]:

$$\begin{aligned} \varepsilon^2 \partial_t u &= \varepsilon \mathrm{div}\left(D\nabla(u)\right) + ku(1-u)(u-a) - uz \quad (1.a) \\ \partial_t z &= -(ku(u-a-1)+z)) \quad (1.b) \end{aligned} \tag{1}$$

where u is a normalized action potential (between 0 and 1), z is a dynamic variable modeling the repolarization, k controls the repolarization, ε controls the coupling between the action potential and the repolarization variable z, and a controls the reaction phenomenon. The depolarization time of a point is computed as the first time such that $u(t) = 0.5$. A 3D anisotropic model based on the Aliev-Panfilov system was developed in the context of the ICEMA collaborative research action [2,15].

The electrophysiological measures are usually available on the endocardium or the epicardium, so as a first methodical and essential stage before going on to the 3D problem, we treat a simplified and tractable problem by considering a surface model. In this manner, we simulate the Aliev and Panfilov model on a surface triangulation $\mathcal{S}$ with N vertices and L triangles. We name $\mathcal{V}$ the set of vertices and $\mathcal{T}$ the set of the triangles. Hence, the tridimensional propagation is simplified to a propagation on the 2D surface of the epicardium. Furthermore, the fiber directions are not relevant in the 2D model since they are not tangential to the epicardial surface, and we consider an isotropic propagation i.e. $D = d\ \mathrm{diag}(1,1,1)$ in system (1), where the diffusion coefficient d is proportional to a conductivity. System (1) is normalized, the model is only 2D and the 3 parameters a, k and d all influence the depolarization times. Hence it is not possible to estimate an electrical conductivity from the depolarization times and we will call d the *apparent conductivity* in the sequal. The temporal integration of the system (1) is done with an explicit Euler scheme. The spatial integration is performed with the finite elements method with linear triangular elements. The numerical issues and the implementation are described in [11].

In this article we present results on the inversion of the Aliev-Panfilov electrophysiological model leading to a regional estimation of apparent conductivities. In Section 2, we first achieve a coarse global estimation of the parameter k that properly scales the electrical propagation. In Section 3, we perform the regional estimation of the *apparent conductivity* by minimizing an error function between

the measured and simulated depolarization times. In Section 4, a case study on dog hearts shows the efficiency of the presented approach for inverting the Aliev-Panfilov electrophysiological model. Finally in Section 5, we sum up this work and present its perspectives.

2 Global estimation of the parameter k

The parameter ε is chosen according to the grid size, and the parameters of the model a, k, or d can vary between different individuals or species. We choose to estimate the parameter k from the depolarization times while standard values are assigned to the other parameters.

As stated in [7], the velocity of the depolarization wave on a 1D domain can be expressed as follows

$$c = \sqrt{2kd}(0.5 - a) \tag{2}$$

In 2D, this velocity is not constant in space. At each point in the mesh, it is equal to the velocity in 1D (Equation (2)) minus a term proportional to the curvature of the front [7]. Since we only need a global estimate of the propagation velocity on a surface, we neglect, as a first approximation, the front curvature and simply approximate the velocity c of the depolarization wave by its expression in Equation (2).

Luckily, the depolarization velocity can also be computed from the gradient of the measured depolarization times on the surface, $\boldsymbol{\nabla}_x t : 1/c = \|\boldsymbol{\nabla}_{\mathbf{x}} t\|$. Then, we can estimate a median value of the parameter k over the whole mesh: $\text{median}\left(\|\boldsymbol{\nabla}_{\mathbf{x}} t\|\right)^{-1} = \sqrt{2kd}(0.5 - a)$.

A direct inversion of this equation would be a comparison between a theoretical 1D velocity and an apparent velocity computed on a 2D surface. As a consequence, we use a velocity estimated from a first guess simulation, that we computed on the same mesh as the one used for the measures. As the velocity c is proportional to $1/\sqrt{k}$, a ratio between measured c^m and simulated c^s propagation velocity can be computed as follows.

$$\frac{\text{median}\,\|\boldsymbol{\nabla}_{\mathbf{x}} t^m\|}{\text{median}\,\|\boldsymbol{\nabla}_{\mathbf{x}} t^s\|} = \frac{c^s}{c^m} \approx \frac{\sqrt{k^s}}{\sqrt{k^m}}. \tag{3}$$

The measured and the simulated depolarization times are denoted by t^m and t^s respectively. k^s is the value for the parameter k used to compute the first guess simulation and k^m is the value computed to adjust the measures. k^m can be computed as follows.

$$k^m = k^s \left(\frac{\text{median}\,\|\boldsymbol{\nabla}_{\mathbf{x}} t^s\|}{\text{median}\,\|\boldsymbol{\nabla}_{\mathbf{x}} t^m\|} \right)^2 \tag{4}$$

3 Local estimation of the electrical *apparent conductivity*

With a simulation globally fitting the measures, a local adjustment of the model is possible. We choose the *apparent conductivity* d as the spatially varying parameter. Indeed, we can give a clinical interpretation of its variation: a region

with a low *apparent conductivity* (AC) value is a region where the electrical wave does not propagate as fast as in the other regions and consequently may be pathological. The AC that we estimate cannot be compared to the electrical conductivity because we used normalized Aliev Panfilov equations. Moreover, we only estimate one parameter of the equation whereas the depolarization times also depend on a and k. Consequently, we detect variations of parameter d which are influenced by the other parameters.

Estimating the AC from patient specific data can be addressed as a data assimilation problem. None of the classical methods of data assimilation, like Kalman filtering and variational methods are truly suited for the model and the measures of our problem. Indeed, classical methods generally require an explicit functional relationship between the results of the model and the measures. Such a relationship is not available between action potentials and depolarization times since the depolarization time is an implicit function of the action potential.

In the discretized model ([11]), an AC value is assigned to each triangle. Consequently, we look for an AC map $(\mathbf{d}) = (d_j)_{0 \leq j \leq L-1}$, where L is the number of triangles in the triangulation. This AC map should minimize $C(\mathbf{d}) = \sum_{v \in \mathcal{V}} (t_v^m - t_v(d_0, \ldots, d_{L-1}))^2$ where $\mathcal{V}$ is the set of the vertices in the triangulation, t_v^m is the measured depolarization time at vertex v and $t_v(d_0, \ldots, d_{L-1})$ the depolarization time at vertex v resulting from a simulation with the conductivities $(d_0, \ldots, d_{L-1})$.

In order to have a robust estimation of the AC, we split the heart surface into different connected regions and estimate one AC value for each region. Let $(R_k)_{0 \leq k \leq K-1}$ be a partition of the surface in K regions. For each region R_k, $d_j = d_{R_k}$ for all j such that the j^{th} triangle of the surface belongs to R_k. Then, the new minimization problem is to find $(\mathbf{d}) = (d_{R_k})_{0 \leq k \leq K-1}$ that minimizes $C(\mathbf{d}) = \sum_{v \in \mathcal{V}} (t_v^m - t_v(d_{R_0}, \ldots, d_{R_{K-1}}))^2$

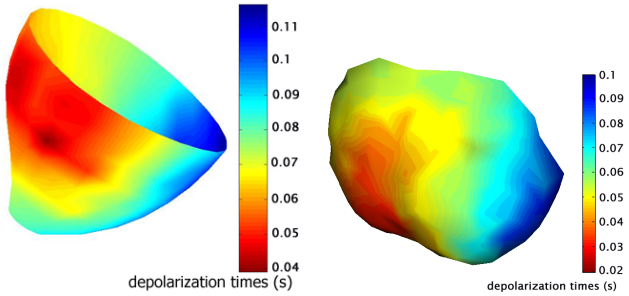
We look for the minimum of $C(\mathbf{d})$ with respect to K variables: $d_{R_0}, \ldots d_{R_{K-1}}$. Instead of using a generic method to solve for this multidimensional minimization, we consider the causality of the electrical wave propagation: the depolarization times in one region mostly depend on the apparent conductivities of the regions that were depolarized before. Hence, we estimate the AC for one region after the other, following the order of depolarization. During the estimation of d_R, the conductivities of the other regions remain constant.

We transform a K-dimensional minimization problem to K successive one-dimensional minimization problems:

$$C(d_R) = \sum_{v \in \mathcal{V}} (t_v^m - t_v(d_R))^2 \tag{5}$$

We simplify the criterion $C(\mathbf{d})$ by taking into account only the vertices of the region R because there are enough vertices in a region to provide a robust estimate. Equation (5) then yields $C(\mathbf{d}) = \sum_{v \in R} (t_v^m - t_v(d_R))^2$

The values of the function $\mathbf{t}(d_R)$ can only be computed after simulating the propagation. Therefore the derivative is computationally expensive to estimate. We favoured a minimization method that does not involve any derivative, an



(a) (b)

Fig. 1. Measured depolarization times. (a) Normal heart. (b) Case of an infarct on the anterior wall.

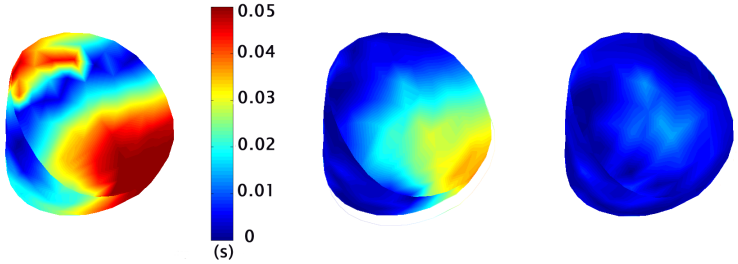
iterative inverse parabolic interpolation derived from the Brent method [13]. This very consistent method replaces the function to be minimized by a well-chosen parabola. The minimum of the function C is approximated by the easily and efficiently computed minimum of the parabola. Given three points on the curve $(d_a, C(d_a))$, $(d_b, C(d_b))$ and $(d_c, C(d_c))$, there is a unique parabola $f(x) = \alpha x^2 + \beta x + \gamma$ described by these points. It reaches its extremum at point x such that

$$x = d_b - \frac{1}{2}\frac{(d_b - d_a)^2(C(d_b) - C(d_c)) - (d_b - d_c)^2(C(d_b) - C(d_a))}{(d_b - d_a)(C(d_b) - C(d_c)) - (d_b - d_c)(C(d_b) - C(d_a))}. \quad (6)$$

From these remarks, we construct an iterative process which is a simplified version of Brent's method [13], to find the minimum from an initial bracketing of this minimum. We call a bracketing of the minimum of function C three points d_a, d_b and d_c such that $d_a < d_b < d_c$, $C(d_b) < C(d_a)$ and $C(d_b) < C(d_c)$. We repeat the parabolic estimation until we are satisfied with the computed value: if (d^k) is the sequence of successively estimated minima, we consider that convergence is reached when the difference between two successive estimations is smaller than a given precision value p i.e. $|d^{k+1} - d^k| < p$.

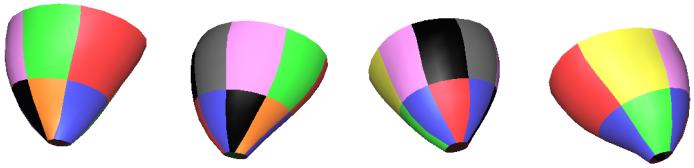
4 Results on *in vivo* measures

The *in vivo* measures used in this section were acquired on adult male mongrel dogs using a multi-electrode epicardial sock during an artificial pacing on the right ventricle. The surgery, experimental layout and the data acquisition are described in [11,15]. In this paper, we present two cases. The first case which is a normal heart, will be used to describe the procedure (Figure 1.a). The depolarization times were computed from a recording of electrical potentials on 128 electrodes and interpolated on a 192 vertices surface mesh. The second case is that of a heart with an anterior wall infarct (Figure 1.b). The depolarization times were computed from a recording of electrical potentials on 247 electrodes.



(a) (b) (c)

Fig. 2. Absolute error on the depolarization times between measures and simulations before (a) and after (b) the global automatic estimation and after the local estimation (c).



(a) (b) (c) (d)

Fig. 3. The regions chosen on the epicardium, according to the propagation of the depolarization wave. The large red region contains the pacing site.

The first step toward a parameter estimation is a good initialization since the propagation is very sensitive to the localization of the pacing regions. We thus selected from the measures (Figure 1) the points with the smallest depolarization times to initialize the propagation.

4.1 Global estimation of the parameter k

Applying the method presented in Section 2 to the data of the normal heart, we obtained a global value of $k^m = 25.2$ starting from a crude initialization $k^s = 8$.

The absolute error between the simulated depolarization and the measured depolarization times before the automatic estimation of k is presented on Figure 2.a. After this estimation, the error is significantly lower as shown on Figure 2.b. Before the estimation , the mean error was 20.6 ms. After the automatic estimation, the mean error was 10 ms compared to the total duration of the depolarization wave which lasts around 120 ms.

4.2 Local estimation of the *apparent conductivity*

We now apply the presented method to perform the local estimation of the *apparent conductivity* (AC). We first need to partition the epicardium into different

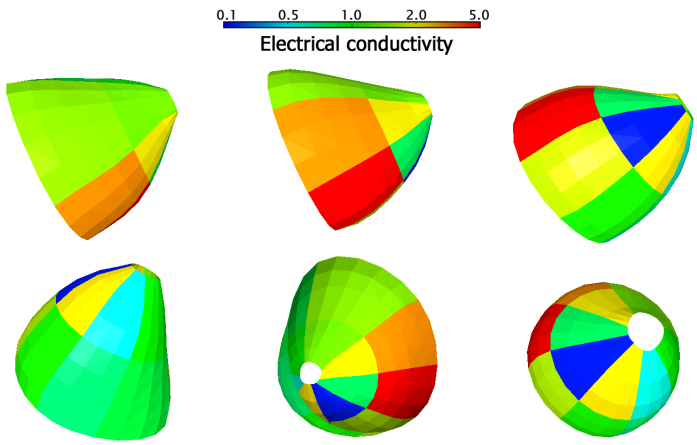
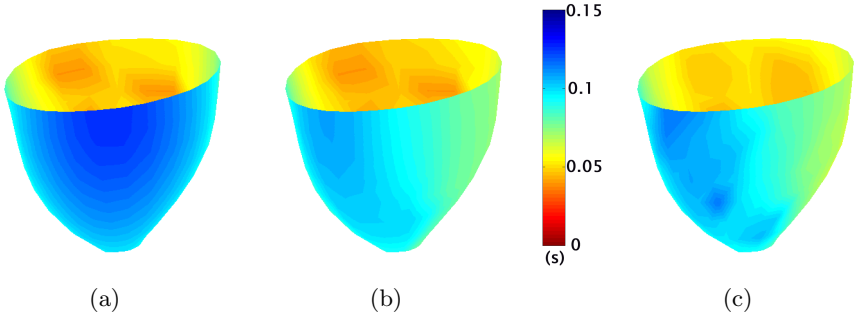


Fig. 4. *Apparent conductivity* map estimated from the first set of data.

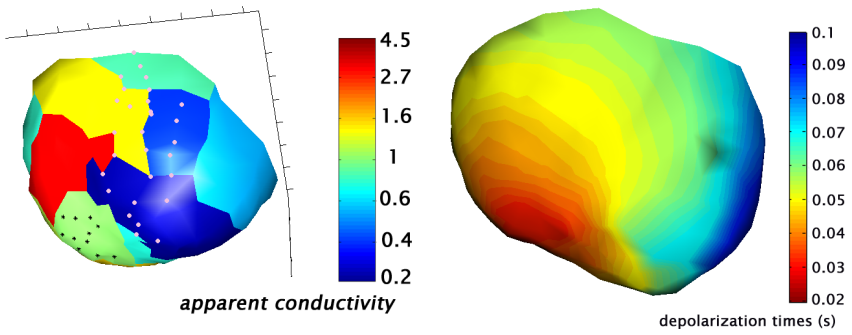


(a) (b) (c)

Fig. 5. Depolarization times before (a) and after (b) the local estimation compared with the measures (c). The absolute error on the depolarization times after the local estimation of the parameters is displayed Figure 2.c.

regions. We create a partition of the epicardium according to the electrical propagation. In this way, this partition is adapted to the particular artificial pacing of this experiment. In practice, we split the epicardium in successive regions following the isochrones of the depolarization times map as closely as allowed by the mesh resolution, and we then split these regions orthogonally to the isochrones. Figure 3 show a partition in 14 regions. We sort out the regions of Figure 3 in the order of their depolarization.

We then estimate one AC value for each region successively. The convergence on each region is quick and stable. Figure 4 presents the AC map that we obtain for the case of the normal heart.



(a) (b)

Fig. 6. AC estimated for the case of the anterior infarct (a). The points marked with a bright circle design the localization of the infarct. The points marked with a dark star design the pacing region. Depolarization times computed with these AC values (b).

4.3 Discussion

Although the variations of the computed AC for the normal heart do not have a physiological meaning, they closely reflect the asymmetry of the measures. These variations are probably due to the modeling of the epicardium as an homogeneous medium, without distinguishing the left and right ventricles nor taking into account the fibers direction.

Figure 5 displays the depolarization times simulated by the model before (5.a) and after (5.b) the local estimation of the AC, and compare them to the measures (Figure 5.c). The depolarization times computed with a constant AC are in the proper range of values, but from Figure 5, when comparing these results with the measures (5.c), we notice that the shape of the depolarization front is much closer to the measures with the local adjustment.

The quality of this estimation is also assessed by the visualization of the absolute error (Figure 2.c) on the depolarization times in the epicardial surface. We can see on Figure 2 that the absolute error decreased significantly after both the global and the local estimation.

We also applied the AC estimation method on the case of an infarct on the anterior wall. The AC values are displayed on Figure 6.a, the purple circles correpond to the infarcted region. The depolarization times computed from a simulation taking into account these values are displayed on Figure 6.b. In the infarcted region, the shape of this depolarization front reproduces the shape of the measured depolarization front (Figure 1.b).

A large portion of the infarct is detected in the two regions with the lowest conductivity values, but we see that a part of the infarct is not detected as a low conductivity region. The heterogeneous infarct geometry in the heart wall can explain this observation: the infarct can be transmural (i.e. extending from

the inner surface to the outer surface) or non-transmural (i.e. extending from the inner surface to somewhere in the wall), and when considering vertices in the mesh, where the infarct is non-transmural, electrical conductivity can be almost normal. In addition, a low conductivity is estimated in normal regions. As seen in the first case, this may be due to the modeling of the epicardium as an homogeneous medium. We are currently working on the inclusion of the fiber directions in this model.

5 Conclusions and perspectives

We addressed the problem of estimating a set of parameters for the action potential propagation modeled by Aliev and Panfilov from measured depolarization times. In order to evaluate the quality of our results, we used a criterion based on the difference in depolarization times between the model and the measures. We first presented a procedure to globally estimate a set of parameters so that the electrical propagation in the model occurs in the same time and space scale as the measures. We then presented a method to locally estimate the electrical *apparent conductivity* (AC) region by region. We successfully estimated global and local parameters of the model from *in vivo* measures of a canine heart. The simulation of the model with these new values showed that the error on the depolarization times was significantly decreased. Moreover, the variations of the AC values that we computed are consistent with the measures. When this method was applied to an infarcted heart, a large part of the infarcted region was assigned a low AC value.

In order to have a fully automatic process, we still need to build automatically the epicardium's partition. The next step will be to estimate the parameters of a 3D model of the heart by establishing a correspondence between 2D measures and a 3D mesh. A proper physiological validation would require the application of our method to a benchmark of pathological and normal measures analyzed by experts. At that time, only the AC is estimated, but other measures, as the action potential duration, would allow us to estimate more parameters. An advantage of the proposed local estimation is that it is not dependent on the model since it only uses simulations of the direct model. Thus, it can easily be adapted to more complex models that can reproduce specific pathologies.

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[1] http://www-rocq.inria.fr/sosso/icema2/icema2.html

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