Volumetric Prediction of Cardiac Electrophysiology using a Heart Model Personalised to Surface Data

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Abstract. Predictive cardiac electrophysiology models can provide a substantial aid in the success of the treatment of cardiac arrhythmias. Sufficiently accurate model predictions highly depend on the personalisation of the model i.e. estimation of patient-specific model parameters. In this paper, we evaluate the prediction ability of a simplified ionic 3D cardiac electrophysiology model, the Mitchell-Schaeffer model (2003), after personalisation. The personalisation is performed by optimising the model parameters, using the epicardial surface depolarisation and repolarisation maps obtained *ex-vivo* from optical imaging of large porcine healthy heart. We also evaluate the sensitivity of the personalisation method to a pacing location and the estimated parameter values. This is done by comparing the personalisation results obtained with left ventricle endocardial pacing location to those obtained with right ventricle epicardial pacing location. Later, using the personalised electrophysiology model, we predict the volumetric depolarisation and repolarisation time isochrones for right ventricle endocardial and left ventricle epicardial pacing locations and evaluate the epicardial isochrones against the actual maps obtained from the optical data.

1 Introduction

Modeling of the cardiac electrophysiology has been an important research interest for the last decades, but in order to translate this work into clinical applications, there is an important need for personalisation of such models, i.e. estimation of the model parameters which best fit the simulation to the clinical data. Cardiac model personalisation is required to develop predictive models that can be used to improve therapy planning and guidance. For instance, Radiofrequency (RF) ablation therapy on patients suffering from atrial fibrillation and ventricular tachycardia has a success rate of only 50% due to non availability of clinical consensus on optimum RF ablation patterns. Thus the procedure is a trial and error process highly depending on cardiologist experience. Whereas personalised cardiac models could provide sufficiently accurate and optimum RF ablation patterns, consecutively increasing the success rate of RF therapy. In this paper, we propose a robust personalisation method for cardiac electrophysiology and apply it to test the prediction of a personalised model. The personalisation

and prediction evaluation are done using the fusion of optical and MR imaging, in order to have high quality *ex-vivo* data for the evaluation.

A variety of mathematical models describing the cardiac electrophysiology have been developed and simulated at various scales. These models can be broadly categorised into three main categories: Ionic Models (IM), Phenomenological Models (PM) and Eikonal Models (EM). IM [1] characterise ionic currents flowing through the cardiac cell membrane and have a lot of parameters and variables, thus are not well suited to solve inverse problem. However they do have analytic biological interpretation of the parameters and their influence on the behavior of the model. EM [2] are very simple, describing only the time at which a depolarisation wave reaches a given point without precisely modeling the reaction part. At the intermediate level are PM [3], which describe the action potential generation and propagation along the cell membrane, and are divided into mono-domain, modeling the transmembrane potential variable, and bi-domain modeling the intra- and extra-cellular potential variables. Here, we personalise the Mitchell-Schaeffer model [4], described by two nonlinear ordinary differential equations for transmembrane potential variable and a gating variable for sodium current depicting the repolarisation phase.

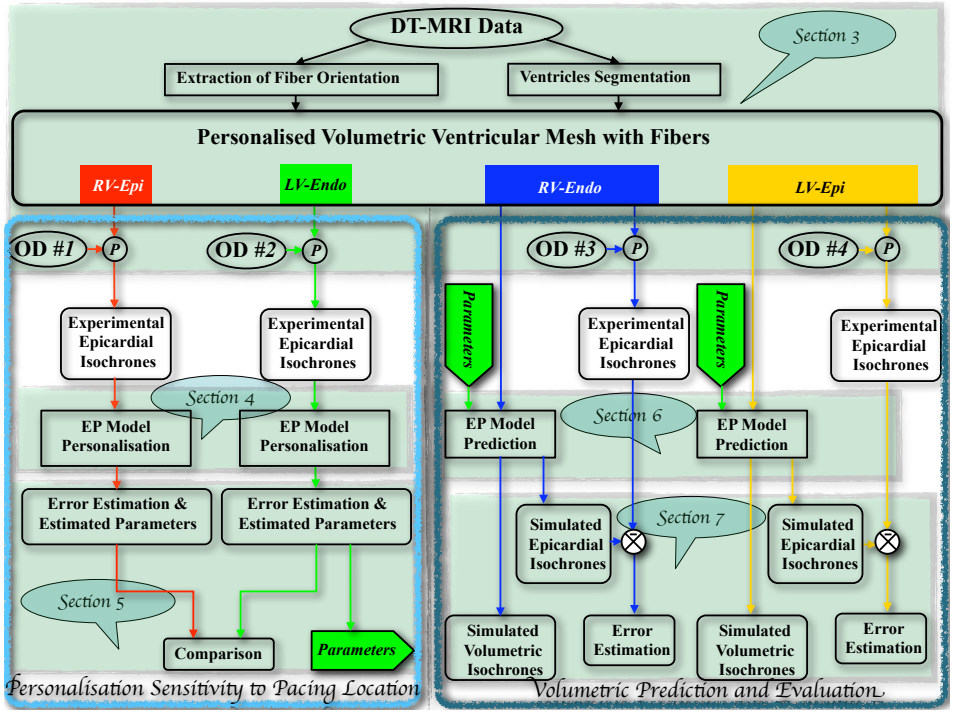


Fig. 1. A Flowchart describing the outline of the paper, where OD: Optical Data, P: Projection and EP: Electrophysiology, with Pacing Locations LV-Epi, RV-Epi, LV-Endo and RV-Endo

Authors have focused recently on the estimation of parameters using EM [5] and PM [6], but only on 2D surface, whereas personalisation of PM on 3D volumes [7] was studied but without any prediction analysis. The two main contributions of this paper is outlined in Fig.1 and they are 1) The estimation of the sensitivity of the personalisation method to a pacing location and 2) A quantitative evaluation of the predictive power of the personalised model. Moreover we use here the Mitchell-Schaeffer model which has a better physiological justification than the Eikonal and Aliev-Panfilov models used in the cited papers.

2 Electrophysiology Model Simulation

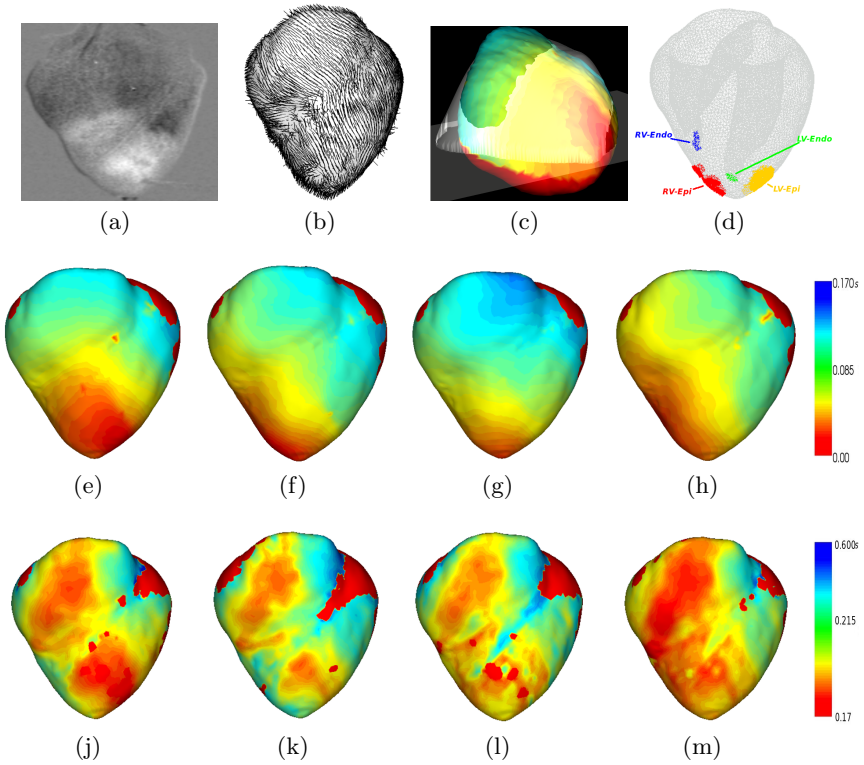
Mitchell-Schaeffer (MS) model [4] is a simplified ionic model derived from the Fenton Karma (FK) [8] ionic model. The MS model contains two ODEs corresponding to sodium and potassium currents:

$$\begin{cases} \partial_t u = div(D\nabla u) + \dfrac{zu^2(1-u)}{\zeta_{in}} - \dfrac{u}{\zeta_{out}} + J_{stim}(t) \\ \partial_t z = \begin{cases} \dfrac{(1-z)}{\zeta_{open}} \; if \; z < z_{gate} \\ \dfrac{-z}{\zeta_{close}} \quad if \; z > z_{gate} \end{cases} \end{cases} \tag{1}$$

u is a normalised transmembrane potential, and z is the gating variable for sodium ion influx which depicts the repolarisation phase. $J_{in} = (zu^2(1-u))/\zeta_{in}$ represents the combination of inward sodium current which raises the action potential voltage and $J_{out} = -u/\zeta_{out}$ represents the outward potassium current that decreases the action potential voltage describing repolarisation. J_{stim} is the stimulation current, at the pacing location. The parameters ζ_{open} and ζ_{close} control the repolarisation variable, with ζ_{close} directly related to the Action Potential Duration (apd). The diffusion term in the model is controlled by the diffusion tensor D. This spatial diffusion can be related to a pseudo-conductivity. In the longitudinal direction of the fibre, this pseudo-conductivity is set to d which is one of the parameters we adjust, and to $d/2.5^2$ in the transverse directions. This electrophysiology model is spatially integrated using a tetrahedral mesh of the myocardium created from MR image, taking into account the fiber orientation as well, and is temporally integrated using an optimum time integration scheme. Here optimality is defined as the best compromise between computational time and accuracy. Several time integration schemes were tested, and for MS model the optimum time integration scheme is Modified Crank-Nicolson/Adams-Bashforth (MCNAB) scheme [9] with $\delta t = 0.1ms$ and optimum edge length $h = 1.5mm$, with one time step computation time $\approx 1s$.

3 Optical and DT-MR Image Data

In this paper we performed the adjustments using optical recordings obtained on a healthy porcine heart. The experimental setup is similar to the one described in details in [10].The data acquired allows the fusion of anatomical MRI, Diffusion tensor MRI and optical imaging. We thus obtain electrical activation maps on a volumetric myocardial mesh with local fiber orientation.



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

(e) (f) (g) (h)

(j) (k) (l) (m)

Fig. 2. (a) Optical Data, (b) Volumetric myocardial mesh generated from DT-MRI data with fibres, (c) Projection of depolarisation time isochrones (in s) derived from the filtered optical data to Volumetric Myocardial Mesh, (d) 4 pacing locations for LV-Epi, RV-Epi, LV-Endo and RV-Endo, (e) - (h) epicardial depolarisation isochrones and (j) - (m) repolarisation isochrones for LV-Epi, RV-Epi, LV-Endo, RV-Endo successively.

We use here 4 different optical datasets from the same heart, paced at a frequency of 1.1 Hz, but obtained using 4 different pacing locations:
Near the apex of :-

- The Left Ventricle Epicardium (LV-Epi) (marked as yellow).
- The Right Ventricle Epicardium (RV-Epi) (marked as red).
- The Left Ventricle Endocardium (LV-Endo) (marked as green).
- The Right Ventricle Endocardium (RV-Endo) (marked as blue).

4 Electrophysiology Model Personalisation

Estimation of the model parameters that result in a simulation which is similar to the measured data is defined as personalisation. Here, we match both the depolarisation time isochrones and the action potential duration, both derived from the optical data. The adjustment of d in order to match the depolarisation isochrones is achieved in two successive phases (Calibration and Iterative Adjustment) while ζ_{close} is estimated in a direct manner.

Calibration : This step is used to initialise the model parameter values using analytical relationships between the measures and the parameters. The calibration function used here is similar to [7] and is given as $c(d) = \alpha\sqrt{d} + \beta$, where c is the conduction velocity and the constants α and β are determined by performing several model simulations for a range of d and computing corresponding c, and then fitting the function in non-linear least squares sense to the measures c. Once the relationship is estimated, it is used to determine the initial parameter value d for the median value of c computed for the actual reference data.

Iterative Adjustment : This step is used to optimise the d parameters with calibration result as initial guess. In order to keep computations reasonable, we divide the left ventricle into 17 zones as defined by American Heart Association (AHA) and a similar division of 9 zones for the right ventricle, when an iterative adjustment is performed. The algorithm used here is a trust region method [11] which finds the minimum of a subproblem, such as a quadratic model created using gradient and approximate hessian matrix at the current search point, and which is implemented using the Trilinos solver package. Here we use an objective function that minimises the difference between the simulated and measured depolarisation times by iteratively adjusting the d parameter value for each zone.

For ζ_{close}, the maximum action potential duration for a single cardiac cycle is directly given by the model [4] as follows: $apd = \zeta_{close} ln(1/h_{min})$ where $h_{min} = 4\zeta_{in}/\zeta_{out}$. As we only have one measured apd available from the data, we choose to adjust ζ_{close}, while keeping the other parameter values from the literature. It is defined by the model that c has no relationship with ζ_{close}, which provides no coupling between the action potential duration and the conduction velocity. Thus we can simultaneously adjust parameter d and ζ_{close}. The defined relationship between ζ_{close} and apd remains valid also in 3D thus allowing us to directly estimate locally at each vertex, the parameter ζ_{close} without calibration and iterative adjustment. The parameter ζ_{close} is estimated locally at each vertex for the epicardium and the mean of the epicardial values for a given zone is assigned to the remaining zone vertices, as shown in Fig.6.

The personalisation method described here is generic and could be used for clinical applications, where optical epicardial data can be replaced by clinical electro-anatomical mapping data for the endocardium.

5 Personalisation Sensitivity to Pacing Location

To evaluate the sensitivity of the personalisation method and the estimated parameter values to a pacing location, First we personalise the model with two different pacing locations: right ventricle epicardium and left ventricle endocardium. Then we compare the apd and depolarization time errors after personalisation and the estimated parameter values for both pacing locations. As the electrophysiology personalisation is performed on the same heart but under different scenarios (pacing locations), we should expect the personalisation results to be similar, thus low sensitivity of the personalisation method to different pacing locations. Before model personalisation, the error maps for apd and de-

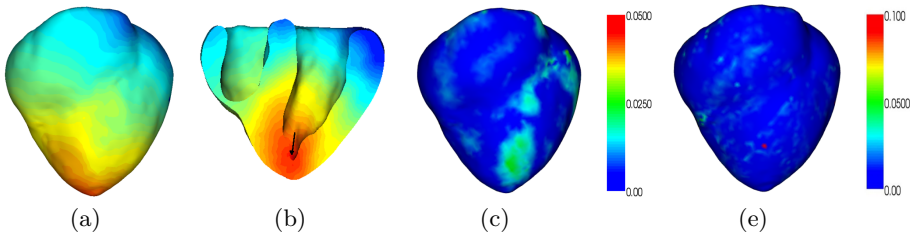


Fig. 3. After Personalisation with LV-Endo (arrow), the simulated volumetric isochrones for depolarisation time (a) Epicardial view (for values refer Fig.2), (b) Long axis view, (c) the depolarisation time error maps,and (d) the *apd* error maps. (in *s*)

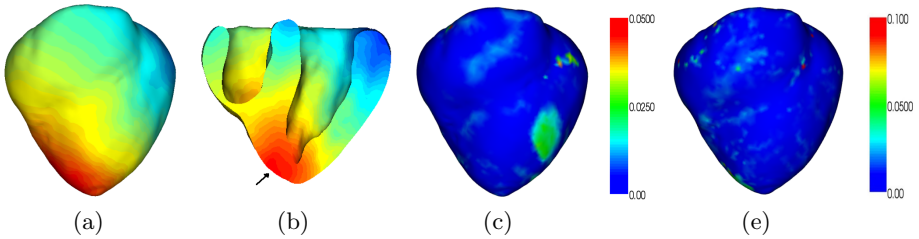
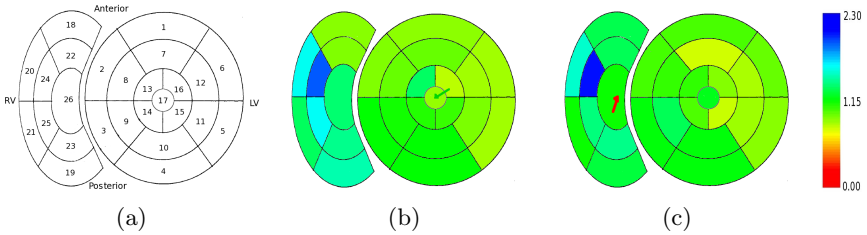


Fig. 4. After Personalisation with RV-Epi (arrow), the simulated volumetric isochrones for depolarisation time (a) Epicardial view (for values refer Fig.2), (b) Long axis view, (c) the depolarisation time error maps,and (d) the *apd* error maps. (in *s*)

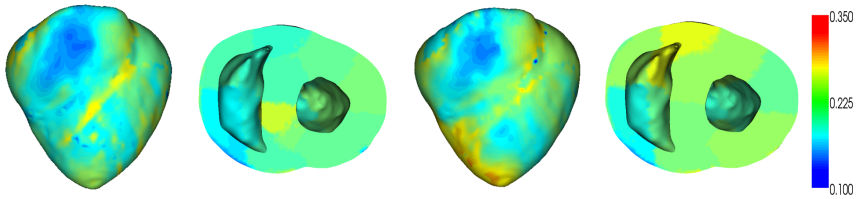
polarisation times are computed using a simulation with the parameter values given from literature.

Comparison of the Estimated Parameter Values and Errors : From depolarisation time error maps with two different pacing locations (Fig.3(c) and 4(c)), one can observe that the personalisation method does reduce the overall error with both pacing locations and also it is able to locate the areas having high variation in conduction velocity irrespective of the pacing location (near the apex of LV, as shown in both the error maps). And the *apd* error maps also shows less error with both pacing locations (Fig.3(e) and 4(e)). This shows low sensitivity of the application of the personalisation method for different pacing locations. Fig.5 and Table.1 shows a quantitative comparison of the estimated parameter d with both pacing locations used for personalisation. Here we can observe that the parameter values are mostly similar with both pacing locations, except in regions surrounding the pacing location, which is mainly due to sudden increase in the conduction velocity with the square wave stimulus applied at the pacing location. Whereas the locally estimated parameter ζ_{close} with both pacing locations is also similar as shown in Fig.6 and Table.1. This analysis does show the low sensitivity of the personalisation results irrespective of the pacing location.



(a) (b) (c)

Fig. 5. (a)AHA division for LV and RV, Estimated Parameter d comparison after personalisation with pacing location LV-Endo(b)(green arrow) and RV-Epi(c)(red arrow).



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

Fig. 6. Estimated Parameter ζ_{close} comparison after personalisation with pacing location LV-Endo (a) (b), and RV-Epi (c) (d) (Epicardial and Myocardial (SA) views).

6 Volumetric Electrophysiology Model Prediction

After EP model personalisation using the epicardial surface data for a given pacing location scenario, the model is then used to predict volumetric simulations for different pacing location scenarios. Here we use the estimated EP model parameters d and ζ_{close} obtained with personalisation to a pacing location on the endocardium (LV-Endo), to predict volumetric simulations for pacing locations on the endocardium (RV-Endo) and on the epicardium (LV-Epi).

7 Quantitative Evaluation of EP Model Prediction

Here, we estimate the volumetric predictive power of the EP model for different pacing location scenarios on the endo- and epicardium (RV-Endo and LV-Epi), after personalisation to a *different pacing location* on the endocardium (LV-Endo). A quantitative evaluation of depolarisation time and *apd* error maps is obtained with predicted epicardial isochrones against the actual experimental maps as shown in the Fig.2. This evaluation is shown in (Fig.7(c),8(c)) and (Fig.7(d),8(d)), also stated in Table.1

8 Discussion

In this work, we have described a personalisation method for a simplified ionic model (MS) in 3D, using epicardial activation maps obtained with optical imag-

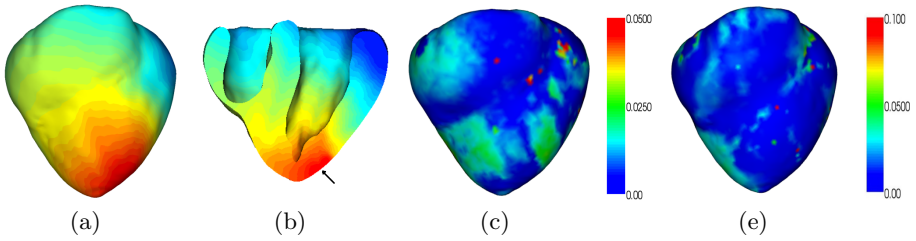


Fig. 7. After Prediction with LV-Epi (arrow), the simulated volumetric isochrones for depolarisation time (a) Epicardial view (for values refer Fig.2), (b) Long axis view, (c) the depolarisation time error maps,and (d) the *apd* error maps. (in s)

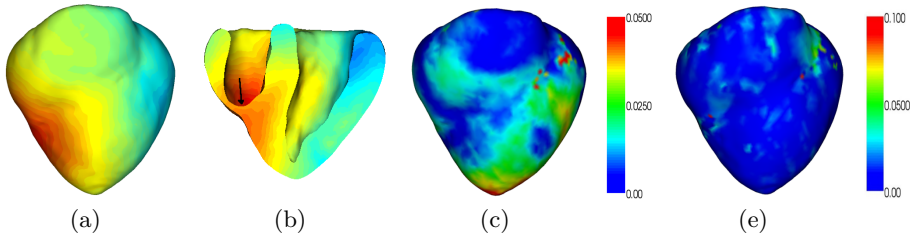


Fig. 8. After Prediction with RV-Endo (arrow), the simulated volumetric isochrones for depolarisation time (a) Epicardial view (for values refer Fig.2), (b) Long axis view, (c) the depolarisation time error maps,and (d) the *apd* error maps. (in s)

	Pacing Location	Parameter d $(\Delta \pm \sigma)$		Mean D Error (ms)	Parameter ζ_{close} $(\Delta \pm (\sigma \times 10^{-4}))$		Mean *apd* Error (ms)
		LV	RV		LV	RV	
1.	LV-Endo	0.95 ± 0.03	1.36 ± 0.16	5.48	0.22 ± 1.25	0.20 ± 4.90	4.98
	RV-Epi	0.96 ± 0.03	1.38 ± 0.11	4.31	0.22 ± 3.04	0.21 ± 6.81	4.73
2.	LV-Epi	-	-	12.16	-	-	8.62
	RV-Endo	-	-	17.21	-	-	7.32

Table 1. Comparison of the estimated parameter values and the mean errors for personalisation (1.) and following prediction (2.) using the estimated parameter values. (Depolarisation time-D, Mean-Δ, Standard Deviation-σ)

ing. Next, we have evaluated the sensitivity of our personalisation method in terms of application to different pacing locations and reproduction of same estimated parameter values irrespective of the pacing location. Last, using the personalised electrophysiology model with a given pacing location on the epicardium, we predicted the depolarisation time isochrones and *apd* for different pacing locations on epi- and endocardium. Volumetric Prediction results did show a good match between simulated and actual epicardial depolarisation and repolarisation time isochrones, for both pacing locations. Such valid cardiac electrophysiology predictions of a personalised model with different pacing locations

on epi- and endocardium opens up possibilities for clinical applications, where typically only the endocardial surface can be mapped and often has an ambiguity of the pacing location. However, we also need to adjust the restitution properties of the myocardium in order to have valid model predictions also at different heart rates, which is important in arrhythmias. This is the topic of our current work.

Acknowledgements

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