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Diffeomorphic Upsampling of Serially Acquired Sparse 2D Cross-Sections in Cardiac MRI

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Abstract

In this paper, we propose a new technique for interpolating shapes in order to upsample a sparsely acquired serial-section image stack. The method is based on a maximum a posteriori estimation strategy which models neighboring sections as observations of random deformations of an image to be estimated. We show the computation of diffeomorphic trajectories between observed sections and define estimated upsampled image sections as a Jacobian-weighted sum of flowing images at corresponding distances along those trajectories. We apply this methodology to upsample stacks of sparse 2D magnetic resonance cross-sections through live mouse hearts. We show that the proposed method results in smoother and more accurate reconstructions over linear interpolation, and report a Dice coefficient of 0.8727 against ground truth segmentations in our dataset and statistically significant improvements in both left ventricular segmentation accuracy and image intensity estimates.

I. INTRODUCTION

Segmented image acquisition techniques as employed for cardiac magnetic resonance (MR), wherein only portions of the imaging data are acquired per heartbeat or breath-hold, are typically acquired at an in-plane resolution several times finer than the slice thickness [1]. Serially assembled image volumes that are acquired at anisotropic resolutions suffer from a lack of smoothness in the out-of-plane imaging axis. The roughness of the resulting image volume is not easily corrected by traditional interpolation or smoothing techniques and can

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cause downstream problems in image registration, segmentation, or construction of parametric representations.

The continuity and smoothness of anatomical structures is a critical assumption in the quantitative investigation and modelling of the variability of anatomical shapes [2] (computational anatomy). The macroscale anatomy of the body is generally known to be composed of continuous structures, even in highly complex anatomical regions. Clearly defined anatomical boundaries enable applications such as atlas-based registration and image segmentation.

General interpolation of shapes is a well-explored field of study. Traditional shape interpolation involves computing smooth trajectories between defined correspondences [3]. Other groups have proposed interpolation of longitudinal datasets and registration of time series [4], interpolation by geodesic flows [5], [6], population models [7], or joint modeling of shape and image intensity [8]. These methods generally involve extraction of image features and segmentation [9] or pairwise optical flow from neighbor to neighbor [10], [11].

Several studies have focused on developing methods to perform 3D reconstruction of the cardiac left ventricle (LV) from sparse MR imagery. These methods either employ interpolation [13] or surface-fitting to endocardial and epicardial contours using some predefined geometry [14]. Other approaches rely on diffeomorphic mapping of a high-resolution LV surface mesh to a set of sparse 2D short axis LV contours [15]. More recently, constrained neural network approaches have been used to incorporate prior anatomical knowledge to enhance sparsely collected 2D cardiac MR imagery [16]. These methods mostly rely on population-based atlases, predefined geometry (prolate-spheroidal) or training on ground truth data sets to reconstruct the 3D LV shape.

In this paper, we propose a method to upsample serially-acquired sparse 2D MR crosssectional cardiac imagery based on a definition of a weighted mean derived from the wellknown statistical template estimation framework in computational anatomy. This method relies solely on the intrinsic constraint provided by the geometry of acquired sparse 2D MR images and does not require training or model fitting. The definition of a sliding windowed average of image slices with arbitrary center along an axis of a 3D image volume provides a flexible but robust framework for computing trajectories between shapes in neighboring image sections.

II. METHODS

A. Data

As a part of ongoing project, in-vivo heart images of 5 adult male wild type (n = 2) and Galectin-3 knockout (n = 3) mice were acquired using Bruker NMR/MRI spectrometer equipped with a 11.7T magnet and a gradient set capable of developing gradient strengths of 740mT/m (Bruker Biospin, Germany). The mice were positioned on the MRI 4-channel surface coil and an MRI gating trigger was established via ECG leads and a respirator pillow was used. Cine MRI was collected (15 frames, echo time (TE) = 1.9708 ms, repetition time (TR) = varied according to the heart rate, slice thickness of 0.8 mm, in plane resolution of

 $0.1307 \times 0.1307 \text{ mm}^2$, flip angle = 12, NEX = 6) at 6–8 short axis slices through the LV. The animal protocol was approved by the Institutional Animal Care and Use Committee of the Johns Hopkins University. The left ventricle was manually segmented in each short-axis acquisition by an independent expert using a freely available semi-automatic software package called Segment [12]. Figure 1 shows some examples of the dataset.

B. Diffeomorphic Trajectories

We constrain the trajectories between corresponding shapes to be diffeomorphisms. Here, we briefly review diffeomorphic image registration under the large deformation diffeomorphic metric mapping (LDDMM) framework and its relation to template estimation. We define the relationship between any two images *I* and *J* of an anatomical structure by some deformation *g* such that $I = J^{\circ} g^{-1}$. As first described in [17], it is possible to restrict the deformation *g* to a diffeomorphism φ by modeling it as a flow parameterized by a timedependent velocity field v_b such that

$$\varphi_l(x) = x + \int_0^t v_l(\varphi_l(x)) dt \tag{1}$$

where we call t = 1 the endpoint of the flow. Diffeomorphisms have the advantage of being smooth, 1-to-1, and invertible, which are desirable properties for preserving topology in anatomy. The image sum-of-squared-error matching problem is then written:

$$\hat{v} = \operatorname{argmin}_{v_t} \int_0^1 \|v_t\|_V^2 dt + \frac{1}{\sigma^2} \|J \circ \varphi^{-1} - I\|_L^2$$
(2)

where σ is a weighting factor on the matching term and subscript *V* indicates the norm of smooth velocity fields in a reproducing kernel Hilbert space. In our case, because we have manual left ventricle segmentations in each section, we employ a multichannel model where each section is represented by a two-channel image, the first being the grayscale image and the second being the segmentation image. This modified matching problem is written:

$$\hat{v} = \operatorname{argmin}_{v_t} \int_0^1 \|v_t\|_V^2 dt + \sum_{c=1}^C \frac{1}{\sigma_i^2} \|J(\cdot, c) \circ \varphi^{-1} - I(\cdot, c)\|_L^2$$
(3)

where C is the number of image channels.

C. Interpolation by Jacobian-Weighted Averaging Along Flow Trajectories

Having constrained ourselves to diffeomorphic trajectories between shapes, we now turn to estimation of a statistical average of shapes in images. We apply the framework of Bayesian template estimation, first described in [18]. Template estimation is traditionally employed to compute atlas images which are minimally distant (in terms of some similarity metric) from a sample of some population of images. We take the same maximum a posteriori approach here, where our population subjects or observations I_i are the neighboring slices to a desired position to be upsampled.

We define our estimate of the data at an unobserved position as a Jacobian-weighted mean of the population along their diffeomorphic trajectories. The diffeomorphic trajectories are solved by the minimization in Eqn. (3). In the classic template estimation case, these minimizations are performed iteratively such that population subjects are mapped to an iterative estimate of the population's centroid or mean. The per-iteration estimate of the mean image is given by a weighted sum at the endpoints of these trajectories:

$$\bar{I}^{(k+1)} = \frac{\sum_{i=1}^{N} I_i \circ \varphi_{\nu_i^{(k)}} | D\varphi_{\nu_i^{(k)}} |}{\sum_{i=1}^{N} | D\varphi_{\nu_i^{(k)}} |}$$
(4)

where $\varphi_{v_n^{(k)}}$ is the diffeomorphism of the velocity field *v* for observation *i* at iteration *k*, *N* is the number of population subjects, and *D* indicates the Jacobian determinant of φ in space. The notion of weighting by the Jacobian determinant $\left| D\varphi_{v_i^{(k)}} \right|$ is a natural one as the Jacobian encapsulates the change of coordinates from each observation to the mean. It is, in a sense, weighting the importance of the observations - for instance, if a pixel in the mean/centroid space maps to many pixels in an observation, that pixel should be more heavily weighted in the computation of the average image by a degree commensurate to its importance. In [18]'s formulation, this process is repeated until the mean image converges to the desired minimally distant population mean.

In the case of image slice upsampling, the two observed slices neighboring the z-position where we want to upsample the volume are the only two population "subjects" or "observations". The mean along the diffeomorphic trajectory between a pair of images is a simpler problem which does not require the notion of a large population's centroid and can be computed in a single shot without an iterative procedure. As such, we define a weighted mean

$$\bar{I}_{r} = \frac{I_{0}\left(\varphi_{0}^{0,\frac{r}{R}}\right) \left| D\varphi_{0}^{0,\frac{r}{R}} \right| \left(1 - \frac{r}{R}\right) + I_{1}\left(\varphi_{1}^{1,\frac{r}{R}}\right) \left| D\varphi_{1}^{1,\frac{r}{R}} \right| \frac{r}{R}}{\left| D\varphi_{0}^{0,\frac{\pi}{R}} \right| \left(1 - \frac{r}{R}\right) + \left| D\varphi_{1}^{1,\frac{\pi}{R}} \right| \frac{r}{R}}$$
(5)

where *R* is the z-axis distance between two observed slices I_0 and I_1 and *r* is the z-axis distance from I_0 at which to estimate the interpolation between the observations. We use Eqn. (5) to directly compute the the midpoint (or any arbitrary point) along the trajectory between I_0 and I_1 in a single iteration. We expect the flow to be symmetric in time, so we constrain φ as in [19]. This formulation is a modification of the Jacobian-weighted mean of Eqn (4) where the population observations are averaged at an intermediate point determined by the diffeomorphic trajectory rather than the estimation of a population's centroid. Here, $\varphi_0^{a, b}$ is the diffeomorphism computed from the time-varying velocity field v_t parameterizing (3) from time t = a to time t = b for the mapping of I_0 to $I_1(\varphi_1^{a, b}$ being the same for I_1 to I_0). The algorithm to upsample a sparse image stack with slice thickness *R* by some factor *S* is then given by:

Algorithm 1 Algorithm for upsampling image stack
Given a stack of <i>M</i> image sections $\mathbf{H} = H_1, H_2, H_3, \dots, H_M$ and slice thickness <i>R</i>
for $i = 1$ to $M - 1$ do
Set observation 1: $I_0 = H_i$
Set observation 2: $I_1 = H_{i+1}$
Compute 2D LDDMM mapping φ_0 from I_0 to I_1 and φ_1 from I_0 to I_1 .
for $s = 1$ to S do
Compute weighted mean image \overline{I}_r , where $r = \frac{sR}{S}$.
end for
end for

For each pair of observed sections I_i and I_{i+1} , convergence of the trajectory estimation step (φ_0, φ_1) is determined by a minimum energy reduction of less than 0.01% between LDDMM iterations (approximately 500 iterations for each direction, with a runtime of about 20 seconds using a custom GPU-accelerated software pipeline running on an Nvidia RTX2080).

D. Evaluation

We apply the proposed algorithm to our mouse cardiac MR dataset and evaluate the accuracy of our estimations by excluding an interior short-axis slice and comparing our estimate with the excluded ground truth. For example, in a heart with 10 slice acquisitions along the left ventricle, we estimated slice 2 using only slice 1 and 3, then we estimated slice 3 using only slice 2 and 4, and so on. In total, the dataset contains 68 such unique triplets of neighboring slices. We evaluate the mean squared error of the grayscale image produced by our estimated with the ground truth image and we compare against traditional linear interpolation. An independent expert has also hand-segmented all estimated slices from end-systole and end-diastole time points for both the proposed method and linear interpolation, and we report the resulting segmentation Dice [20], [21] score against the ground truth.

III. RESULTS AND DISCUSSION

As a first step, we apply the proposed algorithm to the 0.1307 mm \times 0.1307 mm \times 0.8 mm short-axis image stack in order to upsample the volume by a factor of six along the imaging axis to 0.1307 mm \times 0.1307 mm \times 0.1333 mm. The resulting upsampled volume is resliced along the given acquisition's long-axis image plane and compared against the ground truth acquisition alongside other interpolation methods in Figure 2. Because corresponding long-axis acquisitions were not available for all subjects, we present comparison of long-axis reslicing for visual comparison only. Nearest-neighbor interpolation produces the expected step artifacts, and while linear interpolation somewhat smooths these artifacts, they are still evident in panel b of Figure 2. Unlike linear interpolation, the proposed model is capable of modeling physical fluid-like deformations, producing the profile most similar to the ground truth.

For every triplet of sections, the central section is hidden from the proposed model and reconstructed using its neighbors. Figure 4 shows an example of this process in which section 7 from Figure 3 is estimated by both linear interpolation and the proposed diffeomorphic interpolation method. Here, the power of the proposed model becomes evident: obvious ghosting artifacts are present in the linearly interpolated image while the proposed model produces a coherent image with left ventricular boundaries that closely match the ground truth image. Beyond the heart itself, the proposed model clearly produces more accurate estimations in regions with thin features, such as the ventral chest surface on the right side of the panels of Figure 4.

We first quantify the accuracy of our estimation by comparing the absolute intensity difference between our estimated images and the ground truth. Figure 5 shows the difference image for the estimation of section 7 from Figure 4 for both linear interpolation and the proposed model. The difference image shows a close estimate of the ground truth image intensity by the proposed method. Averaged over the entire dataset, we report a mean percent reduction in absolute intensity error of 12.7% \pm 3.26%. We also report that 100% of slices estimated by the proposed model showed lower absolute intensity error compared to linear interpolation. We performed a one-sided Wilcoxon rank-sum test between the sets of individual error values for slice between the two methods and report a p-value of 1.31×10^{-8} , indicating that our method produces significantly more accurate intensity estimates.

In addition to comparing raw intensity, we evaluate our model by comparing manual segmentations of estimated slices by an independent expert against segmentations of the ground truth by the same expert. We evaluate the Dice coefficient of each dense 2D segmentation and observe marked improvement in estimation of the LV boundary when comparing our model (mean Dice score across slices of 0.87 ± 0.085) to linear interpolation (mean Dice score across slices of 0.79 ± 0.11). We again performed a Wilcoxon rank-sum test between the two groups of Dice scores and report a p-value of 1.53×10^{-4} , indicating significantly improved accuracy in the left ventricular region using the proposed method. Sample segmentations for each model overlayed with the ground truth segmentations are shown in Figure 6. The right column of this figure shows close alignment between the ground truth (green) and proposed model (red), whereas linear interpolation (blue) is generally less accurate.

Alongside improved upsampling accuracy, an additional benefit of the proposed deformation-based model is its ability to carry information associated to the sparse observations into the upsampled region. For instance, we can apply each section's computed Jacobian-weighted averaging to the associated sparse segmentations to produce a densely segmented and upsampled volume; this is not possible by linear or nearest-neighbor interpolation. Figure 7 shows an example of this effect on a long-axis reslicing of an upsampled short-axis stack.

IV. CONCLUSIONS

We presented and evaluated a method for estimating 3D dense reconstructions of left ventricular myocardium using diffeomorphic shape interpolation algorithm. Unlike other methods, the proposed approach does not require model training or identification of correspondences, and the Jacobian weighted population-mean model is a more accurate averaging method than other models that sample single geodesics or perform unweighted population averaging. We also show other applications of the method to the data such as upsampling of sparse segmentations into smooth volumes for downstream processing.

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Fig. 1.

Sample images from the mouse cardiac MR dataset. a) A long axis section interposed with short axis sections. b) Short-axis cine with manual segmentation. c) Short-axis image stack resliced along the long axis at native resolution. d) True long-axis cine image.



Fig. 2.

Long axis view through left ventricle, resampled from several interpolation methods applied to short-axis image stack alongside ground truth long axis image. a) Nearest neighbor interpolation applied to short-axis stack. b) Linear interpolation applied to short-axis stack. c) Our proposed shape-based interpolation applied to short-axis stack. d) Ground truth long axis scan.



Fig. 3.

Sample of three consecutive 0.8 mm thickness short-axis sections acquired at end-systole from a single subject. Sections move closer to the apex as section # increases.



Fig. 4.

Estimation of an intermediate section (section 7 from Figure 3) by linear interpolation (left) and the proposed model (center). The ground truth is shown on the right. The images are zoomed to the left ventricle for clarity.



Fig. 5.

Sample absolute intensity difference image zoomed to the left ventricle between a) ground truth slice and linearly interpolated estimation, and b) ground truth slice and diffeomorphically interpolated estimation. Colorbar has units of % mean intensity of the ground truth image.



Fig. 6.

Sample manual segmentations of linearly interpolated estimations (left, blue), diffeomorphically interpolated estimations (left center, red), ground truth (right center, green), and all three overlayed on the ground truth (right).



Fig. 7.

Comparison of sparse segmentations upsampled by a&b) the proposed model, c&d) nearest neighbor interpolation, e&f) linear interpolation, alongside upsampled grayscale intensity images. Segmentation by linear and nearest neighbor methods are identical in the case of 50% thresholding.