A Spatiotemporal Volumetric Interpolation Network for 4D Dynamic Medical Image

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Abstract

Dynamic medical images are often limited in their application due to the large radiation doses and longer image scanning and reconstruction times. Existing methods attempt to reduce the volume samples in the dynamic sequence by interpolating the volumes between the acquired samples. However, these methods are limited to either 2D images and/or are unable to support large but periodic variations in the functional motion between the image volume samples. In this paper, we present a spatiotemporal volumetric interpolation network (SVIN) designed for 4D dynamic medical images. SVIN introduces dual networks: the first is the spatiotemporal motion network that leverages the 3D convolutional neural network (CNN) for unsupervised parametric volumetric registration to derive spatiotemporal motion field from a pair of image volumes; the second is the sequential volumetric interpolation network, which uses the derived motion field to interpolate image volumes, together with a new regression-based module to characterize the periodic motion cycles in functional organ structures. We also introduce an adaptive multi-scale architecture to capture the volumetric large anatomy motions. Experimental results demonstrated that our SVIN outperformed state-of-the-art temporal medical interpolation methods and natural video interpolation method that has been extended to support volumetric images. Code is available at \textsuperscript{1}.

1. Introduction

Dynamic medical imaging modalities enable the examination of functional and mechanical properties of the human body and are used for clinical applications, e.g., four-dimensional (4D) computed tomography (CT) for respiratory organ motion modelling [33], 4D magnetic resonance (MR) imaging for functional heart analysis [9], and 4D ultrasound (US) for echocardiography analysis [40]. These 4D modalities have high spatial (volumetric) and temporal (time sequence) sampling rate to capture the periodic motion cycles of organ activities, and this information is used for clinical decision making. However, the acquisition of these dynamic images requires larger radiation doses which may cause harm to humans, and longer image scanning and reconstruction times; these factors limit the use of 4D imaging modalities to broader clinical applications [32, 10].

Figure 1. The cardiac motions in two-time phases: End-Systole (ES) and End-Diastole (ED). The red bounding boxes highlight the heart structure. All images are shown in transaxial views, cropped in varying scales, to enlarge the heart.

To mitigate these factors, reducing the temporal sampling has been widely employed but this compromises valuable temporal information [23, 15]. In these approaches, the intermediary temporal frames can be used to improve visual inspection, quantitative modelling (e.g., dynamic motion...
and accurate interpretation / diagnosis. These benefits apply to various clinical applications, e.g., motion compensation in image-guided therapy [37], organ motion modeling [1] and alignment or fusion of 4D multi-modal images [1, 40]. Such interpolation methods are reliant on either non-rigid registration [6, 28, 40] or optical flow-based [30, 19] algorithms. Non-rigid registration approaches calculate the dense image volume correspondences that occur from one volume to another, and then uses the calculated correspondences to generate the intermediary volumes. Such approaches, however, often generate artifacts or fuzzy boundaries and do not perform well when the variations in anatomy or organ activity (e.g., size and shape) are large. An alternative approach was to use optical flow-based methods (using deep learning) [19, 38] to estimate a dense motion (i.e., deformation) field between image pairs. However, these methods were limited to 2D image interpolation and therefore did not utilize the rich spatial information inherent in medical image volumes. They are also limited when the motion between the image sequences are not in linear trajectory and are not changing in a constant velocity. Therefore, these approaches are not applicable to volumetric temporal imaging modalities that exhibit large non-linear motions in spatiotemporal space.

2. Related Works

We partitioned the related works into three categories which we deemed relevant to our research: (1) Medical dynamic image interpolation; (2) spatiotemporal motion field calculation for medical image and (3) natural video interpolation approaches.

2.1. Dynamic medical image interpolation

Many existing medical image interpolation methods rely upon optical flow-based or non-rigid registration methods to generate a linearly interpolated image by averaging pixel values between the adjacent image sequences [6, 22, 30, 28, 40, 37]. For instance, Ehrhardt et al. [14] presented an optical flow-based method to establish spatial correspondence between adjacent slices for cardiac temporal image. Zhang et al. [40] used non-rigid registration-based method to synthesize echocardiography and cardiovascular MR image sequences. The main advantage of these approaches is that they track spatiotemporal motion field, in a pixel-wise manner, between the neighboring images to estimate the interpolation. However, their assumption limited the spatiotemporal motion between the adjacent images to be in a linear trajectory, and thus disregarded the complex, non-linear motions apparent in functional organ structures. Recently, there are two CNN based methods for temporal interpolation via motion field for MR images from Lin Zhang et al. [25] and Kim et al. [19]. They achieved outstanding performance compared with previous works. However, their method did not support full 3D volumetric information and did not perform well when there were large variations in motion.

2.2. Learning spatiotemporal motion fields from volume image sequence

Many studies used deformable medical image registration techniques to estimate the motion field between the input image sequences. The deformable medical image registration techniques can be divided into two parts: non-learning based [36, 2, 20, 5, 13] and learning-based methods [21, 39, 35]. The typical non-learning based approaches are free-form deformations with B-splines [2], Demons [36] and ANTs [3]. These approaches optimize displacement vector fields by calculating the similarity of the topological structures. Deep learning-based methods, in recent years, used labelled data of spatiotemporal motion field and have shown great performances [21, 39, 35]. However, their performance was dependent upon the availability of large-scale labelled data. To address this, several unsupervised methods were proposed to predict the spatiotemporal motion field [12, 24, 4]. Although these methods demonstrated promising results, [12] and [24] were only useful in patch-based volumes or in 2D slices. Jiang et al. [4] recently developed
a CNN, VoxelMorph which used full 3D volumetric information. However, it was not designed for dynamic image sequences where it has large variations in motion.

2.3. Natural video interpolation approaches

Video interpolation is an active research task in natural scenes, e.g., model-based tracking, patch identification, and matching and framerate upsampling [17, 11, 27, 29]. Niklaus et al. [31] developed a spatially-adaptive convolution kernel to estimate the motion for each pixels. Liu et al. [26] divided the frame interpolation into two steps, optical flow estimation and image interpolation. Their network learnt an input pair of consecutive frames in an unsupervised manner and then refined the interpolation based on the outputs of the estimation. Jiang et al. [18] presented Slomo – a technique which interpolates frame motion by linearly combining bi-directional optical flows, and then further refining the estimated motion flow field through an end-to-end CNN. Recently, Peleg et al. [34] presented a multi-scale structured architecture neural network to better capture the local details from high resolutions frame. However, when considering the application of these methods to dynamic medical images interpolation, this is a challenging problem as the temporal sampling in medical image volume sequences are much lower than that of natural scene videos. In addition, the deformations and visual differences in dynamic medical images are comparatively more complex and non-trivial than natural scene videos.

3. Proposed Method

Let \( \{I_T, T = 1, 2, ..., N\} \) be a sequence of volumetric images representing the cardiac motion from end-diastole (ED) \( (T = 1) \) to end-systole (ES) \( (T = N) \) phase, and let \( \{I_i, I_j \mid (i, j) \in T\} \) be a pair of cardiac images indicating two random time points within the cardiac motion. Our aim is to interpolate the intermediate image \( I_t, (t \in T) \). For this work, we used images at ED (denote as \( I_{ED} \)) and ES (denote as \( I_{ES} \)) phase to interpolate the complete the cardiac motion. \( \{\phi_{i \rightarrow j}, \phi_{j \rightarrow i}\} \) denotes the motion field between \( I_i \) and \( I_j \) in bi-directions.

Fig. 2 shows the overall proposed method. Initially, spatiotemporal motion network was used to learn and capture bi-directional motion fields between \( I_{ED} \) and \( I_{ES} \) in an unsupervised manner. Two linearly interpolated intermediate images were then coarsely created using the learned spatiotemporal motion fields, \( \phi_{ED \rightarrow ES} \) and \( \phi_{ES \rightarrow ED} \). Using the coarsely interpolated intermediate images and their corresponding deformation fields, we further refined the coarse intermediate images by the volumetric interpolation network. Specifically, both of our volumetric motion estimation and interpolation networks are using an adaptive multi-scale architecture which enables to capture various types motions - both small and large volume spatiotemporal deformations (see Fig. 2 and 3).
3.1. Spatiotemporal volumetric motion field estimation

Fig. 3 presents the architecture of 3D CNN for spatiotemporal motion field estimation. We estimate a motion field that can represent the voxel-wise motion flow of volume images at two individual time points. This can be represented as a function $D_\theta(I_i, I_j) = \phi_{i\rightarrow j}(\Delta x, \Delta y, \Delta z)$, where $\phi_{i\rightarrow j}(\Delta x, \Delta y, \Delta z)$ indicates the vectors that represent the movement in 3D space and $\theta$ are the learnable parameters of the network. We used an encoder-decoder architecture with skip connections for generating $\phi_{i\rightarrow j}$ by given $I_i$ and $I_j$.

In order to produce a volumetric motion field that can cover various types of deformations, we propose an adaptive multi-scale architecture that embeds both a global and a local learning. More specifically, for global learning, our motion field estimation network focuses on large deformation, while the volumetric images in a low-scale level would ignore the local details while more detailed information will be covered when the volumetric image in a high-scale. In addition, the global deformation from low-scale is integrated to high-scale, which reduces the difficulty of the network for learning and constrains the network to pay more attention to detailed deformation. Our deformation field can be defined as:

$$\phi_{i\rightarrow j} = D_\theta(I_i, I_j) \quad \text{or} \quad \phi_{j\rightarrow i} = D_\theta(I_j, I_i)$$ (1)

$$I_j = \zeta(I_i|\phi_{i\rightarrow j}) \quad \text{or} \quad I_i = \zeta(I_j|\phi_{j\rightarrow i})$$ (2)

where $\zeta(I_i|\phi_{i\rightarrow j})$ representing the warped image by the spatial vector field $\phi_{i\rightarrow j}$ with bilinear interpolation.

For training our motion field estimation network, we used an image-wise similarity loss and a motion field smoothness regularization loss with an adaptive multi-scale network architecture (as shown in Fig. 3). Given the network output $\phi_{ED\rightarrow j}^n \{ n = 1, 2, 3 \}$, where $i$ denotes the volumetric images at different scales (we used 3 different scales in total), we define a motion field smoothness regularization loss as:

$$L_\phi(D_\theta(I_i, I_j)) = \sum_{c=1}^{3} \| \nabla \phi_{\cdot \rightarrow j}^c \|_1$$ (3)

Where $\nabla$ is the gradient operator. The image-wise similarity loss was leveraged from VoxelMorph [4] and this can be defined as:

$$L_s(\zeta(I_i|\phi_{i\rightarrow j}), I_j) = \sum_{c=1}^{3} \| \zeta(I_i|\phi_{\cdot \rightarrow j}^c) - I_j^c \|_2$$ (4)

3.2. Sequential volumetric interpolation network

Based on the derived deformation fields $\phi_{ED\rightarrow ES}$ and $\phi_{ES\rightarrow ED}$, we used linear interpolation approach to synthesize the intermediate deformation fields, as shown in follows:

$$\phi_{ED\rightarrow t} = t\phi_{ED\rightarrow ES}$$ (5)

$$\phi_{ES\rightarrow t} = (1 - t)\phi_{ES\rightarrow ED}$$ (6)

Based on Eqs. 1 and 2, the linear interpolation based deformation field for $I_t$ can be approximated as:

$$\tilde{I}_t = (1 - t)\zeta(I_{ED}|\phi_{ED\rightarrow t}) + t\zeta(I_{ES}|\phi_{ES\rightarrow t})$$ (7)
To improve the consistency in bi-directions, Eq. 5 and 6 can be modified to as follows:

\[
\begin{align*}
\phi_{ED\rightarrow t} &= t(1-t)\phi_{ED\rightarrow ES} \\
&\quad - t^2 \zeta (\phi_{ES\rightarrow ED} | \phi_{ES\rightarrow ED}) \\
&\quad + t(1-t)\phi_{ED\rightarrow ED} \\
\phi_{ES\rightarrow t} &= -(1-t)^2 \zeta (\phi_{ED\rightarrow ES} | \phi_{ED\rightarrow ES} ) \\
&\quad + (1-t)\phi_{ES\rightarrow ED} 
\end{align*}
\]

(8)

(9)

In addition, we introduce a hyper-weight map \( \gamma \) to balance the importance of using deformation from the bi-directions (forward and backward directions) and this can be defined as:

\[
\gamma_{ES} = 1 - \gamma_{ED}
\]

(10)

Thus, the linear image interpolation based on bi-directional deformation and \( \gamma \) can be defined as:

\[
\tilde{I}_t = (1-t)\gamma_{ED} \zeta (I_{ED} | \phi_{ED\rightarrow t}) \\
&\quad + t \gamma_{ES} \zeta (I_{ES} | \phi_{ES\rightarrow t})
\]

(11)

As exemplified in right-side of Fig. 2, we used an adaptive multi-scale network architecture to ensure the synthesized intermediate volumetric images will have a high spatial-temporal resolution.

3.3. Regression-based module for interpolation constraints

Since most biological movements have a relatively fixed motion pattern, especially in cardiac motion [8], we present a regression-based module to model the relationship between cardiac motion of the cardiac cycle and time phase (as shown in Fig. 4). Specifically, we attempted to build a regression model representing the population-based cardiac motion vector which indicate the shape variability at individual time point. The population-based cardiac motions at individual time point was then used to constrain the appearance of the synthetic intermediate volumetric images. Our regression estimation \( R_{\theta} \) at time point \( t \) is defined as:

\[
\hat{t} = R_{\theta}(\phi_{ED\rightarrow t} - t\phi_{ED\rightarrow ES}; \phi_{ES\rightarrow t} - (1-t)\phi_{ES\rightarrow ED})
\]

(12)

3.4. Training details for volumetric interpolation

For training our sequential volumetric interpolation network, our loss function is defined as a sum of an image-wise similarity loss \( L_{\text{similar}} \), a regression loss \( L_r \) and a regularization loss \( L_g \):

\[
\mathcal{L} = \lambda_s L_{\text{similar}} + \lambda_r L_r + \lambda_g L_g
\]

(13)

where image-wise similarity loss \( L_{\text{similar}} \) is used to evaluate the similarity of the predicted synthetic intermediate images and the real intermediate images at multiple image scales and is defined as:

\[
\mathcal{L}_{\text{similar}} = \sum_{c=1}^{N} \sum_{k=1}^{3} \| \tilde{I}_{tk} - I_{tk} \|_2
\]

(14)

where \( \sum_{c=1}^{3}() \) represents a 3-scales volumetric image loss. \( \{ I_{tn} \}_{n=1}^{N} \) represents the real intermediate volumetric images and \( \{ \tilde{I}_{tn} \}_{n=1}^{N} \) represents the predicted synthetic intermediate volumetric images. The regression loss \( L_r \) is defined as the appearance difference at individual time point:

\[
L_r = \sum_{k=1}^{N} \| \hat{t}_k - t_k \|_1
\]

(15)

Regularization loss \( L_g \) is used to constrain the predicted motions to be consistent in bi-directions and is defined as:

\[
L_g = \sum_{c=1}^{3} \| \nabla \phi_{ED\rightarrow t} + \nabla \phi_{ES\rightarrow t} \|_1
\]

(16)

The weights \( \lambda_r = 1; \lambda_s = 500; \lambda_g = 50 \) have been set empirically using a validation set.

4. Experiments

4.1. Materials and implementation details

We demonstrate our method with two datasets: 4D Cardiac CT (4D-C-CT), and ACDC (4D-MR cardiac cine or tagged MR imaging) [7]. Fig. 5 shows a snapshot of randomly sampled cardiac sequence volume slices. The 4D-C-CT dataset consists of 18 patient data, each having 5 time points (image volumes) from ED to ES. Image volume is characterized by a high-resolution ranging from 0.32 to 0.45 mm in intra-slice (x- and y-resolutions) and from 0.37mm to 0.82mm in inter-slice (z-resolution). The ACDC dataset contains 100 patient data. On average, each patient has 10.93 time points from ED to ES and it has an imaging resolution from 1.37 to 1.68 mm in x- and y-resolution and 5 to 10 mm in z-resolution. All scans of 4D-C-CT were resampled to a 128x128x96 grid and crop resulting images to
96x96x96. For ACDC dataset, we resampled all scans to 160x160x10. We pad ACDC data in z-axis by 0, increasing its size to 160x160x12 to reduce the border effects of 3D convolution. We randomly selected 80 training / 20 testing patient data and applied contrast-normalization to both of datasets, consistent to other similar researches [16].

We implemented all the networks using Pytorch library and was trained on two 11GB Nvidia 1080Ti GPUs. All models were trained with a learning rate of 0.0001. In all our evaluations, we used 3-fold cross-validation on both the datasets.

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4.2. Evaluation and metrics

In order to evaluate the two networks in our SVIN, we conducted an ablation study. For the unsupervised spatiotemporal motion network, we compared it with state-of-the-art CNN based deformable medical image registration – VoxelMorph [4]. For the interpolation network, state-of-the-art image interpolation methods were used in the comparison including (i) RVL [40] – registration-based volume linear interpolation for medical images, (ii) MFIN [25] – CNN-based medical image interpolation (2D slice-based), and (iii) Slomo – natural video interpolation [18] in 2D as well as its extension to work on medical image volumes (3D-Slomo). For image volume interpolation, we interpolated 3 intermediate volumes in between the ED-ES frames (see Fig 5), evenly distributed across the time points.

We used the standard image interpolation evaluation metrics including Peak Signal-to-Noise Ratio (PSNR), Structural Similarity Index (SSIM), Mean Squared Error, and Normalized Root Mean Square Error (NRMSE). We used the same evaluation metrics for the spatiotemporal motion field estimation, consistent to other medical image registration approaches [25]. In addition, we further used Dice Similarity Coefficient (DSC) to measure the usefulness of our interpolation in medical imaging applications.

5. Results and Discussion

5.1. Ablation study – spatiotemporal volumetric motion field estimation

The results of motion field estimation on two datasets - 4D-C-CT and ACDC are shown in Table 1 and 2. Our results show that motion estimation network with our adaptive architecture outperforms the recent VoxelMorph [4] across all metrics on 4D-C-CT dataset, achieving the PSNR score of 33.176, NRMSE of 0.1388, SSIM of 0.9185 and MSE of 0.00197. Similarly, it also had better scores across all metrics on ACDC dataset. Our motion estimation architecture had higher improvements on 4D-C-CT dataset than that of ACDC dataset relative to VoxelMorph. We attribute this to our robust multi-scale adaptive 3D CNN which can effectively learn both large and small variations in motion.

Fig. 6 shows the synthesized volumes based on the derived motion field and their corresponding warped segmentation results. It clearly shows that the warped segmentation results from the motion field learnt by our motion architecture are more similar to the ground truth.

5.2. Comparison with the state-of-the-art interpolation methods

Table 3 and 4 represent the interpolation results of different time points from ED to ES on 4D-C-CT and ACDC.
datasets, respectively. As expected, results show that the intermediate volumes that are in later time points had better performances. This is due to the fact that the earlier time points have larger motion variations, which contributed to its lower accuracy.

Table 3. Multi-volume cardiac sequence interpolation results on the 4D-C-CT dataset.

|        | MSE($10^{-2}$) | PSNR   | NRMSE  | SSIM  |
|--------|----------------|--------|--------|-------|
| 1st-point | 0.45           | 29.45   | 0.211  | 0.830 |
| 2nd-point | 0.43           | 29.47   | 0.210  | 0.825 |
| 3rd-point | 0.28           | 31.52   | 0.165  | 0.863 |

Table 4. Multi-volume cardiac sequence interpolation results on the ACDC dataset.

|        | MSE($10^{-2}$) | PSNR   | NRMSE  | SSIM  |
|--------|----------------|--------|--------|-------|
| 1st-point | 1.22           | 39.34  | 0.109  | 0.934 |
| 2nd-point | 0.95           | 40.42  | 0.087  | 0.950 |
| 3rd-point | 0.28           | 45.86  | 0.052  | 0.977 |

The comparative quantitative results for volume interpolation are shown in Table 5 and 6. SVIN outperformed all other state-of-the-art interpolation method on 4D-C-CT dataset across all measures. Similarly, it also had the best scores across all metrics on the ACDC dataset. We attribute this to our adaptive multi-scale architecture capturing the variant type of motions and regression-based module which effectively constrains the intermediate volumetric motions and learn relevant inherent functional motion patterns (see Fig. 7 and 8). Our results show that the RVLI was the closest to our results. However, the RVLI was not able to accurately interpolate the volumes when there were artifacts as evident in Fig. 7 and 8. MFIN and Slomo also did not consider full 3D volumetric information, i.e., limited to 2D space, which contributed to its lower scores. As expected, our implemented 3D-Slomo produced a better result relative to the 2D methods. The 3D-Slomo, however, was not able to accurately synthesize the clear organ boundary and estimate the motion trajectory when there are large changes of cardiac activities (see Fig. 7).

Table 5. Performance comparisons on the 4D-C-CT dataset.

|        | MSE($10^{-2}$) | PSNR   | NRMSE  | SSIM  | Dsc  |
|--------|----------------|--------|--------|-------|------|
| MFIN  | 1.06           | 26.84  | 0.308  | 0.709 | 0.844|
| Slomo | 1.13           | 26.52  | 0.308  | 0.704 | 0.839|
| 3D-Slomo | 0.92         | 26.33  | 0.303  | 0.713 | 0.872|
| RVLI | 0.54           | 28.70  | 0.237  | 0.806 | -    |
| Ours  | **0.39**       | **30.15** | **0.196** | **0.840** | **0.917** |
Table 6. Performance comparisons on the ACDC dataset.

|          | MSE(10^{-1}) | PSNR | NRMSE | SSIM |
|----------|--------------|------|-------|------|
| MFIN     | 1.082        | 30.69| 0.309 | 0.607|
| Slomo    | 1.001        | 31.08| 0.296 | 0.630|
| 3D-Slomo | 0.341        | 35.27| 0.178 | 0.845|
| RVLI     | 0.331        | 35.66| 0.173 | 0.860|
| Ours     | 0.081        | 41.87| 0.085 | 0.953|

6. Conclusion

6.1. Summary

We presented a novel interpolation method for 4D dynamic medical images. Our proposed two-stage network was designed to exploit the volumetric medical images that exhibit large variations between the motion sequences. Our SVIN outperformed state-of-the-art temporal medical interpolation methods as well as natural video interpolation methods that have been extended to support volumetric images. Ablation study further exemplified that our motion network with our SVIN was able to better represent the large functional motion compared with the state-of-the-art unsupervised medical registration methods.

6.2. Extensions implementation

In Section 4, we discussed our multi-scale architecture for learning the spatial appearance volume in different scales to retain the spatial information for volume synthesis. Rather than learning a spatial transform model, as future work, we will implement our architecture in other volume synthesis task.

We leveraged a regression based constrain module to explore the potential ‘rule’ associated with functional motion. This could be extended to other 4D volumetric medical image tasks having periodic cycle motion.

Although we demonstrated our SVIN model on cardiac imaging modality, there is no restriction of our method to be applied to other dynamic images. We suggest that our method is broadly applicable to other 4D medical images, as well as to non-medical image volume interpolation problems where the motion field can be modeled.

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