Active learning based Cardiac Tissue Parameter Estimation for Personalized model exploiting predictive uncertainty

Pradeep Bajracharya[1], Anton J. Prassl[2], Karli Gillette[2], Gernot Plank[2], Linwei Wang[1]

[1] Rochester Institute of Technology, Rochester, USA
[2] Gottfried Schatz Research Center: Division of Medical Physics and Biophysics, Medical University of Graz, Graz, Austria

Abstract

Personalized cardiac models are crucial intervention tools for a multitude of cardiac health issues. As cardiac simulations become more complex and expensive, machine learning (ML) models demonstrated the potential to enable efficient model personalization and cardiac tissue parameter estimation. Prior studies however depend on "globally" accurate ML models trained with large simulation data to predict tissue parameters. Such a global ML model is not only expensive to train, but its success also relies on the assumption that real-world data would fall within the range of the training data. We establish a novel active-learning method for cardiac parameter estimation by steering the training of the ML model towards the unknown region of interest in the parameter space.

1. Introduction

Personalized cardiac models plays a pivotal role for designing effective intervention strategies for multiple cardiac problems [1–3]. In recent years, there have been development in the area of machine learning based surrogate models [4–6] that provide accurate estimation of various cardiac parameters. Such models are assumed to be "globally" accurate after training on a large amount of labelled data. These models, however, pose two important limitation. First, acquisition of large amount of labelled data to train the model is very expensive. Second, parameter estimation using such models inherently assume that the real world data would fall under the scope of training data used to acquire the "global" perspective of cardiac mechanism.

In this paper, we propose a novel active-learning method for cardiac parameter estimation that tackle these limitations. We train a machine learning model using limited set of labelled data, and augment the labelled exploiting the predictive uncertainty on the test data. This process is driven with a particular focus on guiding the training process towards the unknown region of interest in parameter space. By doing so, we are able to train a model with limited labelled data but covering a larger scope of parameter space based on test-data.

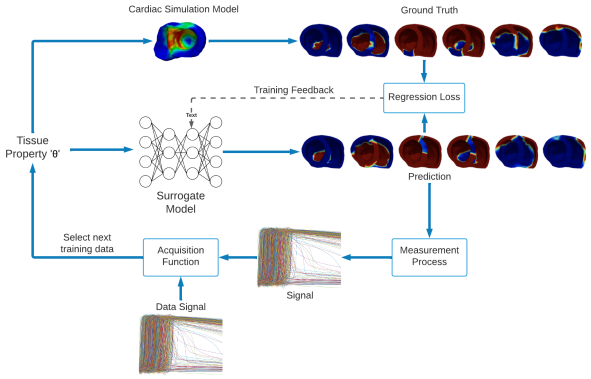

Figure 1. Block diagram of of the proposed method.

We evaluated our method on healthy heart data from MedalCare-XL dataset [7]. The dataset includes 16900 data from 13 patients equally distributed into the 8 groups (healthy control and 7 cardiac pathologies) [7]. Each data has 20 dimensional parameter space that represents important concepts like the activation location, action potential duration, etc. The data also includes 12-lead ECG data lasting 10s sampled at 500 Hz. We compared our method with a MLP based "global" model trained on large training set to learn the parameters from the input ECGs. The results demonstrate an improved accuracy of parameter estimation in our method compared to a global-ML model that too using limited labelled training data size.

2. Method

The ECG signals are considered as a function of 20 cardiac tissue parameters which represent the pacing site on the left and right ventricles, action potential duration parameters, etc.

$$y = M(\theta_1, \theta_2, ..., \theta_{20}) \quad (1)$$

where y is the ECG signal, M is the simulation model and $\{\theta_i\}_{i=1}^{20}$ are the cardiac tissue parameters.

2.1. Active Learning

The overview of the proposed active learning method is shown in Figure 1. Active learning involves first training an initial model on limited labelled data. Next, using the trained model, we estimate the cardiac parameters for given ECG signal and match the predicted signal with ground truth signal to get an error estimate as an objective function. We add the set of parameter estimated and predicted signal to the labelled data and retrain the model to update it. This process is repeated until the error estimate converges. By adding back the estimates along the way, we constantly explore the unknown region of interest and allow the model to refine on limited data in comparison to requirement of large labelled data upfront. We now look at the training and parameter estimation steps in detail.

2.2. Initial Model Training

Consider $L = (x_i, y_i)_{i=1}^{|L|}$ be the initial labeled data where x represents the tissue parameters, y represents the ECG signal and $|L|$ is the initial labelled data size. Let $T = (x_{test}, t_{test})$ be the test data where for given y_{test} ECG signal we need to estimate the parameter as close as possible to the ground truth x_{test}.

We initially train a base model $f(x)$ on the labelled data L to learn the forward relation from cardiac parameters to the ECG signal as depicted in 1. We try to reduce the error between the prediction y_{pred} and ground truth y.

$$Loss = \frac{1}{|L|} \sum_{i=1}^{|L|} (y_i - y_{pred_i}) \quad (2)$$

We train the model with dropout [8] which is known to model predictive uncertainty [9].

2.3. Parameter Estimation

Our main task is to estimate the cardiac parameter x_{est} such that the corresponding predicted ECG y_{est} is as close as possible to the actual ECG. This error between the test ECG y_{test} and y_{est} is defined as the error E:

$$E = ||y_{test} - y_{est}||^2 = ||y_{test} - f(x_{est})||^2 \quad (3)$$

Thus, our new objective function becomes:

$$\begin{aligned} x_{est} &= argmin_x E(y_{test}, y_{est}) \\ &= argmin_x ||y_{test} - f(x)||^2 \end{aligned} \quad (4)$$

We begin with a sample point of parameter x_{est} within the bounds of the parameter space x. The initial trained model provide us with ensemble of prediction due to the use of dropout and thus provide us an estimate of uncertainty in the error E. We can now use optimization method like Bayesian optimization to optimize for the cardiac parameters.

$$\begin{aligned} EI(x) = (\mu(x) - E^+)\Phi(\frac{\mu(x) - E^+}{\sigma(x)}) \\ +\sigma(x)\phi(\frac{\mu(x) - E^+}{\sigma(x)}) \end{aligned} \quad (5)$$

where, E^+ is the maximum of the objective function obtained so far, $\mu(x)$ and $\sigma(x)$ are the mean and standard deviation of the error E respectively, and ϕ and Φ are density function and CDF of the standard normal distribution respectively.

3. Experiments and Results

3.1. Setup

Experiments were performed on 1000 healthy sinus heart data from MedalCare-XL dataset[7]. Each data point includes 20 cardiac parameters which represented activation site on left ventricles (anterior endocardium, posterior endocardium and septum) and right ventricle in UVC coordinate, and action potential duration parameters. Each data also had a 12-lead ECG signal of 10s duration sampled at 500 Hz. All of the data was split into train data and test data. The train data was obtained by considering all data points that lied in intersection of 70% of apicobasal height and 70% rotation of the heart and the rest was considered as test data.

The proposed method is compared with a passive "global" neural network (MLP) model which takes 12-lead ECG as input and cardiac parameters as the output. Each ECG signal had 451 time steps thus the input to the MLP is a 5412 dimensional signal. The structure of the model was composed as 5412 - 2048 - 1024 - 512 - 20 with a batch normalization and LeakyReLU signal after each layer. The network was trained with all of the training data for 300 epochs and tested on both in and out-distribution test-data.

3.2. Results

The proposed method was initially trained on 40 labelled data followed by parameter estimation step for 100 epochs. During the process a total of 42 points were added to labelled data. In comparison, the passive model was trained with all of the training data (i.e. 300).

The mean relative error for estimated parameter of test-data are shown in Table 1. The table shows comparison

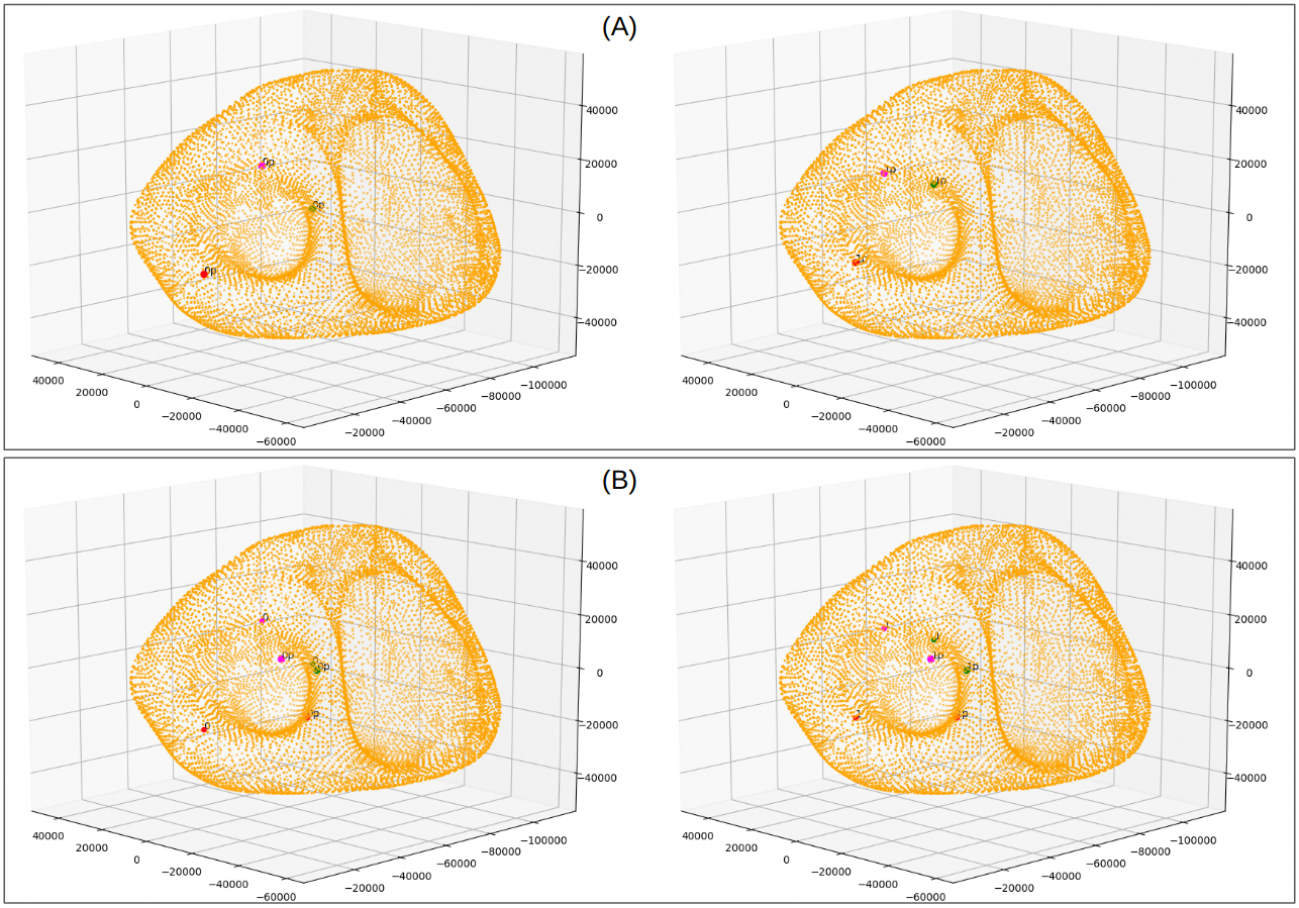

Figure 2. Estimation of activation sites on left ventricle on two test data (test data identifier 0 and 1) on proposed method (A) and passive MLP model (B). The red, green and magenta points represent activation site at anterior endocardium, posterior endocardium and septum respectively. The larger sizes on same color with 'p' added to identifier indicate the respective predictions from parameter estimation.

	p1	p2	p3	p4	p5	p6	p7	p8	p9	p10
Active Learning	**0.05**	**0.14**	**0.03**	**0.05**	**0.4**	**0.28**	**0.56**	**0.2**	**0.29**	**0.79**
Passive MLP	0.75	0.58	0.26	0.69	1.25	0.75	1.4	1.1	0.71	3.22

	p11	p12	p13	p14	p15	p16	p17	p18	p19	p20
Active Learning	**1.05**	**0.37**	**0.57**	**0.34**	**0.18**	**0.42**	**1.02**	**0.24**	**0.24**	**1.21**
Passive MLP	2.1	1.71	2.1	0.84	0.92	1.91	3.31	0.82	0.9	2.73

Table 1. Mean relative error over all in-distribution data across the 20 dimensional parameter space for proposed method (Active learning) and passive/global model (MLP)

of our-proposed method (Active Learning) with the global model across all 20 parameters. The results show that our proposed method has a low relative error on prediction of cardiac parameter across all dimensions in comparison to the "global" model. This shows improved parameter estimation capability of active learning driven model in compare to the globally trained model.

The visualization of activation site on the left ventricle (anterior endocardium - red, posterior endocardium - green and septum - magenta) are shown in Figure 2. Figure 2A shows active learning based method was able to exactly predict the activation site (shown by the overlap of ground truth and prediction activation site). The global model, despite being trained with a larger training size, was not able to capture the activation site as shown inf Figure 2B.

4. Discussion

The quantitative and qualitative results above show the advantage of our proposed method in comparison to using a surrogate trained on a large labelled data. We demonstrate the benefit of our method in two ways. First, in terms of the number of labelled data required. The global model was trained on entire training data to learn the relation from ECG to cardiac parameters but despite such large dataset the results showed a lacking performance. On the other hand, the active learning model was trained total of 82 data points and yet was able to estimate parameters more accu-

rately. This is particularly due to the second benefit of our method i.e. intelligent search of data to be labelled. During active learning step, we use the uncertainty in the error between the ground truth ECG and its prediction to search for data to be labelled in unknown region in parameter space. This intelligent steering of simulation to generate next data to be labelled helps cover a larger scope of parameter space and updates the model with fewer data than used in the other surrogates.

5. Conclusion

We propose a cardiac tissue parameter estimation framework for personalized model using an active-learning approach by exploiting the predictive uncertainty. Experiments showed that the performance of the active learning based parameter estimation model outperformed machine learning surrogate on both the number of training data required as well as the relative error performance. We showed that exploiting predictive uncertainty allows us to intelligently select the data required to update the model and improve estimation of the parameters circumventing the requirement of large number of training data which is both expensive and unavailable in almost all situations. Future works will examine this observation in a larger cohort as well as data with cardiac problems.

Acknowledgments

This study was supported by funding provided by National Institutes of Health (NIH)/National Heart, Lung, and Blood Institute (NHLBI) award R01HL14559, and National Science Foundation (NSF) award OAC-2212548. This research was also funded by InstaTwin grant FO999891133 from the Austrian Research Promotion Agency (FFG)

References

[1] Chakshu NK, Sazonov I, Nithiarasu P. Towards enabling a cardiovascular digital twin for human systemic circulation using inverse analysis. Biomechanics and modeling in mechanobiology 2021;20(2):449–465.

[2] Prakosa A, Arevalo HJ, Deng D, Boyle PM, Nikolov PP, Ashikaga H, Blauer JJ, Ghafoori E, Park CJ, Blake III RC, et al. Personalized virtual-heart technology for guiding the ablation of infarct-related ventricular tachycardia. Nature biomedical engineering 2018;2(10):732–740.

[3] Arevalo HJ, Vadakkumpadan F, Guallar E, Jebb A, Malamas P, Wu KC, Trayanova NA. Arrhythmia risk stratification of patients after myocardial infarction using personalized heart models. Nature communications 2016;7(1):11437.

[4] Babaei H, Mendiola EA, Neelakantan S, Xiang Q, Vang A, Dixon RA, Shah DJ, Vanderslice P, Choudhary G, Avazmohammadi R. A machine learning model to estimate myocardial stiffness from edpvr. Scientific Reports 2022; 12(1):5433.

[5] Zhou Y, He Y, Wu J, Cui C, Chen M, Sun B. A method of parameter estimation for cardiovascular hemodynamics based on deep learning and its application to personalize a reduced-order model. International Journal for Numerical Methods in Biomedical Engineering 2022;38(1):e3533.

[6] Dhamala J, Ghimire S, Sapp JL, Horáček BM, Wang L. High-dimensional bayesian optimization of personalized cardiac model parameters via an embedded generative model. In Medical Image Computing and Computer Assisted Intervention–MICCAI 2018: 21st International Conference, Granada, Spain, September 16-20, 2018, Proceedings, Part II 11. Springer, 2018; 499–507.

[7] Gillette K, Gsell MA, Nagel C, Bender J, Winkler B, Williams SE, Bär M, Schäffter T, Dössel O, Plank G, et al. Medalcare-xl: 16,900 healthy and pathological 12 lead ecgs obtained through electrophysiological simulations. arXiv preprint arXiv221115997 2022;.

[8] Gal Y, Ghahramani Z. Dropout as a bayesian approximation: Representing model uncertainty in deep learning. In international conference on machine learning. PMLR, 2016; 1050–1059.

[9] Gal Y, Islam R, Ghahramani Z. Deep bayesian active learning with image data. In International conference on machine learning. PMLR, 2017; 1183–1192.

Address for correspondence:

Pradeep Bajracharya
1 Lomb Memorial Drive, Rochester, NY-14623, USA
pb8294@rit.edu