From Body Surface Potential to Activation Maps on the Atria: a Machine Learning Technique

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Abstract

The treatment of atrial fibrillation has greatly changed in the past decade. Ablation therapy, in particular pulmonary vein ablation, has quickly evolved. However, the sites of the trigger remain very difficult to localize. In this study we propose a machine-learning method able to non-invasively estimate a single site trigger. The machine learning technique is based on a kernel ridge regression algorithm. In this study the method is tested on a simulated data. We use the monodomain model in order to simulate the electrical activation in the atria. The ECGs are computed on the body surface by solving the Laplace equation in the torso.

1. Introduction

The inverse problem in cardiac electrophysiology also known as electrocardiography imaging (ECGI) is a new and a powerful diagnosis technique. It allows the reconstruction of the electrical potential on the heart surface from electrical potentials measured on the body surface. This non-invasive technology and other similar techniques like the electroencephalography imaging interest more and more medical industries. The success of these technology would be considered as a breakthrough in the cardiac and brain diagnosis. However, in many cases the quality of reconstructed electrical potential is not sufficiently accurate. The difficulty comes from the fact that the inverse problem in cardiac electrophysiology is well known as a mathematically ill-posed problem. Different methods based on Thikhnov regularization [1] have been used in order to regularize the problem, but still the reconstructed electrical potential is not sufficiently satisfactory. In this study we present a machine learning method based on Reproducing Kernel Hilbert Space (RKHS) [2]. The idea is to learn on a data base of body surface potentials (BSPs) and their correspondent electrograms (EMGs) in order to construct a metamodel. This is called the "learning phase". Afterwards the evaluation of the metamodel on a new BSP provides a statical guess of the correspondant heart potential (EGM). This second phase is called the "reconstruction phase".

2. Methods

In the present work the data base used for the learning phase is made of a set of couples (BSPs,EGMs) provided by our ECG simulator. In paragraph 2.1, we present the mathematical models and methods used in order to simulate the electrical potential on the atria and its correspondent BSP. In paragraph 2.2, we present the machine learning method solving the inverse problem.

2.1. Forward problem

The bidomain model is considered as the state-of-the art model describing the electrical wave propagation inside the heart [3]. Less complex and easier to solve is the monodomain model. It has been shown that the modomain model is a good approximation of the bidomain model [3, 4]. The monodomain model is a reaction-diffusion equation coupled to an ordinary differential equations system,

$$\begin{cases} A_{\rm m}\big(C_{\rm m}\partial_t v_{\rm m} + I_{\rm ion}(v_{\rm m},w)\big) - \operatorname{div}(\boldsymbol{\sigma}_{\rm m}\boldsymbol{\nabla} v_{\rm m}) = I_{\rm stim}, \\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad \text{in } \Omega_{\rm H}, \\ \boldsymbol{\sigma}_{\rm m}\boldsymbol{\nabla} v_{\rm m}.\boldsymbol{n}_{\rm H} = 0, \text{ on } \Sigma. \\ \partial_t \boldsymbol{w} + \boldsymbol{g}(v_{\rm m},\boldsymbol{w}) = 0, \text{ in } \Omega_{\rm H}. \\ v_{\rm m}(0,.) = v_0, \text{ and } \boldsymbol{w}(0,.) = \boldsymbol{w}_0 \text{ in } \Omega_{\rm H}. \end{cases} \tag{1}$$

where $v_{\rm m}$ is the transmembrane potential.Constants $A_{\rm m}$ and $C_{\rm m}$ represent the rate of membrane surface per unit of volume and the membrane capacitance, respectively. The myocardium conductivity tensor is represented by $\boldsymbol{\sigma}_{\rm m}$. The function $I_{\rm stim}$ and $I_{\rm ion}$ are the stimulation and the transmembrane ionic currents. The field of variables $\boldsymbol{w}$ is a vector containing different chemical concentrations and various gate variables. Its time derivative is given by the vector of functions $\boldsymbol{g}$. Constants v_0 and $\boldsymbol{w}_0$ are the initial

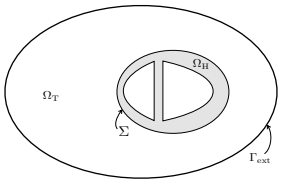

Figure 1. Two-dimensional geometrical description: heart domain Ω_{H}, torso domain Ω_{T} (extramyocardial regions), heart-torso interface Σ and torso external boundary Γ_{ext}.

conditions of the monodomain problem. The precise definitions of $\boldsymbol{g}$ and I_{ion} depend on the electrophysiological transmembrane ionic model. In the present work we make use of one of the human myocyte model Beeler Reuter [5].Ω_{H} stands for the heart domain which is in our case the atria. In order to simulate the body surface potential we first need to compute the extracellular potential in the heart. Supposing the the extracellular conductivity tensor $\boldsymbol{\sigma}_{\mathrm{e}} = \lambda \boldsymbol{\sigma}_{\mathrm{i}}$, where $\boldsymbol{\sigma}_{\mathrm{i}}$ is the intracellular conductivity tensor and $\lambda \in \mathbb{R}$. The extracellular potential satisfies

$$(\lambda + 1)\,\mathrm{div}(\boldsymbol{\sigma}_{\mathrm{i}} \boldsymbol{\nabla} u_{\mathrm{e}}) = -\,\mathrm{div}(\boldsymbol{\sigma}_{\mathrm{i}} \boldsymbol{\nabla} v_{\mathrm{m}}). \tag{2}$$

One can easily check that

$$u_{\mathrm{e}} = \frac{1}{(1+\lambda)}(< v_{\mathrm{m}} > - v_{\mathrm{m}}) \tag{3}$$

is a solution of equation (2). Morover, it is the unique solution satisfying $\left(\int_{\Omega_{\mathrm{H}}} u_{\mathrm{e}}\right) = 0$.
Here, $< v_{\mathrm{m}} >= \frac{1}{|\Omega_{\mathrm{H}}|}\int_{\Omega_{\mathrm{H}}} v_{\mathrm{m}}$ is the mean value of v_{m} in space. In order to compute the body surface potential we need to solve a Laplace equation on the torso with a Dirichlet boundary condition on the heart-torso interface [4].

$$\begin{cases} \mathrm{div}(\boldsymbol{\sigma}_{\mathrm{T}} \boldsymbol{\nabla} u_{\mathrm{T}}) = 0, \text{ in } \Omega_{\mathrm{T}}, \\ \boldsymbol{\sigma}_{\mathrm{T}} \boldsymbol{\nabla} u_{\mathrm{T}}.\boldsymbol{n} = 0, \text{ on } \Gamma_{\mathrm{ext}}, \\ u_{\mathrm{T}} = u_{\mathrm{e}}, \text{ on } \Sigma. \end{cases} \tag{4}$$

The forward problem algorithm is: (a) compute the transmembrane potential by solving equation (1), (b) compute the extracellular potential using the formula (3), (c) compute the torso potential by solving (4). As it was explained in the introduction we build a synthetic data base of BSPs and their correspondant EGMs. Each sample of BSPs and EGMs corresponds to a stimulation location. We simulated n heart beats, each one corresponds to a given I_{stim}. We use finite element method in order to solve equations (1) and (4), a space discretisation of the heart and torso domains is then needed. Since we are interested in targeting ectopic beats in the atria, we only consider the electrical

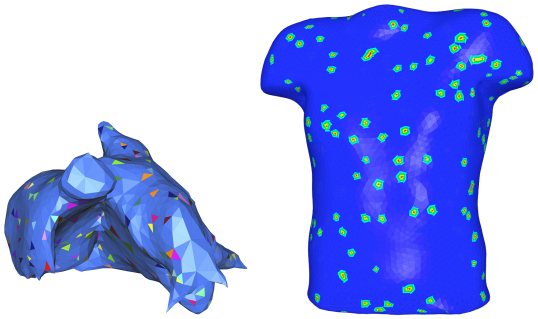

Figure 2. Finite element computational domains: Atria geometry with the different locations of stimulus used to construct the training data set (lfet). Torso geometry with different BSP measurements locations (right).

activation in the atria. The finite element geometry of atria is given in Figure 2.1 (left). it was embedded in a torso geometry given in Figure 2.1 (right) [6].

2.2. Inverse problem: a regression method

As explained in the previous paragraph, we have n samples of BSP and EGMs. The sequence $(BSP_i, EGM_i)_{i=1\ldots n} \in \mathbb{R}^{p\times m} \times \mathbb{R}^{q\times m}$ is the data set of our metamodel. Here p (respectively, q) is the number of potential measurement locations on the body surface (respectively, on the heart surface), and m is the number of time steps. We denote by $(x_k)_{k=1\ldots p}$ (respectively, $(y_k)_{k=1\ldots q}$) the positions of the BSP measurements (respectively, positions of EGMs measurements) and $(t_l)_{l=0\ldots m-1}$ the times of the recordings. For the i^{th} element of our data set we have, $BSP_i \in \mathbb{R}^{p\times m}$, where $BSP_i(l \times p + k) = u_{\mathrm{T}}(x_k, t_l)$, for $k = 1, ..., p$ and $l = 0, ..., m-1$, and $EGM_i \in \mathbb{R}^{q\times m}$ where, $EGM_i(l \times q + k) = u_{\mathrm{e}}(y_k, t_l)$, for $k = 1, ..., q$ and $l = 0, ..., m-1$.

The main goal is to build a function f able to accurately map a BSP to an EGM. We use a kernel ridge regression method based on the gaussian kernel

$$K(\mathbf{x}, \mathbf{y}) = \mathbf{e}^{-\frac{|\mathbf{x}-\mathbf{y}|^2}{2\sigma^2}}, \quad \forall \mathbf{x}, \mathbf{y} \in \mathbb{R}^{m\times p}.$$

We look for f in a *Reproducing Kernel Hilbert Space* (RKHS) $(\mathcal{H}, \langle\cdot,\cdot\rangle_{\mathcal{H}})$ characterized by the following property,

$$\forall f \in \mathcal{H}, \quad \forall \mathbf{x} \in \mathbb{R}^{m\times p}, \quad f(\mathbf{x}) = \langle \mathbf{f}(\cdot), \mathbf{K}(\cdot, \mathbf{x})\rangle_{\mathcal{H}}. \tag{5}$$

where $\langle\cdot,\cdot\rangle_{\mathcal{H}}$ is the inner product in $\mathcal{H}$. The use of the Gaussian kernel can be motivated by the following property (see [7]): given a compact subset K of $\mathbb{R}^{m\times p}$, the set of the restriction to K of functions from $\mathcal{H}$ is dense in the set of continuous functions from K to $\mathbb{R}$. In other word,

$\mathcal{H}$ is rich enough to approximate any possible continuous mapping from the BSP to a given lead of the EGM.

Consider in $\mathcal{H}$ the following regularized least square problem: given a training set $\{(\mathbf{x_i}, \mathbf{y_i})\}_{\mathbf{i=1}}^{\mathbf{n}} \in (\mathbb{R}^{m\times p} \times \mathbb{R})^n$, solve

$$\min_{f\in\mathcal{H}} \left\{ \frac{1}{n}\sum_{i=1}^{n}(f(\mathbf{x_i}) - \mathbf{y_i})^{\mathbf{2}} + \lambda\|\mathbf{f}\|_{\mathcal{H}}^{\mathbf{2}} \right\}, \qquad (6)$$

where $\lambda > 0$ is a given regularization coefficient and n is the number of the data set element. The representer theorem ([6]) states that the solution to (6) can be written as:

$$\sum_{i=1}^{n} \alpha_i K(\cdot, \mathbf{x_i}),$$

where $\alpha = (\alpha_i)_{i=1\dots n} \in \mathbb{R}^n$ is the new unknown. Defining the Gram matrix $\mathrm{K} = (K_{ij})_{i,j=1\dots n}$ with $K_{ij} = K(\mathbf{x_i}, \mathbf{x_j})$, the training problem (6) is equivalent to solving:

$$\min_{\alpha\in\mathbb{R}^{\mathrm{n}}} \left\{ \frac{1}{n}(\mathrm{K}\alpha - \mathbf{y})^{\mathbf{T}}(\mathrm{K}\alpha - \mathbf{y}) + \lambda\alpha^{\mathbf{T}}\mathrm{K}\alpha \right\},$$

whose solution is given by

$$\alpha = (\mathrm{K} + \lambda n\mathrm{I})^{-1}\mathbf{y}. \qquad (7)$$

Here $\mathbf{y} \in \mathbb{R}^n$, and the i^{th} element of $\mathbf{y}$ represents an element of EGM_i meaning the value of u_{e} in a fixed position at at a given time. In order to consider all the positions on the atria surface and all the time sequence. The training phase consists in solving this system:

$$\mathrm{A} = (\mathrm{K} + \lambda n\mathrm{I})^{-1}\mathrm{Y}, \qquad (8)$$

with $\mathrm{A}, \mathrm{Y} \in \mathbb{R}^{n\times(q\times m)}$, where $\mathrm{Y} = (EGM_i^T)_{i=1\dots n}$. Once the training phase is completed, the reconstruction of EGM from a given heart beat BSP $\in \mathbb{R}^{p\times m}$ is obtained, according to (5), by

$$\mathrm{EGM} = \widetilde{\mathrm{K}}\mathrm{A}, \qquad (9)$$

with $\widetilde{\mathrm{K}}_i = K(BSP, BSP_i)$, $i = 1\dots n$.

3. Results

In this section we present numerical simulations of the forward and inverse problems. We first built $n = 400$ heart beats using our computer simulator as described in section (2.1). In this work we reconstruct the EGMs on all the whole atria surface ($q = 1994$), from 264 BSPs ($p = 264$). In figure 3 we present two example of simulation depending on the location of the stimulus, in each case we show two snapshots one at 10ms (left) and the other at 90 ms (right). In the top two figures we show an example of simulation where the atria is activated in the left superior pulmonary vein and in figure 3 (bottom) the right atria appendage is activated. After building the metamodel from equation (8), we propose to test the regression method on different example. As expected the reconstruction of EGMs from BSPs belonging to the training data set is perfectly accurate. On the contrary, if the BSP does not belong to the training data set, the accuracy of the EGMs reconstruction is not accurate especially in terms of amplitude where the l^∞ relative error could reach 50%, an example is given in figure 4 where the amplitude of the exact solution (continuous red line) is twice higher then the RKHS solution (dashed green line). Nevertheless, the reconstructed and original signals are synchronized. We then computed the activation times following the maximum time derivative of the extracellular potential at each node of the mesh. The maximal error is 6ms. The location of the stimulus corresponds to the location of the minimal activation time. For the sake of illustration we show in fig-

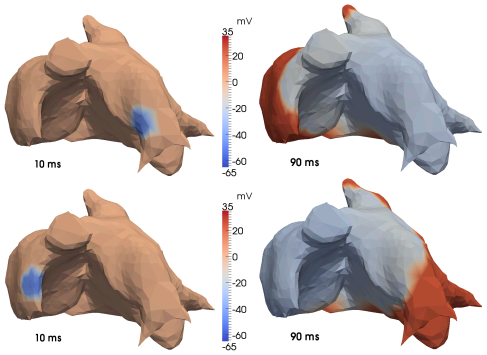

Figure 3. Snapshots of the simulated extracellular potential. The atria is activated in the pulmonary vein (top) and in the right atria (bottom).

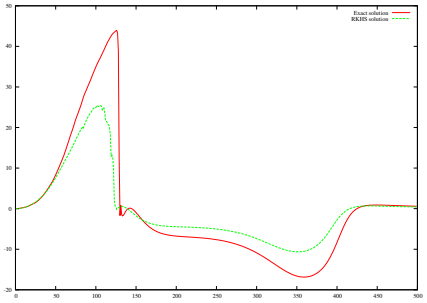

Figure 4. Comparison between the exact and the reconstructed EGM at a given location on the atria: Exact solution (red continuous line) and the one reconstructed with RKHS (green dashed line).

ure 4 a comparison of the activation times computed from the original signal (left) and the reconstructed (right). The activation site is localized with a 0.5 cm of accuracy, which is expected since the average of the distance between the stimulus sites in the training set is 0.42 cm.

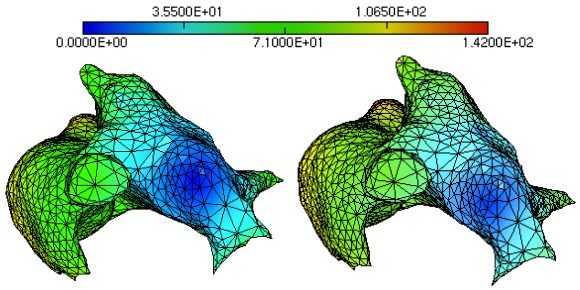

Figure 5. Comparison of the activation times: exact activation times (left) and activation times reconstructed with RKHS metamodel (right).

4. Discussion

In this work we showed an original approach based on a machine learning technique in order to solve the inverse problem in electrocardiography. This method allows solving the inverse problem in real time: since the metamodel could be build off-line, in practice we only need to evaluate the metamodel according to equation (9). This does not require solving any linear system. The reconstruction of EGMs is accurate if the training data base is sufficiently rich. The accuracy of the produced EGMs depends on how close is the BSP from the elements of the training set. This means that it is difficult to reproduce an information which is far from the training data base. It is for instance difficult to reproduce accurate EGM for a multiple sites activation based on a data set containing only simulation with single site stimulus. This limitation could be tackled by including multiple site stimulations in the training data set, at the same time this will increase the complexity of the training phase. But since this phase is off line, the computational time of the reconstruction would be slightly affected.

5. Conclusion

In this work we have considered a machine learning approach, based on the kernel ridge regression method, in order to construct activation maps on the atria from a set of BSP measurements. The procedure has been trained using synthetic data from numerical simulations, based on a 3D mathematical model of the ECG involving a mathematical description of the electrical activity of the heart and the torso. Several examples showed the method is able to reconstruct conveniently the EGM information included in the training data set, and is robust when reconstructing situations close to the training data set. In this study we showed that a single site stimulus is localized with 0.5 cm error. The accuracy could be improved if the training set is much rich. In the proposed approach, the solution depends on all training examples, which may be too expensive. This point could be improved in future works. In future works this method would be trained and tested on clinical data. The ECG simulator would be used in order to enrich the clinical data.

Acknowledgements

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