Synthetic Echocardiographic Image Sequences for Cardiac Inverse Electro-Kinematic Learning

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Abstract. In this paper, we propose to create a rich database of synthetic time series of 3D echocardiography (US) images using simulations of a cardiac electromechanical model, in order to study the relationship between electrical disorders and kinematic patterns visible in medical images. From a real 4D sequence, a software pipeline is applied to create several synthetic sequences by combining various steps including motion tracking and segmentation. We use here this synthetic database to train a machine learning algorithm which estimates the depolarization times of each cardiac segment from invariant kinematic descriptors such as local displacements or strains. First experiments on the inverse electro-kinematic learning are demonstrated on the synthetic 3D US database and are evaluated on clinical 3D US sequences from two patients with Left Bundle Branch Block.

1 Introduction

Despite advances in both medical image analysis and intracardiac electrophysiological mapping technology, the understanding of the relationship between the cardiac electrophysiology and the cardiac motion visible in images is only partial. However such understanding would be very valuable as it would open possibilities in non-invasive electrophysiological mapping. Since 3D echocardiography (US) is readily available, an important topic of interest for cardiologists would be the estimation of the cardiac electrophysiology function from the analysis of 3D US images. This is specifically important, for example, in the evaluation of the Cardiac Resynchronization Therapy (CRT) where the placement and tuning of pacemaker leads play a crucial role in the outcome of the therapy. In this context, cardiologists need to interpret time series of US images in order to detect and characterize kinematic patterns (motion asynchrony, delayed contraction) and then infer possible electrical conduction disorders.

While there is an important literature on the estimation of the cardiac kinematics from 3D US sequences (see for instance [3] and references therein), there exists no such tools to estimate the electrical wave propagation from such image sequences. However, the relationship between cardiac motion and electrical activation has been investigated in several studies [5–7].

In this paper, we propose to study the inverse electro-kinematic relationship through the creation of a large database of synthetic 3D US images. Because it is difficult to obtain a large number of cases where both electrophysiological mapping and 3D US images are available, we use an electromechanical (E/M) model of the heart to produce synthetic but realistic image sequences for which the electrical stimulation is known. Previous work [6, 7] has mainly focused in detecting E/M wave directly from the displacement and strain patterns estimated from image sequences during the contraction and relaxation of the myocardium. Since the relationship between those mechanical waves and electrical waves is certainly complex, our approach is to learn it through an E/M model of the heart. Compared to [5], instead of estimating displacements and strains from the E/M model, we propose a more realistic estimation by first simulating 3D US images and then using an image-based motion tracking algorithm. Furthermore, rather than learning the activation forces over time, we have chosen to learn the depolarization times of all American Heart Association (AHA) segments. Finally, our learning approach is optimized in order to detect which kinematic descriptor is most correlated with the electrophysiology waves.

Different studies have been conducted for the creation of simulated 3D US sequences, e.g. [2, 3]. Instead of simulating the ultrasonic image formation process, in this paper, we propose a new approach to create synthetic 3D US sequences by deforming a real 3D US sequence and combining simulated myocardium displacements with the visible motion of the surrounding environment (blood pool speckle, mitral valve). This approach has the advantage of providing a realistic 3D US sequence at little computational cost and including all neighboring structures. A vast database of electrical propagations along with corresponding synthetic sequences based on the E/M simulation was created. On this database, invariant kinematic descriptors were extracted from each synthetic sequence and then fed to a machine learning algorithm which estimates the electrical pattern from kinematic descriptors during the cardiac cycle. The created synthetic 3D US sequences are of realistic quality and first experiments on the inverse electro-kinematic learning using this database are discussed.

2 Creating Synthetic 3D US Sequences

2.1 3D US Sequence Non-Rigid Registration

We use as input to our method a real 3D US sequence acquired by the iE33 Philips probe on a patient suffering from heart failure. The first step in the pipeline was to segment semi-interactively or automatically the left ventricle (LV). The binary mask was then used to apply the iLogDemons non-rigid registration algorithm [4] which had been applied in the cardiac cine MR sequence analysis. This motion tracking algorithm enforces the incompressibility of the myocardium during the cardiac motion which provides an additional prior information to regularize the visible motion in the image sequence. With this non-rigid registration algorithm, the displacement field (DF) u between the end diastole (ED) image and each image of the real 3D US sequence was estimated

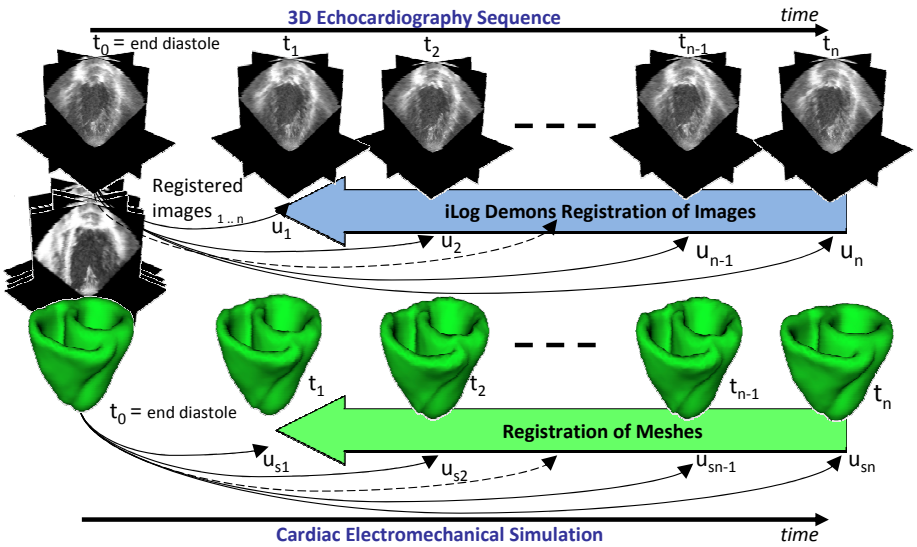

Fig. 1. Registration of Images and Meshes. iLog Demons registration method is applied to all images in the sequence to register them to the ED reference image. All meshes in a simulation cycle are also registered to the ED mesh.

(see Fig. 1). Thanks to the diffeomorphic nature of u, we computed its inverse and thus resampled each image of the sequence in the ED geometry.

2.2 Deformation of Registered 3D US Images Using E/M Simulation

From the segmented images of the myocardium at ED, we created a computational tetrahedral mesh which was suitable for the simulation of a cardiac E/M model [8] whose myocardium motion is used for the generation of the synthetic sequences. This required additional work since only part of the LV and right ventricle (RV) were visible in the image. Registration of a template mask of the 2 ventricle was used to infer the missing parts.

With this model, we simulated the cardiac motion after specifying an electrophysiological pattern (see Section 2.3). We sampled the cardiac simulated motion to follow the temporal resolution of the real 3D US sequence and then computed the DF between the reference configuration (ED) and the deformed position at each time of the sequence using the linear interpolation of the displacement of each vertex of the tetrahedral mesh rasterized in a 3D image having the same size and spatial resolution as the real 3D US image (see Fig. 2). This dense synthetic DF of the myocardium was then merged with the DF estimated from the non-rigid registration. The synthetic DF completely overwrites the registration DF within the myocardium. Additionally, the synthetic DF within the eroded myocardium is diffused by solving the Laplace equation and fused with

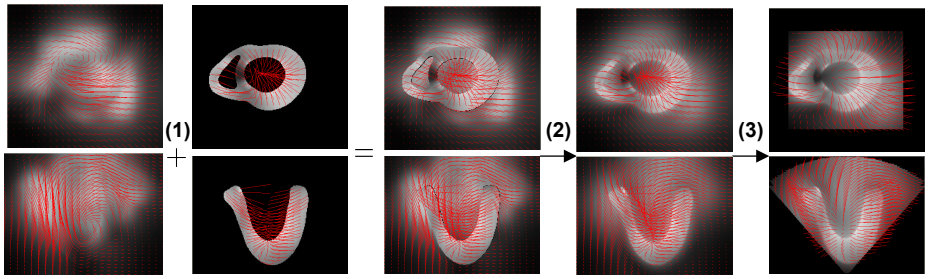

Fig. 2. Fusion of the Displacement Fields. (1) The DF estimated from the iLog Demons registration (left) is combined with the myocardium DF from the E/M simulation (second left). The two fields are fused, (2) smoothed, (3) inversed and cropped along the acquisition cone.

the registration DF to smooth the transition outside the myocardium. Then, the new DF was inversed and applied to each real image previously resampled in the ED configuration. Finally, a 3D cone mask was applied to remove all the displacements outside the cone, as observed in real acquisitions. With this approach, most of the image will stay unchanged in the synthetic image compared to the original sequence. We preserve the dynamics of the image, in particular the speckle visible in 3D US for most voxels. Only in the myocardium is the image texture slightly warped, the amount of warping depending on the difference between the simulated cardiac motion and the motion in the original images.

2.3 Generation of Healthy and Pathological Cardiac Motion

Different simulation scenarios were performed including normal and pathological cases such as left bundle branch block (LBBB) and right bundle branch block (RBBB) by blocking the LV and RV initial electrical activation respectively, LBBB with LV pacing, RBBB with RV pacing and also LBBB and RBBB with biventricular (BV) pacing. The different pacing positions were based on the LV AHA segments (see Fig. 3). Table 1 summarizes the electrical and mechanical parameters used for the 120 simulations done from each real 3D US sequences.

3 Learning Electro-Kinematic Inverse Relationship

3.1 Kinematic Descriptors

With the method described previously, a large database of synthetic 3D US images was created. We then tracked the cardiac motion from those synthetic images by using the iLogDemons registration algorithm [4]. More precisely, we registered all the images of the synthetic sequence to its reference ED image. As an input to a machine learning algorithm, we needed to first extract kinematic descriptors which describe in a compact and exhaustive way the cardiac motion.

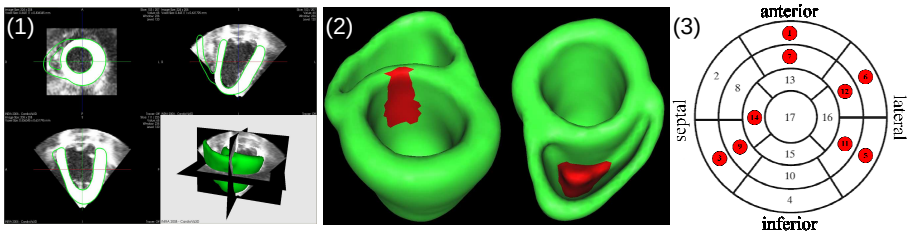

Fig. 3. Cardiac Geometry and Electrical Stimulation. (1) LV segmentation (2) Initial electrical activation area for the normal stimulation (3) Positions of the stimulation leads in the LV AHA zones

Simulation Number	Initial Electrical Activation Position	Global Conductivity	Global Contractility
1-4	LVRV (Normal)	50/30	0.09/0.05
5-8	LV (RBBB)	50/30	0.09/0.05
9-12	RV (LBBB)	50/30	0.09/0.05
13-36	RV + AHA 1/5/6/7/11/12 (LV Pacing)	50/30	0.09/0.05
37-48	LV + AHA 3/9/14 (RV Pacing)	50/30	0.09/0.05
49-120	AHA 1/5/6/7/11/12 + AHA 3/9/14 (BV Pacing)	50/30	0.09/0.05

Table 1. Simulation Database. Parameters of the 120 simulations. Global conductivity (cm/s) is the conduction velocity of the electrophysiology model and global contractility (adimensioned) is the peak contractility of the E/M coupling.

To this end, we characterized the motion of each AHA segment by fitting in the least-square sense an affine transformation $f(p) = Ap + B$ to the iLogDemons estimated DF. The strain tensor was computed from the affine matrix $E = \frac{1}{2}(A^T A - I)$. We propose to extract kinematic descriptors that are invariant to any change of reference frame (or rigid transformation). For the strain matrix E, the three Euclidean invariants are written as $x_1 = \text{trace}(E)$, $x_2 = \text{trace}(E^2)$, and $x_3 = \det(E)$. For the displacement vector, we only extracted its norm as invariant: $x_4 = \|u\| = \|Ab + B - b\|$, where $\|u\|$ is the displacement norm of the zone centroid with b the initial position of the centroid. Finally, we also used the strain in the direction of displacement as the last invariant $x_5 = \frac{1}{2\|u\|^2}(u^T E u)$. These 5 descriptors for the 17 AHA zones during the 19 time instances of a cardiac cycle were used to create a vectorial kinematic descriptor for each simulation: $X = x_i \in \mathbb{R}^d$ where d=5 (Descriptors) $\times$ 19 (Times) $\times$ 17 (Zones) = 1615.

3.2 Inverse Electro-Kinematic Learning

In the inverse electro-kinematic learning process, the non-linear relationship between the kinematic descriptors and the electrical propagation was estimated based on a training set extracted from the synthetic database. To represent the

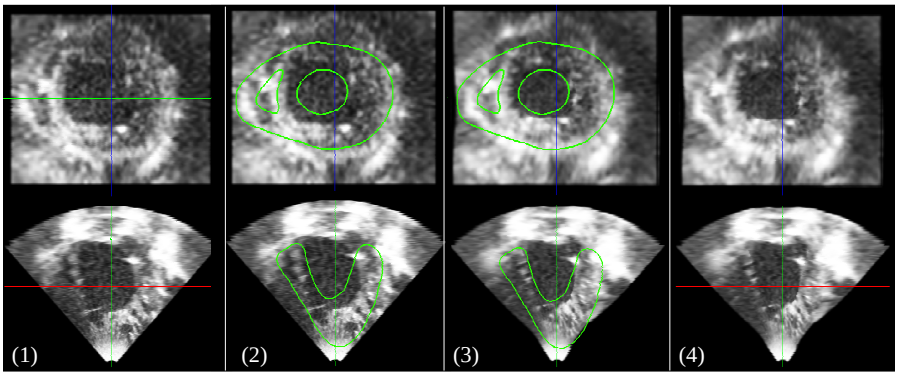

Fig. 4. Synthetic 3D US. (1) original real image with (2) contour of the mesh at the corresponding time from the model simulation overlayed, (3) synthetic image generated with the model simulation with model contour overlay, (4) synthetic image.

cardiac electrophysiology, we considered the activation time when the electrical potential starts to depolarize at a point of the myocardium. The activation time was averaged for all points in each AHA segment. Therefore, the vector characterizing electrophysiology for each simulation is $\mathrm{Y} = \mathrm{y}_i \in \mathbb{R}^{\mathrm{r=17}}$ (AHA Zones) $= log(\text{Activation Times})$.

We modelled the non-linear relationship using Least-Square Support Vector Machine (LS-SVM) $Y = f(X) = Ak(x_i, X) + b$ with the Radial Basis Function (RBF) $K(x_i, x_j) = e^{-z}$ as the Kernel function where $z = \sum_{k=1}^{5} \left(\frac{|x_i^k - x_j^k|}{\sigma_k \alpha_k} \right)^2$. In this kernel function, σ_k is the standard deviation of each descriptor and α_k is a dimensionless coefficient which weights the importance of the descriptor in the learning process. Finally, following the LS-SVM theory, $k(x_i, X)$ is a kernel vector while matrix A is computed as $\mathrm{A} = Y^T \left(\lambda \mathrm{I} + K\right)^{-1}$. In order to have a good generalization of the model, the α_k parameters and the regularization parameter λ were optimized with a downhill simplex method using leave-one-out cross-validation based on Allen's predicted residual sum-of-squares (PRESS) statistic [1].

4 Results

The proposed synthetic 3D US generation method produces realistic synthetic 3D US sequence (cf. Fig. 4) with a seamless fusion of simulated myocardium motion with neighboring moving structures. The created synthetic 3D US database contains 120 different cardiac cases consisting of a sequence of 19 3D US images describing a complete cardiac cycle. In total, $120 \times 19 = 2280$ synthetic 3D US images were generated.

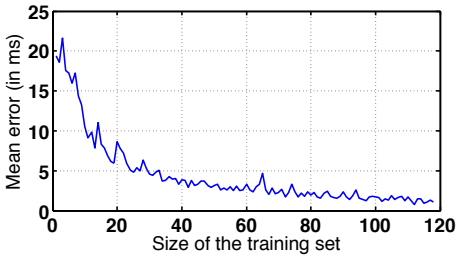

Fig. 5. RMS Residual vs Size of Training Data. Less than 10 ms RMS residual is obtained by using more than 15 training cases.

4.1 Machine Learning Validation on Synthetic Data

We evaluated the learning process on synthetic data and estimated the minimum size of the training set to have a small regression error for the remaining entries of the database. Fig. 5 shows a good generalization with a root mean square (RMS) error of less than 10 ms of residual by using at least 15 training datasets.

4.2 Machine Learning Evaluation on Real Data

After optimizing the PRESS criterion on the whole synthetic database, we obtained the following LS-SVM parameters : $\lambda = 7.89 \times 10^{-31}$, $\alpha_1 = 463.65$, $\alpha_2 = 2.29 \times 10^{13}$, $\alpha_3 = 8.02 \times 10^{12}$, $\alpha_4 = 14.37$ and $\alpha_5 = 174.51$. This clearly shows that the kinematic descriptors x_1, x_4 and x_5 are the only meaningful ones to learn the electro-kinematic relationship. We did a first evaluation of this learning process on clinical 3D US sequences for two patients with LBBB. After performing non-rigid registration and extracting the vector X of kinematic descriptors, the electrophysiology vector Y was estimated from the LS-SVM. Very similar estimated depolarization times were obtained for these two patients (cf. Fig. 6). Moreover, the activation patterns correspond to what was expected: depolarization starts from the septum towards the lateral wall, and the difference between the first activated zone and the last activated zone, which indicates the QRS duration, is around 150 ms which is also a characteristic of the LBBB.

5 Conclusion

We developed a pipeline to create realistic synthetic 3D US sequences using the deformation from an E/M model simulation. Those sequences represent in themselves a valuable result for instance to benchmark motion tracking algorithms. As these synthetic 3D US sequences have electro-kinematic "ground truth" information, we thus performed an inverse electro-kinematic learning on this database. Invariant kinematic descriptors were extracted from the DF obtained from the synthetic 3D US images registration. The non-linear inverse relationship between the electrical activation times and the kinematic descriptors was modelled using

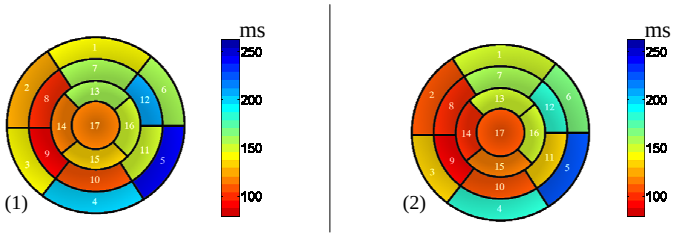

Fig. 6. Depolarization Time Estimation from Clinical 3D US Sequences. First evaluation of the learning process on patient (1) and patient (2). Both patients have LBBB.

LS-SVM. Evaluation of the learning process for the synthetic 3D US sequences database shows good generalization and the first evaluation on clinical 3D US sequences shows encouraging results.

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