A PREDICTIVE PATIENT SPECIFIC MODEL FOR THE HUMAN ATRIUM

C. Corrado¹, S. Williams¹, G. Plank², M. O’Neill¹, and S. Niederer¹

¹King’s College London, London, SE17EH, {cesare.corrado, steven.williams, mark.oneill, steven.niederer}@kcl.ac.uk
²Medical University of Graz, Harrachgasse 21, 8010, Graz gernot.plank@medunigraz.at

SUMMARY

We propose and validate a novel method to generate patient-specific models of the left atrium that captures tissue heterogeneities. A personalised model is generated from a set of measured local activation times (LATs) obtained by pacing the left atrium in the proximity of the coronary sinus with an $s_1$-$s_2$ pacing protocol. The model is then validated by evaluating the correlation between a set of measured LATs, obtained by pacing on the high right atrium and a set numerically computed LATs. Validation is performed on 4 clinical cases.

Key words: Patient-specific models, local activation times, parameter fitting

1 INTRODUCTION

Atrial fibrillation (AF) is a common arrhythmia, affecting almost 2.5 million people in the US, [1] and is associated with an increased incidence of cardiovascular disease, stroke and premature death [2]. Biophysical model enabled the study of the mechanisms that underpin arrhythmia’s in the ventricle and the atria, [3]; however, their inability to capture the significant variability in physiology typical of AF patients limits their potential to make quantitative predictions of patient response to treatment and thus to inform clinical procedures. In this work we apply the algorithm developed in [4] to locally constrain the model parameters of the modified Mitchell-Schaeffer (mMS) ionic model [5], when the conduction velocity (CV) restitution and the effective refractory period (ERP) are known for a single $s_1$ cycle length. Differently from other data assimilation techniques, [6] this approach allows the generation of locally personalised computational models of the human atrium in a clinical time scale when local tissue variability is not negligible. Local parameter values are constrained from a set of LATs obtained by applying an external stimulus in the proximity of the coronary sinus (CS), following an $s_1$-$s_2$ pacing protocol [7], and measuring the local electrograms (EGM) with a multi-polar catheter. The model is then validated by comparing the LATs generated by applying the $s_1$-$s_2$ pacing protocol and stimulating on the high right atrium region (HRA), with those obtained by numerical simulations of the same experiment. The validation process is applied on 4 clinical cases.

2 METHODS

From a set of LATs recording, local CV restitutions are evaluated with the procedure described in section 2.1 and then used to locally constrain the model parameters as described in section 2.2. From the evaluated local parameter values, a computational model is finally obtained as described in section 2.3. The pipeline to generate a computational model from multi-polar catheter measurements is depicted in Figure 1.
Figure 1: Sketch of the pipeline used to generate the computational model

Table 1: Parameter values used for building the data set. A set of parameter values ranging from the minimum to the maximum value in increments of the step value is created. The data set of candidate solutions was generated by models with each of the permutations of the Cartesian products of all of the parameter value sets.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>min</th>
<th>0.25</th>
<th>0.05</th>
<th>1.0</th>
<th>65</th>
<th>65</th>
</tr>
</thead>
<tbody>
<tr>
<td>max</td>
<td>4.0</td>
<td>0.4</td>
<td>9.0</td>
<td>215</td>
<td>185</td>
<td></td>
</tr>
<tr>
<td>step</td>
<td>0.375</td>
<td>0.05</td>
<td>1</td>
<td>10</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

2.1 LATs and local CV evaluation

An external stimulus is applied either on CS or on the HRA and following an \( s_1 \), \( s_2 \) pacing protocol where 3 stimuli are applied with an inter-pacing interval \( s_1 = 470 \text{ ms} \), followed by a premature pacing \( s_2 \). The protocol is repeated for 28 values of \( s_2 \), ranging between 343 and 200 ms. Bipolar EGM were recorded on the surface of the left atrium with a multi-polar catheter and up to 100 locations per case. For each location an EGM was available, LATs were evaluated as the time corresponding to the first peak on the EGM trace, and then linearly interpolated on the region covered by the catheter. For each \( s_2 \) applied in the pacing protocol, local CV modulus was determined as the inverse of the magnitude of the gradient of LATs and used to build local CV restitution curves.

2.2 Local electrophysiology and parameter fitting

Atria tissue electrophysiology is modelled with the mono-domain approximation \([8]\) of the bidomain model \([9]\), when intra- and extra- cellular conductivities are proportional up to a constant. The mMS ionic model described in \([5]\) was chosen to characterise the source term; similarly to the original Mitchell-Schaeffer model \([10]\), mMS captures the measured CV and ERP restitution properties with the smallest numbers of parameters to constrain, and it is proven to be stable to pacemaker behaviour independently of the choice of its parameter values. Parameters are fitted by applying the algorithm described in \([4]\); this algorithm fits the CV restitution and the ERP value (here approximated by the \( s_1 \), \( s_2 \) functional block) to a set of pre-computed CV restitutions and ERP, obtained by solving a computational model with a set of known parameters. In this work, a data set of 16436 restitutions were evaluated with the parameter values summarised in Table 1, and keeping the gate potential value fixed and equal to \( v_{\text{gate}} = 0.05 \).

2.3 Computational model

The parameter values were interpolated on regions where no measurements were available through a harmonic extension operator; a Gaussian filter with covariance \( \sigma^2 = 2 \) and a median filter were then applied to smooth the parameter values and to remove possible outliers. A computational mesh with an imposed edge length \( h = 215 \mu\text{m} \) was generated on the 2D surface describing the anatomy and obtained from the NavX electroanatomical mapping system. The computational model was then discretized in space with linear finite elements;
the non-linear term describing the ionic current was treated with a splitting technique. The ionic model was discretized in time with a forward-Euler scheme, while the diffusive parabolic PDE with a Crank-Nicholson scheme; a constant time step $dt = 50\mu s$ was chosen for both sub-problems. Simulations were performed with the Cardiac Arrhythmias Package (CARP), an electrophysiology solver suitable for hyper-computing.

3 VALIDATION PROCESS

A set of LATs were computed by simulating the atrium electrophysiology following an external stimulus applied on the HRA and with the $s_1,s_2$ pacing protocol, with $s_2 = [280, 292, 298, 304, 310, 322, 329, 336, 343]$. On the computational model, the external stimulus was applied to the circular region with radius $R = 1$ and centred on the measured early depolarisation for a coupling interval $s_2 = 343\,\text{ms}$. For each of the $s_2$ considered in the validation process, the mean difference between the measured and the computed LATs was evaluated and used as an offset on the computed LATs; this to take into account of the time required by the depolarization front to propagate from the right atrium to the left atrium. The correlation between computed and measured LATs was then evaluated through 4 indicators: the linear regression coefficients $(m,q)$ of the regression line $y = mx + q$, where points $(x,y)$ correspond to the measured and computed LATs and over the whole set of coupling interval $s_2$ tested in the validation; the coefficient of determination $r$ between measured and computed LATs; and $sl$ expresses the ratio between the two principal components of the covariance. The overall validation process is depicted in Figure 2.

4 RESULTS AND CONCLUSIONS

The validation of the proposed method was applied to 4 cases suffering from paroxysmal atrial fibrillation who underwent to pulmonary veins isolation. For each clinical case, the scatter plot of the measured and computed LATs is depicted in Figure 3, while the indicators are summarised in Table 2.

Case 1 to 3 presented small discrepancies between measured and evaluated data, while all the cases presented a coefficient of determination greater than 0.8 and a ratio between the principal components of the covariance not greater than 0.1.

REFERENCES

Figure 3: Scatter plot of the estimated (y-axis) vs measured (x-axis) LATs; each colour corresponds to a different $s_2$ coupling interval. The linear regression line $y = mx + q$, is plotted in red, the line $y = x$ in black. The red ellipse corresponds to the covariance ellipsoid of $x$ and $y$.

<table>
<thead>
<tr>
<th>Case</th>
<th>$m$</th>
<th>$q$</th>
<th>$r$</th>
<th>$sl$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.09</td>
<td>-8.91</td>
<td>0.91</td>
<td>0.05</td>
</tr>
<tr>
<td>2</td>
<td>1.06</td>
<td>-7.37</td>
<td>0.89</td>
<td>0.06</td>
</tr>
<tr>
<td>3</td>
<td>1.04</td>
<td>-5.26</td>
<td>0.9</td>
<td>0.05</td>
</tr>
<tr>
<td>4</td>
<td>0.95</td>
<td>4.94</td>
<td>0.81</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Table 2: Correlation indicators for each of the 4 cases


