Temporal Registration for MRI Time Series

by

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B.E., Electronic Engineering, Tsinghua University, 2015

Submitted to the Department of Electrical Engineering and Computer Science
in partial fulfillment of the requirements for the degree of

Master of Science
in Electrical Engineering and Computer Science
at the Massachusetts Institute of Technology

June 2017

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Abstract
Time-course analysis in medical image series often suffers from serious motion. Registration provides voxel correspondences among images, and is commonly employed for correcting motion in medical images. Yet, the registration procedure fails when aligning volumes that are substantially different from template. We present a robust method to correct for motion and deformations in MRI time series. We make a Markov assumption on the nature of deformations to take advantage of the temporal smoothness in the image data. Forward message passing in the corresponding hidden Markov model (HMM) yields an estimation algorithm that only has to account for relatively small motion between consecutive frames. We demonstrate the utility of the temporal model by showing that its use for in-utero MRI time series alignment improves the accuracy of the segmentation propagation through temporal registration. Our results suggest that the proposed model captures accurately the temporal dynamics of deformations present in in-utero MRI time series. We also demonstrate that our method can be used for cardiac cine MRI. By propagating segmentation labels of one volume to the other frames in the cine MRI through deformation estimated by our method, 4D (3D+time) cardiac MRI series can be segmented.

Thesis Supervisor: Polina Golland
Professor of Electrical Engineering and Computer Science
Acknowledgments

I would like to thank my supervisor, Polina Golland, for her continuous guidance and support of my study at MIT. I knew her before I came to MIT, when I was thinking about applying for graduate school as a senior undergraduate student. We had a chat in the MICCAI conference, 2014. I spoke with her about my summer internship project at Brigham and Women’s Hospital and my interest in applying for MIT. I have forgotten the detail of our conversation, but I do remember that while she was occupied chairing that conference, she was patient and listened to me carefully, which is what she has always been. During my two-year study at MIT, I have been going through the process of knowing what research is and how to do research. Polina has not only given me high-level advice, but also guided me in a hands-on way. Her devotion has helped me, a very junior researcher, have a much deeper understanding of my research than when I just started two years ago. I am truly grateful.

My families, especially my grandparents and my parents, have given me tremendous support and love. Their love without reservation has been my deepest motivation of contributing to this world and making it better, and my source of being happy and optimistic.

I have been fortunate to work in a research lab full of helpful and smart people. Adrian Dalca, George Chen, Danielle Pace, Kayhan Batmanghelich, and Miaomiao Zhang have offered me lots of help from specific technical problems to being adjusting to graduate school life. Polina Binder, Mazy Abulnaga, Jay Patel have also made this lab a friendly and fun place. It has been my great pleasure to work with my collaborators Mehdi Moghari, Elfar Adalsteinsson, Ellen Grant, Esra Turk, and Jie Luo.
## Contents

Abstract .............................................. 3
Acknowledgments .................................... 4
List of Figures ....................................... 9

1 Introduction ...................................... 11  
   1.1 Motivating application .......................... 11  
   1.2 Related Work .................................... 12  
   1.3 Proposed Method ................................. 13  
   1.4 Roadmap .......................................... 13  

2 Methods ........................................ 15  
   2.1 HMM and Filtered Estimates ..................... 15  
   2.2 Estimating Temporal Deformations in HMM ......... 17  
   2.3 Implementation Details ......................... 18  

3 Experiments and Results ......................... 19  
   3.1 Data ............................................. 19  
   3.2 Experiments ..................................... 20  

4 Additional Application: Cardiac MRI .......... 25  

5 Discussion and Conclusions ..................... 27  

Bibliography ........................................ 29
1.1 Example twin pregnancy case from the study. The same cross-section from frames $J_1$, $J_2$, $J_{74}$, and $J_{75}$ is shown. Arrows indicate areas of substantial motion of the placenta (red), fetal head (green), and fetal body (yellow). ................................................................. 11

2.1 A graphical model showing the hidden Markov model in the context of temporal deformations. The likelihood term $p(J_n|\varphi_n; I)$ acts as a data term in registration. The transition probability $p(\varphi_n|\varphi_{n-1})$ encourages temporal smoothness of deformations in the series. .................................................... 16

3.1 Each volume is split into even and odd slices, and the empty slices on an isotropic 3mm$^3$ image grid are linearly interpolated from the adjacent slices. The blue and green blocks represent odd and even slices, and the red hollow blocks represent the interpolated slices. .................................................... 19

3.2 Two example cases from the study. For each case, we display the reference frame $J_1$ with manual segmentations, the reference frame $J_1(\varphi_{75}^{-1})$ transformed into the coordinate system of frame $J_{75}$, frame $J_{75}$ with manual segmentations, and frame $J_{75}$ with segmentations transferred from the reference frame $J_1$ via $\varphi_{75}$. Both cases are twin pregnancies. Segmentations of the placentae (pink), fetal brains (green), and fetal livers (yellow) are shown. Two-dimensional cross-sections are used for visualization purposes only; all computations are performed in 3D. .................................................... 20

3.3 Volume overlap between transferred and manual segmentations: (a) placentae, (b) fetal brains, and (c) fetal livers. The cases in the study are reported in the increasing order of placentalar volume overlap for our method. Duplicate case numbers correspond to twin and triplet pregnancies. Statistics are reported for our method (red), pairwise registration to the template frame (green), and no alignment (blue). .................................................... 22
3.4 MRI intensity change in three ROIs (placenta, one brain, one liver) in one in-utero image series. The red curves are computed from images after our temporal alignment, and the blue curves are from those without registration. ................................................................. 23

4.1 One example case from the study. We display the template (EDV) phase with segmentations from the 3D semi-automatic segmentation algorithm and the ESV phase with segmentations transferred from the template frame via our estimated transformation. A representative short-axis view and 3D models of both ventricles generated from the segmentation labels are shown; all computations are performed in 3D. ................................. 26

4.2 Ventricular measurements from manually segmented breath-hold 2D images and semi-automatically segmented 3D cine datasets (n=5). Values are mean ± standard deviation. EDV, end-diastolic volume; ESV, end-systolic volume; SV, stroke volume; and difference percentage, 2 × |2D − 3D|/(2D + 3D). ................................................................. 26
Chapter 1

Introduction

This thesis demonstrates robust temporal image registration framework. Large motion presents significant challenges for time-course analysis in medical image series. Image registration produces voxel correspondences between images and is commonly employed for correcting motion in medical images. Yet, the registration procedure often fails for volumes that are substantially different from the template. We take advantage of the temporal continuity to achieve robust alignment of volumetric MRI time series. This work is motivated by two different clinical applications, which we briefly introduce below.

1.1 Motivating application

In-utero blood oxygenation level dependent (BOLD) magnetic resonance imaging (MRI) is a promising imaging tool for studying functional dynamics of the placenta and fetal organs [14, 26, 28, 29]. Changes in fetal and placental oxygenation levels with maternal hyperoxygenation can be potentially used for detecting placental dysfunction [1]. The temporal MRI data suffers from serious motion artifacts due to maternal respiration, unpredictable fetal movements, and signal non-uniformities [30], as illustrated in Fig. 1.1. Moreover, the deformation induced by the movements of multiple organs, contains different types of motion. The fetal brains move as rigid objects; the placenta movement includes a high degree of non-rigid deformation.

Figure 1.1. Example twin pregnancy case from the study. The same cross-section from frames $J_1$, $J_2$, $J_{74}$, and $J_{75}$ is shown. Arrows indicate areas of substantial motion of the placenta (red), fetal head (green), and fetal body (yellow).
3D cine cardiac MRI promises to provide accurate assessment of ventricular volumes and ejection fractions, and enable detailed visualization of cardiac motion [15, 20]. Manual segmentation of multiple 3D volumes is time intensive and clinically impractical. Temporal registration provides voxel correspondences across volumes, and therefore can be employed to propagate manual segmentation labels of one time point in the series of images to the other time points.

1.2 Related Work

Temporal registration has been studied for time series of cardiac images [8, 18, 22, 31] and lung images [17, 18, 23, 25]. Both cardiac and lung motion patterns are somewhat regular and smooth across time, and lend themselves to biomechanical modeling [17, 22, 31]. For instance, ECG-gating or respiratory gating can be incorporated in the cardiac or lung image motion correction, by either enforcing the transformation models to be periodic or penalizing non-periodic transformations in the cost functions. These approaches cannot be generalized to non-periodic motion correction or for images that contain complex motion patterns.

Existing registration techniques for dynamic medical imaging data can be categorized into two distinct groups. The first group of methods performs registration based on the differences between each two consecutive frames. In a pairwise manner, each two consecutive frames are serially aligned, and the estimated deformations are concatenated to estimate alignment of all images in the series [7, 23]. In application to long image series, this approach leads to substantial accumulated errors after several concatenation steps. Such methods only take the moving image and the reference image into account in each pairwise registration step, and ignore essential temporal information from the other images in the series. The second group applies groupwise registration to simultaneously align individual images to a group template – estimated or selected to be one of the input images – which is expected to yield acceptable registration results for all images in the series [3, 5, 11, 16, 18, 19, 25, 27, 33]. Taking this approach in our application, registration fails for a great number of images that are substantially different from the template if the optimization is performed in a pairwise manner, where no temporal continuity of the data is taken into account. Alternatively, a global objective function based on pairwise differences between each individual image in the series and an implicitly defined template frame can incorporate the temporal information [18]. This leads to a global optimization, i.e., the algorithm performs pairwise registration of consecutive frames iteratively until the entire series comes into alignment. The optimization in a global manner, however, is challenging for large image sets.

The problem of temporal alignment has also been investigated in longitudinal image data analysis, which often involves characterizing temporal variations [9, 11, 12, 13, 24]. The goal is to examine the behavior of a biological system driven by external or internal forces [12]. The statistical analysis can be performed via temporal shape regression in Riemannian manifold [9, 11, 12, 13], aimed to find a trajectory that characterizes the
shape variation across time. Longitudinal data is often sparsely distributed in time, and temporal smoothness constraint is therefore imposed. Typically, the challenges in longitudinal analysis involve growth or degeneration, and require modeling tools that are different from those employed in analysis of MRI time series with motion present.

1.3 Proposed Method

We assume a Markov structure in the image series that induces temporal smoothness and offers an efficient way to estimate the deformations by serially solving the optimization problem in a pairwise manner. This is in contrast to the methods that serially perform pairwise registration and concatenate the estimated deformations. Temporal continuity is taken into account at every estimation step. Unlike the groupwise registration where temporal smoothness is incorporated in a global cost function, our method includes the temporal smoothness as the Markov structure in the generative model and solves the optimization in a serial pairwise manner. Our approach is related to filtering methods in respiratory motion modeling \[17\]. We do not model the motion explicitly, but rather capture it through deformations of the template image, to adapt to complex motion patterns.

We derive filtered estimates of the deformations from the hidden Markov model that represents the MRI series. The resulting sequential procedure determines the non-rigid transformation of the template to each frame in the series. This work provides a flexible framework for temporal alignment of MRI time series. We demonstrate and evaluate the proposed method in the context of the in-utero BOLD MRI time series by providing registration-based tracking of organs of interest. Our experiments show robust improvements in alignment of placenta, fetal brains, and fetal livers, compared to the serial pairwise registration without temporal smoothness.

1.4 Roadmap

This thesis is organized as follows. In the next chapter, we present the generative model of temporal deformations and observed images using hidden Markov model and derive the deformation estimation algorithm using filtered estimates, followed by implementation details. In Chapter 3, we introduce the in-utero BOLD MRI data and report the experimental results. In Chapter 4, we demonstrate another application of our method in 4D cardiac MRI. In Chapter 5, we discuss future directions, including bias correction for our in-utero MRI data and potential extension on other transformation models, and conclusions.
We employ Hidden Markov model (HMM) to represent the temporal deformations in the MRI time series. One image in the MRI time series is chosen as a template image, whose deformations are used to represent the rest of the images in the series. The deformation of each image in the series from the template image is modeled as the hidden state, and each image is the observation dependent on the corresponding hidden state. The deformations are estimated using filtered estimates. In the following sections, we review the inference in HMM, demonstrate its instantiation in the context of temporal registration, and describe the implementation details.

2.1 HMM and Filtered Estimates

In this section, we introduce HMM notation in the context of temporal registration and review filtered estimates – an efficient inference method in HMMs [4,6]. The temporal dynamics of latent (hidden) states in HMM has the Markov property, where the current state depends on the history, only through the state at the previous time point. By integrating the information passed from the state at the previous time point and information from the corresponding observation, the current latent state can be efficiently inferred, which is equivalent of performing inference based on the current observation and all the previous observations.

In our application, one image is chosen as the template image $I$, which is a global parameter shared by all observed images. We assume that the template $I$ deforms at each time point, and the deformation $\varphi_n$ – the anatomical transformation from the template to the image at that time point – defines the latent state at time $n \in \{1, \ldots, N\}$, where $N$ is the number of images in the series. The observed image $J_n$ at time $n$ can be viewed as generated by applying the anatomical transformation $\varphi_n$ to the template $I$, independently of all other time points. Fig. 2.1 illustrates this model.

Our aim is to estimate each latent state variable $\varphi_n$ from the observations $J_{1:n}$, where we use $J_{k:m}$ to denote sub-series $\{J_k, J_{k+1}, \ldots, J_m\}$ of the MRI time series $\{J_1, J_2, \ldots, J_N\}$. Formally, posterior distribution $p(\varphi_n|J_{1:n}; I)$ is constructed, and the estimation of the latent variable $\varphi_n$ is reduced to maximization of $p(\varphi_n|J_{1:n}; I)$. This posterior distribution, referred to as a filtered estimate of the state, can be efficiently inferred using forward message passing [4,6], also known as sequential estimation. The mes-
Figure 2.1. A graphical model showing the hidden Markov model in the context of temporal deformations. The likelihood term \( p(J_n | \varphi_n; I) \) acts as a data term in registration. The transition probability \( p(\varphi_n | \varphi_{n-1}) \) encourages temporal smoothness of deformations in the series.

The forward message sent from the latent variable node \( n-1 \) to the node \( n \) is determined by integrating a previous message \( m_{(n-2) \rightarrow (n-1)}(\varphi_{n-1}) \) with the temporal dynamics (smoothness) \( p(\varphi_n | \varphi_{n-1}) \) and the likelihood \( p(J_n | \varphi_n; I) \) of the current observation:

\[
\begin{align*}
    m_{(n-1) \rightarrow (n)}(\varphi_n) & \triangleq p(\varphi_n | J_{1:n}; I) \\
    & \propto p(J_n | \varphi_n; I) p(\varphi_n | J_{1:n-1}; I) \\
    & = p(J_n | \varphi_n; I) \int p(\varphi_n | \varphi_{n-1}) m_{(n-2) \rightarrow (n-1)}(\varphi_{n-1}) d\varphi_{n-1}. 
\end{align*}
\]  

(2.1)

where \( m_{0 \rightarrow 1}(\varphi_1) = p(\varphi_1) \), and \( n = \{1, ..., N\} \). Applied recursively, the forward message passing produces the posterior distribution \( p(\varphi_n | J_{1:n}; I) \) for each time point \( n \) in the number of steps that is linear with \( n \). Similarly, backward message passing enables inference of the posterior distribution \( p(\varphi_n | J_{1:N}; I) \), which is based on all data, often referred as smoothing. In this thesis, we investigate advantages of incorporating temporal smoothness in temporal registration by filtering. We discuss the challenges of developing a smoothing algorithm for temporal registration in the Discussion chapter.
2.2 Estimating Temporal Deformations in HMM

As we saw above, a deformation from the template image $I$ to each image $J_n$ in the MRI time series can be represented as a hidden state in the HMM. The problem of aligning the images in the time series reduces to the estimation of the hidden states. The filtered estimates using forward message passing can efficiently solve the inference problem. Here, we derive our algorithm for estimating temporal deformations.

Given a template image $I$ and anatomical transformation $\varphi_n$, the observed image can be reconstructed by transforming this template image. Exponential family likelihood on image similarity determines the likelihood term $p(J_n|\varphi_n; I)$, also known as emission probability in Eq. (2.1):

$$p(J_n|\varphi_n; I) \propto \exp \left(-\text{Dist}(J_n, I(\varphi_n^{-1}))\right),$$

where $\text{Dist}(\cdot, \cdot)$ is a measure of dissimilarity (distance) between images. This probability term measures how different the transformed template and the currently observed image are, given the template image $I$ and the transformation $\varphi_n$.

The state transition probability $p(\varphi_n|\varphi_{n-1})$, acts as a "prior" when estimating the state $\varphi_n$ at time $n$ and encourages both temporal and spatial smoothness in our temporal registration:

$$p(\varphi_n|\varphi_{n-1}) \propto \exp \left(-\lambda_1 \text{Reg}(\varphi_n) - \lambda_2 \|\varphi_n \circ \varphi_{n-1}^{-1}\|^2\right),$$

where $\text{Reg}(\cdot)$ is the regularization term that encourages spatial smoothness or other desired properties, and $\|\cdot\|$ is an appropriate norm that encourages $\varphi_n$ to be close to $\varphi_{n-1}$. $\lambda_1$ and $\lambda_2$ are regularization parameters that control the amount of temporal and spatial smoothness we need. The regularization term $\text{Reg}(\varphi_n)$ is often used in image registration to restrict the estimated deformation in a specific transformation group.

Since it is intractable to integrate over all possible deformation fields, we employed a commonly used approach of approximating message $m_{(n-1) \rightarrow (n)}(\varphi_n)$ as a point estimate that maximizes the probability distribution. In particular, if $\varphi^*_{n-1}$ is the best deformation estimated by the algorithm for time point $n-1$, the message passed from the state at time $n-1$ can be viewed as passing the optimal deformation $\varphi^*_{n-1}$ to node $n$:

$$m_{(n-1) \rightarrow (n)}(\varphi_n) \propto p(J_n|\varphi_n; I) \int p(\varphi_n|\varphi_{n-1}) m_{(n-2) \rightarrow (n-1)}(\varphi_{n-1}) \, d\varphi_{n-1}$$

$$\approx p(J_n|\varphi_n; I) \int p(\varphi_n|\varphi_{n-1}) \mathbb{1}\{\varphi_{n-1} = \varphi^*_{n-1}\} \, d\varphi_{n-1}$$

$$= p(J_n|\varphi_n; I) p(\varphi_n|\varphi^*_{n-1}),$$

yielding the (recursive) estimate of the hidden state at time point $n$:

$$\varphi^*_n = \arg \max_{\varphi_n} p(J_n|\varphi_n; I) p(\varphi_n|\varphi^*_{n-1}).$$
This estimate is then passed to node \( n + 1 \) for estimating \( \varphi_{n+1}^* \), and so on until we reach the end of the series.

Note that this HMM-based temporal deformation model can be easily generalized to various types of similarity metrics between moving images and fixed images, to different transformation models, and to different types of temporal regularization. The model can be readily augmented to include a model of a bias field and a latent reference template that is estimated jointly with the deformations, similar to prior work in groupwise registration \([11, 18, 25, 27]\). In the following section, we describe our implementation for aligning MRI time series.

### 2.3 Implementation Details

We choose the first image \( J_1 \) in the series as the reference template \( I \), and perform the deformation estimation in increasing order of the frames in the series. We manipulate Eq. (2.5)

\[
\varphi_n^* = \arg\max_{\varphi_n} p(J_n|\varphi_n; I) p(\varphi_n|\varphi_{n-1}^*) \\
= \arg\min_{\varphi_n} \text{Dist}(J_n, I (\varphi_n^{-1})) + \lambda_1 \text{Reg}(\varphi_n) + \lambda_2 \left\| \varphi_n \circ (\varphi_{n-1}^*)^{-1} \right\|^2,
\]

and observe that this optimization problem reduces to serial pairwise image registration of the template \( I \) and the observed image \( J_n \).

The algorithm proceeds as follows. Given the deformation estimate \( \varphi_{n-1}^* \) of the template image to represent the image \( J_{n-1} \), we apply the registration algorithm to \( I \) and \( J_n \) by minimizing the cost function in Eq. (2.6), while also using \( \varphi_{n-1}^* \) as an initialization, resulting in the estimate \( \varphi_n^* \).

We implemented our method using symmetric diffeomorphic registration with cross-correlation \([2]\) based on Thirion's demons algorithm \([32]\). We employ (negative) cross-correlation to define the measure of image dissimilarity \( \text{Dist}(\cdot, \cdot) \), because cross-correlation can be well adapted to images with signal non-uniformities, characteristic of in-utero BOLD MRI data. The diffeomorphic demons algorithm adapts convolutional kernels (we use Gaussian kernels for this implementation) on the incremental vector field or/and the updated displacement field at each iteration acting as a regularization in the cost function, which can naturally be implemented upon for our temporal registration method to incorporate temporal smoothness. The size of the local window for computing cross-correlation is set to be 5 voxels in cube. We use the state-of-the-art implementation provided in the ANTS software package \([2]\).
Chapter 3

Experiments and Results

We tested our method on ten in-utero BOLD MRI time series and compared our results with those from registration without incorporating temporal smoothness. In this chapter, we briefly describe our data and experimental setting. We demonstrate our registration results by showing transformed images with the template image and then quantitively evaluate the results.

3.1 Data

Ten pregnant women were consented and scanned on a 3T Skyra Siemens scanner (single-shot GRE-EPI, $3 \times 3\text{mm}^2$ in-plane resolution, 3mm slice thickness, interleaved slice acquisition, $\text{TR}= 5.8 - 8\text{s}$, $\text{TE}= 32 - 36\text{ms}$, $\text{FA}= 90^\circ$) using 18-channel body and 12-channel spine receive arrays. Each series contains around 300 volumes. This study included three singleton pregnancies, six twin pregnancies, and one triplet pregnancy, between 28 and 37 weeks of gestational age. A hyperoxia task paradigm was used during the scans, comprising three consecutive ten-minute episodes of initial normoxic episode ($21\%\text{O}_2$), hyperoxic episode ($100\%\text{O}_2$), and a final normoxic episode ($21\%\text{O}_2$). To enable quantitative evaluation, we manually delineated the placentae (total of 10), fetal brains (total of 18), and fetal livers (total of 18), in the reference template $I = J_1$ and in five additional chosen volumes $(J_{25}, J_{50}, J_{75}, J_{100}, J_{125})$ in each series.

To eliminate the effects of slice interleaving, we resampled odd and even slices of

![Figure 3.1. Each volume is split into even and odd slices, and the empty slices on an isotropic 3mm$^3$ image grid are linearly interpolated from the adjacent slices. The blue and green blocks represent odd and even slices, and the red hollow blocks represent the interpolated slices.](image-url)
Figure 3.2. Two example cases from the study. For each case, we display the reference frame $J_1$ with manual segmentations, the reference frame $J_1(\varphi_{75}^{-1})$ transformed into the coordinate system of frame $J_{75}$, frame $J_{75}$ with manual segmentations, and frame $J_{75}$ with segmentations transferred from the reference frame $J_1$ via $\varphi_{75}$. Both cases are twin pregnancies. Segmentations of the placentae (pink), fetal brains (green), and fetal livers (yellow) are shown. Two-dimensional cross-sections are used for visualization purposes only; all computations are performed in 3D.

3.2 Experiments

To evaluate the validity of the temporal model, we compare it to a variant of our algorithm that does not assume the temporal structure and instead aligns each image in the series to the reference frame using the same registration algorithm used by our method. Algorithmically, this corresponds to setting $\lambda_2$ in Eq. (2.6) to be 0 and initializing the registration step with an identity transformation instead of the previously estimated transformation $\varphi_n^{*}$.

To quantify the accuracy of the alignment, we transform the manual segmentation labels in the reference template to the five segmented frames in each series using the estimated deformations. We employed Dice coefficient [10] to quantify volume overlap between the transferred and the manual segmentations. In our application, the goal is to study average temporal signals for each ROI, and therefore delineation of an ROI provides an appropriate evaluation target. Moreover, the manual segmentation labels drawn in the template frame of one time series are tracked through the image series
by our temporal registration method, and the average MRI intensity in three ROIs were respectively computed. This is compared to the MRI intensity change without transforming the manual delineations in the template frame, i.e. no registration.

**Experimental Results**  
Fig. 3.2 illustrates results for two example cases from the study. We observe that the reference frame was warped accurately by the algorithm to represent a frame in the series that is substantially different in the regions of the placenta and the fetal liver. The delineations achieved by transferring manual segmentations from the reference frame to the coordinate system of the current frame ($J_{75}$ in the figure) are in good alignment with the manual segmentations for the current frame. Fig. 3.3 reports volume overlap statistics for the placentae, fetal brains, and fetal livers, for each case in the study. We observe that temporal alignment improves volume overlap in important ROIs and offers consistent improvement for all cases over pairwise registration to the reference frame. We also note that temporal alignment offers particularly substantial gains in cases with a lot of motion, i.e., low original volume overlap. Fig. 3.4 shows one example case of the intensity change curves in placenta, a fetal brain, and a liver. We will further discuss this result in Chapter 5.
Figure 3.3. Volume overlap between transferred and manual segmentations: (a) placentae, (b) fetal brains, and (c) fetal livers. The cases in the study are reported in the increasing order of placental volume overlap for our method. Duplicate case numbers correspond to twin and triplet pregnancies. Statistics are reported for our method (red), pairwise registration to the template frame (green), and no alignment (blue).
Figure 3.4. MRI intensity change in three ROIs (placenta, one brain, one liver) in one in-utero image series. The red curves are computed from images after our temporal alignment, and the blue curves are from those without registration.
Additional Application: Cardiac MRI

Additionally, we also tested our method on five cine cardiac MRI datasets and demonstrated that our method can be used for 4D cardiac MRI segmentation. In this chapter, we briefly describe our cardiac data and experimental setting. We demonstrate our registration results by showing the segmentation labels transferred from the template volume based on the deformations estimated by our method. We compare ventricular volume measurements between manually segmented 2D MRI images and the segmented 3D cine datasets using our method.

Data  Five patients (4 male, age 17.8 ± 5.8 years) with complex congenital heart disease were recruited and consented. 3D cine SSFP image series were acquired from each patient on a 1.5T MR scanner (Philips Achieva) with anterior coil and the following imaging parameters: voxel size 2mm³, TR/TE=3.4/1.7ms, flip angle 60°, 30 cardiac phases, and SENSE ×3. Scan time was around 10 minutes. To compensate for respiratory-induced heart motion, the reconstruction was performed only using the data acquired within a narrow 5mm acceptance window around end-expiration. As a routine clinical protocol, 11-13 short-axis 2D cine images were also acquired from each patient with the following imaging parameters: voxel size 1.8mm³, slice thickness 8mm, TR/TE= 2.8/1.4ms, flip angle 60°, 2 cardiac phases, and SENSE ×2.

The 3D and 2D cine SSFP datasets were reconstructed online and analyzed retrospectively for segmentation. Following the current clinical practice, the 2D cine datasets were manually segmented only at the end-diastolic and end-systolic cardiac phases by an expert clinician. 5-10 short-axis “reference” slices (out of 50-100) in one 3D volume were manually segmented. The left ventricle (LV) and right ventricle (RV) labels were automatically propagated through the remaining 3D image using a patch-based segmentation algorithm [21].

Experimental Setting  The segmentation labels of the 3D volume by the 3D semi-automatic segmentation algorithm is propagated to the other 29 volumes in each cine dataset using our temporal registration method. The end-diastolic volume (EDV) and end-systolic volume (ESV) for the left and right ventricles are estimated from the segmentations and compared between the two imaging approaches (2D vs. 3D) using
correlation coefficient. The estimation using our proposed algorithm was blinded to the measurements from 2D slices.

**Experimental Results** Fig. 4.1 shows one example case where segmentation labels in the template (EDV phase) are transferred to the ESV phase in the series. We demonstrate a representative short-axis view and 3D models of both ventricles generated from the segmentation labels. Visually, this provides a good segmentation initialization to be refined in the ESV phase and also other phases, as we will discuss in Chapter 5. Fig. 4.2 reports that no significant differences are detected between ventricular volume measurements (including EDV, ESV, and stroke volume (SV)) from manually segmented 2D images and semi-automatically segmented 3D cine datasets using our method. We should also note that the volume measurements from the 2D images are not ground truth but the results from the current clinical routine.

![Figure 4.1.](image)

**Figure 4.1.** One example case from the study. We display the template (EDV) phase with segmentations from the 3D semi-automatic segmentation algorithm and the ESV phase with segmentations transferred from the template frame via our estimated transformation. A representative short-axis view and 3D models of both ventricles generated from the segmentation labels are shown; all computations are performed in 3D.

**Volume Measurements**

<table>
<thead>
<tr>
<th></th>
<th>Left Ventricle</th>
<th></th>
<th>Right Ventricle</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EDV</td>
<td>ESV</td>
<td>EDV</td>
<td>ESV</td>
</tr>
<tr>
<td>Breath-hold 2D (ml)</td>
<td>135.0±35.56</td>
<td>51.2±18.95</td>
<td>83.8±22.44</td>
<td>156.2±108.55</td>
</tr>
<tr>
<td>Free-breathing 3D (ml)</td>
<td>127.0±46.17</td>
<td>51.0±25.04</td>
<td>75.2±22.80</td>
<td>159.3±121.43</td>
</tr>
<tr>
<td>Difference (ml)</td>
<td>8.0±10.73</td>
<td>-0.5±10.73</td>
<td>8.6±6.57</td>
<td>-3.1±17.74</td>
</tr>
<tr>
<td>Difference Percentage</td>
<td>8.64±10.26%</td>
<td>3.88±24.38%</td>
<td>11.17±7.85%</td>
<td>0.50±9.74%</td>
</tr>
<tr>
<td>p-value</td>
<td>0.17</td>
<td>0.91</td>
<td>0.04</td>
<td>0.71</td>
</tr>
</tbody>
</table>

**Figure 4.2.** Ventricular measurements from manually segmented breath-hold 2D images and semi-automatically segmented 3D cine datasets (n=5). Values are mean ± standard deviation. EDV, end-diastolic volume; ESV, end-systolic volume; SV, stroke volume; and difference percentage, $2 \times |2D - 3D|/(2D + 3D)$. 
Chapter 5

Discussion and Conclusions

WE presented a HMM-based registration method to align images in MRI time series. Forward message passing incorporates the temporal model of motion into the estimation procedure. The filtered estimates are therefore based on not only the present volume frame and the template, but also on the previous frames in the series. Our method can be easily extended on other forms of transformation models and image similarity metrics. The experiment on in-utero BOLD MRI time series demonstrates the promise of our approach in a novel and challenging application. The experiments on cine cardiac MRI show that our approach can be used for segmenting 4D (3D+time) cardiac images by transferring labels in the template volume using our estimated transformations.

Future work will focus on obtaining robust estimates of the in-utero MRI signal time courses by augmenting the method with a backward pass and a model of ROI-specific intensity changes. Currently the intensity curves in some ROIs have spikes and drastic fluctuations within short time windows, one example case of which is shown in Fig. 3.4. We can observe that after our temporal alignment, the intensity change curves in the liver and in the placenta are somewhat smoothed, and the intensity change in the placenta does reflect the maternal oxygenation protocol. The intensity change in the brain, however, still has lots of spikes. This is mostly due to that the tracked organs move substantially in the image series that are severely affected by the bias field. Even though the cross-correlation used as the image similarity metric in our temporal registration captures local image differences despite the bias, tracking the intensity changes in corresponding regions across images is still affected by the bias field.

In addition, it is still challenging to fully automatically segment cardiac MRI images [21]. A few manually segmented slices are needed as manual input for segmenting one entire cardiac MRI volume. Our temporal alignment can facilitate generating good segmentation initialization from that segmented (template) volume to the rest frames of the cardiac MRI image series. Refinement from the transferred segmentation labels should be investigated to achieve more accurate segmentation for 4D cardiac MRI. We should also note that we are currently lack of ground truth in the presented cardiac application. Performing more comprehensive validation for 4D cardiac MRI segmentation is part of the future work. Our method can also be extended to segmentation of left and right atrium as well as great vessels from the 3D cine datasets.
Bibliography


BIBLIOGRAPHY

