Ensemble Kalman Filtering Based Calibration of Tissue Parameters Using Emulators of Left Atrial Electrophysiology Models

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Abstract

Atrial fibrillation (AF) is a common cardiac arrhythmia characterised by disordered electrical activity. Standard treatment for AF is catheter ablation, which is invasive and irreversible. Patient-specific computer models (often referred to as digital twins) offer a promising way to improve treatment planning. However, their clinical value depends on our ability to rapidly calibrate electrophysiological parameters from routine measurements. We present a new framework for efficient calibration of atrial tissue properties using local activation times (LAT)s and action potential durations (APD)s derived from an S1S2 stimulation protocol. By combining Gaussian process emulators with a fast data assimilation method, we are able to rapidly estimate key tissue parameters with uncertainty quantification. Our results highlight the feasibility of near real-time calibration, a crucial step towards the clinical translation of digital twins in cardiac electrophysiology.

1. Introduction

Atrial fibrillation (AF) is a common supraventricular arrhythmia affecting around 46.3M individuals worldwide. Moreover, this disease increases the incidence of cardiovascular disease, stroke, and premature death [1]. AF is typically treated by radiofrequency catheter ablation[2], which consists of burning portions of the cardiac tissue to restore the sinus rhythm. This treatment is invasive, irreversible and has mild effectiveness, with many patients requiring multiple procedures to achieve sinus rhythm[3]. Computational models of the human heart improved our understanding of the underpinning mechanisms responsible for arrhythmias in the ventricles and atria[4]. Patient-specific models of the human atria have the potential to tailor the treatment to each patient and, ultimately, improve its effectiveness; their application in clinical practice, however, is hampered by the narrow time scales characterising clinical procedures.

Accurate estimation of tissue parameters in cardiac electrophysiology models is essential for predictive simulations and personalised therapy planning. While traditional methods for parameter inference involve solving the forward problem iteratively, the associated computational cost becomes prohibitive when using the finite element method for three-dimensional tissue simulations for the left atrium.

This paper proposes a computationally efficient framework for parameter calibration in synthetic settings, assuming spatially homogeneous tissue properties. Specifically, we adapt the ensemble Kalman filter (EnKF) to a static inverse problem using Gaussian process (GP) emulators trained on simulations of the modified Mitchell-Schaeffer[5] model. The proposed method used local activation time (LAT) and action potential duration (APD) data to estimate tissue parameters, and we demonstrate its performance using synthetic problems.

2. Methods

We developed a computational framework to calibrate atrial electrophysiology models against synthetic measurements. Left atrial simulations were performed with the modified Mitchell–Schaeffer model under an S1S2 pacing protocol, generating LAT and APD data, see Section 2.1 for details. Parameter inference used a Gaussian process based ensemble Kalman filter as described in Section 2.2.

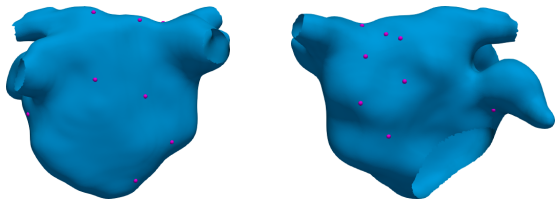
2.1. Electrophysiology Model and Synthetic Data

We model left atrial electrophysiology using the modified Mitchell–Schaeffer model under the monodomain assumption with homogeneous, isotropic tissue. The model is parameterised by four cell-level time constants that describe the different stages of the action potential, and a tis-

sue conductivity parameter. Simulations were carried out with openCARP [6] on ARCHER2[7] on a finite element mesh derived from imaging data [8], using no-flux boundary conditions and resting initial conditions.

A paced activation protocol was applied by stimulating a region near the coronary sinus (CS), as shown in Figure 1. We used an S1S2 pacing protocol, consisting of three S1 stimuli separated by 800 ms, followed by a premature S2 stimulus with a 500 ms coupling interval.

Our analysis focuses on local activation times (LATs), which can be directly measured during electroanatomical mapping. In addition, we computed action potential duration (APD). While APD is not directly measured in clinical practice, it can be approximated from the effective refractory period (ERP), obtained by repeating the S1S2 protocol at progressively shorter coupling intervals until propagation fails. Including APD in this study allows us to assess the potential added value of ERP-like measurements for calibration, relative to their additional experimental cost. To generate synthetic data, we added noise to simulated LAT and APD values at a subset of atrial locations (Figure 1).



(a) (b)

Figure 1: Two views of the left atrium anatomy illustrating the 15 measurement locations (blue dots) and stimulus region (green patch) for the S1S2 pacing protocol.

2.2. Proposed Method: Gaussian Process Assisted Ensemble Kalman Filter

We develop a new approach for calibrating electrophysiological parameters by combining Gaussian process (GP)[9] emulators with the ensemble Kalman filter (EnKF)[10]. GP models provide a flexible, probabilistic surrogate for the simulator, capturing both mean predictions and uncertainty at unseen parameter values. This allows rapid evaluation of activation times and other outputs without running the full simulator.

The EnKF is a Monte Carlo method for combining model predictions with data, commonly used for dynamic state–parameter estimation. We adapt it for static calibration of electrophysiological parameters, where there is no underlying state evolution. Unlike previous work[11, 12], we use artificial parameter dynamics that allows the ensemble to explore the parameter space, and a sequence of perturbed observations ensures a smooth transition from prior to posterior. This method is a simpler variant of the algorithm in [13]. It does not account for the Gaussian process uncertainty, and hence is computationally cheaper.

This EnKF framework using GP emulators, produces an approximate posterior over the parameters while remaining computationally efficient (1). Numerical experiments in [13] have shown that the posterior converges to that of the true simulator as the GP efficiency improves, highlighting the method's potential for rapid, uncertainty-aware calibration in static inverse problems such as patient-specific atrial electrophysiology.

Algorithm 1 EnKF for Static Calibration with a GPE measurement operator

Inputs: Noise covariance matrix R, number of iterations K, process covariance σ_θ, initial distribution $\mathcal{N}_d(\mu_0, \Sigma_0)$, observation vector $Y \in \mathbb{R}^p$.
Initialise: Sample parameters $\theta_0^n \sim \mathcal{N}_d(\mu_0, \Sigma_0)$ for $n = 1, \ldots, N$.
for $k = 0, \ldots, K-1$ **do**
  $\epsilon_y \sim \mathcal{N}_p(\mathbf{0}, KR)$
  $Y_{k+1} = Y + \epsilon_y$ *// Perturb observation*
  for $n = 1, \ldots, N$ **do**
    $\epsilon_\theta \sim \mathcal{N}_d(\mathbf{0}, I)$
    $\tilde{\theta}_{k+1}^n = \theta_k^n + \sigma_\theta \epsilon_\theta$ *// Predict θ*
  end for

$$P_{k+1} = \frac{1}{\sqrt{N-1}} \left[\tilde{\theta}_{k+1} - \langle \tilde{\theta}_{k+1} \rangle \right]$$
$$H_{k+1} = \frac{1}{\sqrt{N-1}} \left[\bar{m}(\tilde{\theta}_{k+1}) - \langle \bar{m}(\tilde{\theta}_{k+1}) \rangle \right]$$

where $\tilde{\theta}_{k+1}, \bar{m}(\tilde{\theta}_{k+1})$ are matrices with nth column $\tilde{\theta}_{k+1}^n$ and $\bar{m}(\tilde{\theta}_{k+1}^n)$. $\langle A \rangle$ denotes the matrix with N identical columns, each being the mean of the columns of A

  $K_{k+1} = P_{k+1} H_{k+1}^T (H_{k+1} H_{k+1}^T + R))^{-1}$
  for $n = 1, \ldots, N$ **do**
    $\theta_{k+1}^n = \tilde{\theta}_{k+1}^n + K_{k+1}[Y_{k+1} - \bar{m}(\tilde{\theta}_{k+1}^n)]$
    // Update θ
  end for
end for

3. Results

We first generated an ensemble of 176 left atrial simulations (using a physiologically feasible space-filling design [13] under the S1S2 pacing protocol, extracting three types of measurements: local activation times (LATs) from S1 and S2, and action potential duration (APD) from S2 at 15 measurement sites (Figure 1). Independent Gaussian process (GP) emulators were trained for each of the 45 outputs, achieving high predictive accuracy with $R^2 > 0.95$

on held-out test cases.

To evaluate calibration performance, we carried out 50 synthetic experiments, each with a different ground truth parameter set and additive observation noise. In each case, the calibrated parameter estimate was taken as the mean of the posterior ensemble produced by the EnKF method. Three data scenarios were considered: (i) S1 only, (ii) S1+S2, and (iii) S1+S2+APD. The comparison between ground truth and estimated parameters, see Figure 2 (a)-(e), shows that τ_{in} and tissue conductivity, D, can be consistently identified, while the other parameters require inclusion of S2 and APD data to be well estimated.

Predictive accuracy was quantified by running simulations with calibrated parameters and computing root-mean-square errors (RMSEs) across the full atrial mesh ($\approx$ 300k nodes). As shown in Figure 2 (f)-(h), S1 predictions improve modestly when S2 data are included, while S2 predictions are only accurate when S2 measurements are used. APD predictions showed consistent improvement as more measurement types were incorporated. Overall, including multiple data types progressively reduced RMSEs and improved recovery of physiologically relevant parameter values.

These results demonstrate that the proposed GP–EnKF framework provides computationally efficient calibration of atrial tissue parameters with the flexibility to incorporate different experimental measurement types, yielding larger performance gains from measurement diversity than from measurement quantity.

4. Conclusions

We presented an efficient calibration framework for tissue parameter estimation in cardiac electrophysiology models, combining a modified Ensemble Kalman Filter (EnKF) with Gaussian process (GP) emulators. This approach substantially reduces the computational cost of forward simulations while preserving high calibration accuracy when tested on synthetic LAT and APD data. In the specific problem configuration considered, incorporating GPs reduced the number of simulations required for calibration from 10,000 to about 200—an approximate 98% reduction. Using this framework, we successfully calibrated two parameters, τ_{in} and tissue conductivity, from LAT data alone. A third parameter, τ_{open}, proved more challenging to infer from S1 LAT data alone, but its calibration improved when using combined S1+S2 LAT data, and further improved with the inclusion of APD data. Although demonstrated for spatially homogeneous parameters, the framework can be extended to spatially heterogeneous fields through more expressive emulators and localization strategies within the EnKF. Future work will focus on validation using patient-specific datasets.

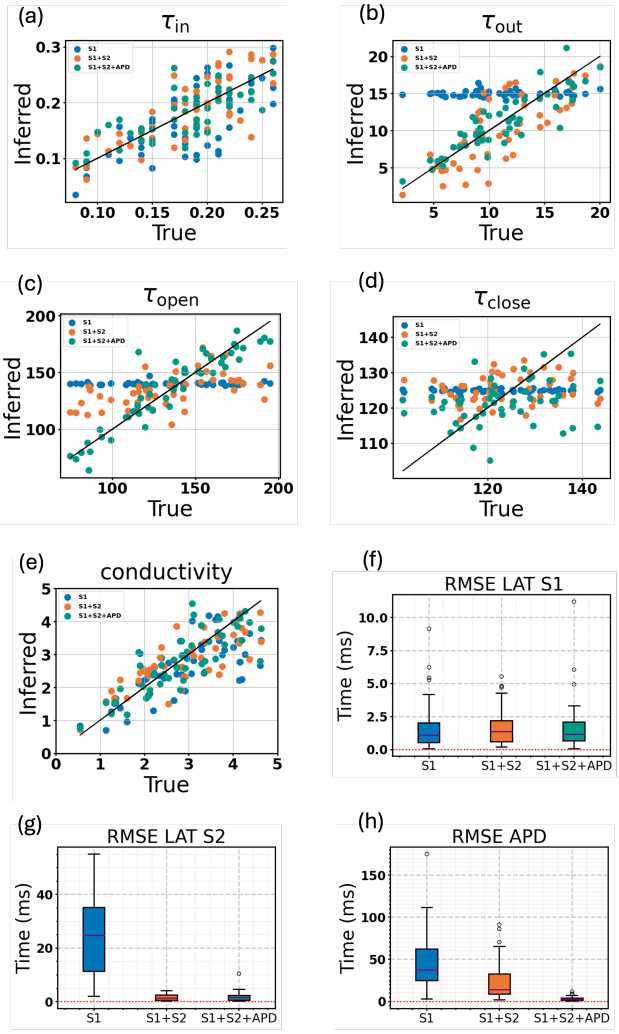


Figure 2: (a)–(e): Estimated versus ground truth values of the tissue parameters obtained from 150 independent calibration trials. Each panel corresponds to a specific parameter, with reference values shown along the x-axis and the corresponding calibrated estimates along the y-axis. Colors indicate the measurement type used during calibration. (f)–(h): Root-mean-square errors (RMSEs) across 50 simulation runs, computed over the left atrial mesh (300 k nodes). Panels show RMSEs for LAT S1, LAT S2, and APD, respectively. Each boxplot compares three calibration settings: (i) LAT (S1) only, (ii) LATs (S1 + S2), and (iii) LATs (S1 + S2) + APD.

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