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Bayesian Optimization for the Inverse Problem in Electrocardiography

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***Abstract*—The inverse problem in electrocardiography is an ill-posed problem where the objective is to reconstruct the electrical activity of the epicardial surface of the heart, given the electrical activity on the thorax' surface. In the forward problem, the electrical propagation from heart to thorax is modeled by the volume conductor equation with Dirichlet boundary conditions in the heart's surface, and null flux coming from the thorax. The inverse problem, however, does not have a unique solution. In order to find solutions for the inverse problem, techniques such as Tikhonov regularization are classically used, but they often deliver unrealistic solutions. As an alternative, we propose a novel approach, where a fixed solution of the volume conductor model with a source in a forward scheme is used to solve the inverse problem. The unknown values for parameters of the fixed solution can be found using optimization techniques. Due to the characteristics of the problem, where each single evaluation of the cost function is expensive, we use a specialized CMA-ES-based Bayesian optimization technique, that can deliver good results even with a reduced number of function evaluations. Experiments show that the proposed approach can deliver improved results for in-silico simulations.**

***Index Terms*—inverse problems, bayesian optimization, ECGI**

I. Introduction

The main cause of more than 17 million deaths annually in the world are heart-related diseases[1]. Understanding the electrical activity of the heart to provide accurate and timely diagnosis is an important key to decrease the risk of death from these diseases. To this aim, different signal analysis techniques such as electrocardiography (ECG), phonocardiography (PCG) and photoplethysmography (PPG) are commonly used [1].

Non-invasive electrocardiographic imaging (ECGI) is an increasingly used imaging modality that is based on the numerical reconstruction of cardiac electrical activity using body surface potential measurements and patient-specific heart and torso geometries [2]. ECGI is also known as the inverse problem of electrocardiography: since the problem is ill-posed, it does not have a unique solution, making each proposed solution unstable. Solutions to the problem can vastly differ with even the slightest noise or disturbance in the electrical and/or geometric input data [2]–[6]. Several solutions have been proposed for the inverse problem of electrocardiography, for example using ECG signal processing methods [4], [7], single/multi-layer approaches [2], [8], and machine learning [9]–[11]. One of the most common techniques used in practice, however, is still Tikhonov regularization [5], [6], [12], [13]. Despite the great number of approaches proposed, finding stable solutions for the inverse problem of electrocardiography remains, at the time of writing, an open problem.

In this work we propose a novel approach to tackling this problem, where a fixed solution of the volume conductor model with a source in a forward scheme is used to solve the inverse problem of electrocardiography. The unknown values for the parameters of the fixed solution are found using optimization techniques. Due to the characteristics of

[1]https://www.who.int/health-topics/cardiovascular-diseases#tab=tab_1

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the problem, where each single evaluation of the cost function is computationally expensive, we use a specialized CMA-ES-based Bayesian optimization technique, that can deliver good results even with a reduced number of function evaluations. Bayesian optimization already has a considerable number of success stories, when applied to medical issues such as assigning personalized dose to patients [14], individualized treatment rules [15], regenerative medicine [16], and deep brain stimulation [17], [18], among many others. The results obtained using Bayesian optimization were the motivation to use it as an alternative solution in the inverse problem of electrocardiography. An experimental evaluation shows that the proposed approach can deliver excellent results for benchmarks where traditional approaches fail.

II. Background

In the following, we provide the reader with the minimal notions related to the inverse problem in electrocardiography and Bayesian optimization that are necessary to introduce the scope of the work.

A. Inverse problem in electrocardiography

Electrocardiography (ECG) is defined as the interpretation of the potentials recorded at the body's surface, typically using AgCl electrodes: the objective is to obtain a qualitative and quantitative representation of the electrical activity of the heart.

To achieve this objective, solutions to the so-called forward and inverse problems in ECG must be sought. The forward problem in ECG consists of calculating the potential distribution at the surface of the thorax (∂T) due to the electrical activity on the heart's surface (∂H) [3], whereas the inverse problem is to reconstruct the electrical activity in the epicardium ∂H from the measured electrical activity at the thorax ∂T [2], [4].

The inverse problem of electrocardiography is considered an ill-posed problem [3], with no unique solution [19]. In the inverse problem of electrocardiography, elements such as perturbation in the electrical and/or geometrical input data, even in small amounts, can lead to errors that negatively affect the accuracy of the reconstructed cardiac activity, making it unstable and highly oscillatory [2]–[4]. To solve this ill-posed problem, it is necessary to regularize the procedure to obtain physical and physiological results. These regularizations techniques could facilitate the inversion by restricting the possible types of solutions using implicit constraints, such as electrical activity of the heart and/or body-surface potentials, which cause the model parameters to be uniquely computed from surface potentials [3], [20]. Some examples of the mentioned models are a multipolar array, one or two moving dipoles, multiple fixed location dipoles, the epicardial potential distribution, and isochrones of activation at the surface of the heart [3]. The most common regularization technique used in the inverse problem of electrocardiography is Tikhonov regularization: this technique seeks to achieve a good balance between the adjustment to the measures and *a priori* information about the solution [5], [13], [20]. Previous works focused on using two-step algorithms with genetic programming [21] and particle swarm optimization [22], but these approaches require a considerable amount of function evaluations, which explode in number as the geometry becomes more dense. While effective on benchmarks, such approaches cannot be applied to real cases, where the number of evaluations they require would be impractical to perform, given the timeliness required by the application. Techniques that use a smaller amount of function evaluations, such as Bayesian optimization, could thus be more suitable for real-world applications.

B. Inverse Problem Formulation

From the geometry of the model, and the boundary conditions of null flux and measured potential at the thorax's surface, we construct an operator considering the following model, using the Finite Element Method (FEM) [23]:

$$\begin{cases} -\nabla \cdot (c\nabla u) = 0 & x \in H, \\ u = u_t & x \text{ on } \partial T, \\ \frac{\partial u}{\partial n} = 0 & x \text{ on } \partial T. \end{cases} \tag{1}$$

This formulation translates to a set of equations, where h, v and t denote nodes in the heart, volume (between heart and thorax), and thorax, respectively:

$$\begin{bmatrix} A_{hh} & A_{hv} & A_{ht} \\ A_{vh} & A_{vv} & A_{vt} \\ A_{th} & A_{tv} & A_{tt} \end{bmatrix} \begin{bmatrix} u_h \\ u_v \\ u_t \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}. \tag{2}$$

Considering no overlapping nodes between the heart and the thorax, we can simplify the system to:

$$\begin{bmatrix} A_{vh} & A_{vv} & A_{vt} \\ 0 & A_{tv} & A_{tt} \end{bmatrix} \begin{bmatrix} u_h \\ u_v \\ u_t \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}. \tag{3}$$

If we solve for u_h, then we can create operator O:

$$O = (A_{tt} - A_{tv}A_{vv}^{-1}A_{vt})^{-1}A_{tv}A_{vv}^{-1}A_{vh}, \tag{4}$$

$$Ou_h = u_t. \tag{5}$$

As mentioned, a classical approach to the solution of the inverse problem is to use Tikhonov regularization. Tikhonov regularization, considers the following functional:

$$min(||Ou_h - u_t||^2 + \lambda||C(u_h - u'_h)||^2) \quad \lambda > 0 \tag{6}$$

We applied the functional in the following form [24]:

$$u_h = [O^T O + \lambda C^T C]^{-1}[O^T u_T + \lambda C^T C u'_h], \tag{7}$$

where C is a constrained matrix. In our case we use the identity matrix ($C = I$) and set $\lambda = 0.001$.

C. Bayesian optimization

Machine learning algorithms often have several hyper-parameters that directly influence performance [25]. Hence, in recent years, different optimization algorithms have been proposed to automate parameter tuning, such as grid search, random search [26] or evolutionary algorithms [27], [28]. Although capable of achieving excellent results, these techniques typically require considerable computational effort to achieve such results, in particular due to the necessity of performing many function evaluations [29].

An alternative to these algorithms are optimization techniques that are designed to get high-quality results using only few function evaluations [25], [30]–[32]. Such algorithms are well-suited for problems where using only few evaluations is critical, for example robotics and machine learning [33]–[36]. A type of expensive optimization is Bayesian optimization. Bayesian optimization has two components: First, apply a Gaussian Process (GP) to the data as a prior probability distribution to infer values. This is known as Gaussian Process Regression. Next, use an acquisition function to evaluate those values and select the next point to evaluate [37], [38]. In this context, each time we modify a hyper-parameter in the algorithm, we consider the result as a sample from the GP. Using the GP as a surrogate model allows us to evaluate a simplified function in comparison to the original.

The acquisition function is described by a covariance matrix (or kernel), a mean, a variance, and the information already gathered on the model. To optimize the acquisition function, either a gradient-based algorithm technique like DIRECT in the BayesOpt library [39], or a global non-linear optimizer such as the evolution strategy with covariance matrix adaptation (CMA-ES) [40], [41] in the Limbo library [42] may be used.

In Bayesian optimization, we will have a set of observed samples (x_0, y_0), (x_1, y_1), ... , (x_n, y_n) where $y_i = f(x_i)$, X is the vector of inputs, and y the vector of outputs. The objective will be to predict the next point x^* that maximizes the acquisition function,

$$x^* = argmax\ f(x). \tag{8}$$

Using a GP the predicted mean $\mu(x_*)$ and predicted variance $\sigma(x_*)$ of the point x_* are given by ([38], [43]):

$$\mu(x_*) = k_*^T(K + \sigma^2_{noise}I)^{-1}y \tag{9}$$

$$\sigma^2(x_*) = k(x_*, x_*) - k_*^T(K + \sigma^2_{noise}I)^{-1}k_*, \tag{10}$$

where $K = K(X, X)$ denotes the covariance matrix computed for each pair of observed inputs, σ^2_{noise} is the noise level, I the identity matrix, k_* is the vector of covariances between the test point x_* and each of the n observed inputs. Examples of covariance functions include the exponential kernel (Eq. 11) and the Matérn $5/2$ (Eq. 12) [37]:

$$K_{sq-exp}(x, x') = \theta_0^2 exp(-\frac{1}{2}r^2) \tag{11}$$

$$K_{M52}(x, x') = \theta_0^2 exp(-\sqrt{5}r)(1 + \sqrt{5}r + \frac{5}{3}r^2) \tag{12}$$

with r given by:

$$r^2 = \sum_{d=1}^{D} \theta_d^2 (x_d - x'_d)^2 \tag{13}$$

with $\theta_d \in$ [0,1] (parameterized) [31]. The values of θ_i are estimated by the log marginal likelihood,

$$\log P(y|x, \theta) = -\frac{1}{2}\log|K| - \frac{1}{2}y^T K^{-1} y - \frac{N}{2}\log 2\pi. \tag{14}$$

which gives a measure of how well the model adjusts to the data [38]. The log marginal likelihood is usually calculated using gradient methods [43], such as the LBFGS-B [44].

With a given covariance function k, a set of inputs X, a set of outputs y, and a σ^2_{noise} noise level, we can optimize an acquisition function, such as an upper confidence bound (UCB) [31], [45]:

$$UCB(x) = \mu(x_*) + \kappa\sigma(x_*), \tag{15}$$

where κ is a parameter to tune the exploration-exploitation trade-off. The overall algorithm is summarized in Alg. 1.

Algorithm 1: Bayesian optimization algorithm.

```
Create n random initial points ;
for Number of Evaluations do
    Optimize log P(y|x, θ);
    Optimize acquisition function ;
    Evaluate selected point x_* in the original function
     ;
    Update sets X, y ;
```

III. Proposed approach

In the inverse problem in electrocardiography, we considered the system in a quasi-static approach, thus each time step is solved independently [23]. We propose to tackle the IPE by applying Bayesian optimization, and speed up the computation by selecting only a subset of points of fixed size, including the ones with the best values obtained up to that moment. From Eq. 7, we have u'_h, that is considered as *a priori* information. Using the model for Multiple Dipole Source Position from [46], we modified to use it as a basis for cardiac sources.

$$u'_{hi} = \frac{1}{4\pi\zeta}\begin{bmatrix} s_0 & s_1 \end{bmatrix}\begin{bmatrix} \frac{N_x - u0_x}{r0^3} & \frac{N_y - u0_y}{r0^3} & \frac{N_z - u0_z}{r0^3} \\ \frac{N_x - u1_x}{r1^3} & \frac{N_y - u1_y}{r1^3} & \frac{N_z - u1_z}{r1^3} \end{bmatrix}\begin{bmatrix} v_x \\ v_y \\ v_z \end{bmatrix} \tag{16}$$

Thus, this would translate to identifying the values of 12 parameters $(\zeta, s_0, s_1, u0_x, u0_y, u0_z, u1_x, u1_y, u1_z, v_x, v_y, v_z)$, where ζ is the conductivity, s_0 is the dipole signal strength of dipole 0, s_1 is the dipole signal strength of dipole 1, $u0_x, u0_y, u0_z$ is the dipole 0 position, $u1_x, u1_y, u1_z$ is the dipole 1 position, v_x, v_y, v_z is the unit vector denoting the orientation of the dipole, and N_x, N_y, N_z are the position on the heart's surface at each point.

Then, having calculated u'_h as *a priori* information, we will solve the original functional in Eq. 7 for each time step (Alg. 2).

Algorithm 2: Bayesian optimization algorithm for the inverse problem in electrocardiography.

for *Each Time Step* **do**
- Create n random initial points to evaluate a source model equation;
- Generate n initial u_h and u_t;
- **for** *Number of Evaluations* **do**
  - Optimize $\log P(y|x,\theta)$;
  - Optimize acquisition function ;
  - Evaluate selected point x_* in the source model equation ;
  - Generate u_h and u_t ;
  - Update sets X, y ;
- Solve Functional $min(||Ou_h - u_t||^2 + \lambda||C(u_h - u'_h)||^2)$;

IV. Results

We performed two experiments: one using simulated data with geometries from [47] and a monodomain model [23], [48] with a one-point source (Experiment 1), and a second one using real-world data from a Langendorf-perfused canine heart [49], [50] (Experiment 2). For Experiment 2, we modified the torso geometry to make it a close surface using Laplacian interpolation, as the provided geometry was non-compliant with the volume conductor model. Then, for both experiments, we generated the transfer matrix using the Garlekin boundary element method [51]. The coupled geometries of heart and torso are displayed in Fig. 1.

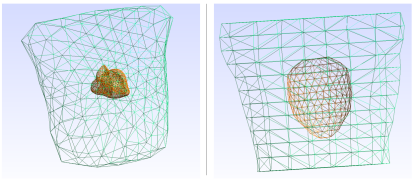

Fig. 1. Geometries used for the experiments. (Left) geometry of human torso and thorax for Experiment 1. (Right) Geometry of torso tank and heart cage for Experiment 2.

A. Experiment 1

For this experiment, we used a geometry of the thorax with 300 nodes, and 1,444 nodes on the heart's surface. First, using the Monodomain model we put an impulse in the left ventricle. Next, we propagate the extracellular potential to the thorax (electrocardiography forward problem) for 200 time steps (Fig.2). Then, using Tikhonov regularization ($\lambda = 0.001$), we reconstruct the extracellular potential in the heart's surface from the thorax' potential (electrocardiography inverse problem), using only the Tikhonov functional and the Bayesian Optimization with a source model, as seen in Fig. 3.

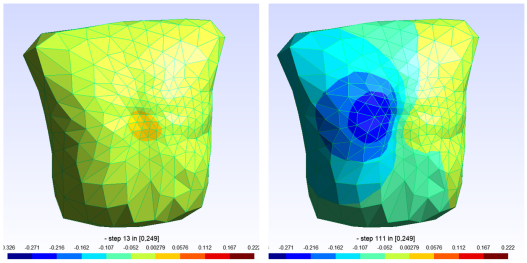

Fig. 2. Thorax simulated potentials at time steps 13 and 111, using the Monodomain Model with a laplace coupling with BEM.

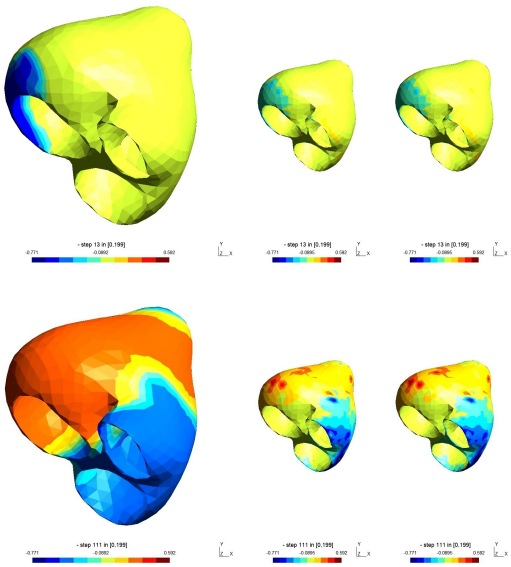

Fig. 3. Measurements of electrical activity in the heart's surface using the Monodomain (Left), reconstruction with Tikhonov only (middle) and reconstruction using Bayesian Optimization (right), for time steps 13 and 111.

B. Experiment 2

In this experiment we have the real-world recordings from a Langendorf-perfused canine heart, for both the thorax' surface and the cardiac cage. Thus, for this case we will close the geometry and interpolate the values in the thorax (Fig. 4) with a Laplace interpolation (229 nodes), and then try to reconstruct the activity measured by the cardiac cage (256 nodes). The activity in the heart is described by an anterior ventricular paced beat (avp) for 220 time steps. First, we build the transfer matrix, or operator using the Garlekin boundary element method. Then, we apply the Tikhonov functional and Bayesian Optimization with a source model and compare it to the actual recordings, as summarized by Fig. 5.

Finally, from the final results and knowing the ground truth, we can compute the error for the two approaches (Table I). The error is defined as:

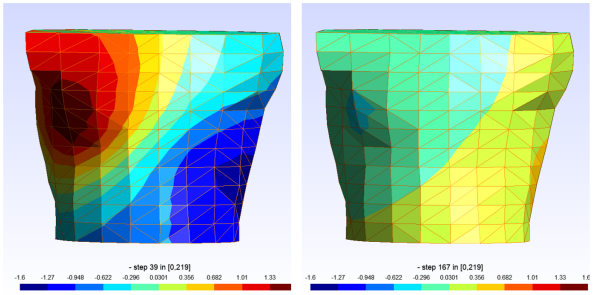

Fig. 4. Interpolated activity of the thorax (torso tank) for time steps 39 and 167.

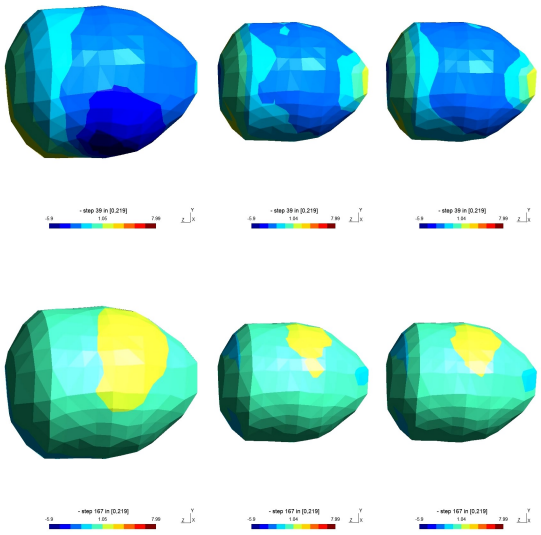

Fig. 5. Measurements of electrical activity in the cardiac cage (Left), reconstruction with Tikhonov only (middle) and reconstruction using Bayesian Optimization (right), for time step 39 and 167.

$$error = \frac{\sum_i^{nodes} \sum_j^{t_{total}} (u_h - u_{sim})_{i,j}^2}{\sum_i^{nodes} \sum_j^{t_{total}} (u_h)_{i,j}^2}, \tag{17}$$

TABLE I
SUMMARY OF ERROR IN THE 2 DIFFERENT EXPERIMENTS.

	Experiment 1	**Experiment 2**
Tikhonov	0.7157	0.3442
BO + Tikhonov	0.6881	0.3352

It is interesting to notice that the numerical value of the error depends on the number of nodes in the geometry, so error values reported for Experiment 1 (using a geometry with 1,444 nodes) and Experiment 2 (256 nodes) are not directly comparable. Still, the proposed approach outperforms the classic Tikhonov method for both experimental configurations. As the objective of solving the inverse problem is to find sources of arrhythmia in the heart without invasive surgery, rule out acute myocardial infarction, or the extent of cardiomyopathy, even small gains in the error correspond to significant improvements from the point of view of patients' safety and comfort.

V. CONCLUSION

In this work, we presented a novel CMA-ES-based Bayesian optimization approach for solving the inverse problem in electrocardiography, a difficult ill-posed problem with unstable solutions but invaluable practical applications for medicine. Compared to previously proposed techniques, the presented algorithm requires fewer function evaluations to achieve the same quality of results, thus being more applicable to real-world scenarios. In addition, the given approach makes it possible to solve each time step independently, thus it can be efficiently parallelized. Simulated and real world data experiments show that the approach is not only faster, but provides better results than established techniques such as Tikhonov regularization.

Although further testing and validation are necessary, this approach could represent a step in the right direction to solve the inverse problem in electrocardiography in real time and with a better precision than the classical Tikhonov regularization. As of now, we have only used a source generation model, but next experiments will focus on using different functions that can approximate the electrical activity and the parameters can be found via Bayesian optimization as shown and more real data-based experiments. Finally, we expect to test further our methodology with other datasets avaialble in the EDGAR repository [49].

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