Symmetry and inverse consistency are two important features for deformable image registration in medical imaging analysis. This work presents a novel registration method computing symmetric and inverse-consistent image alignment efficiently while preserving high accuracy and consistency of the mapping. This is achieved by optimizing a symmetric energy functional estimating forward and backward transformations constrained by the transformations being inverse to each other. In other words, this approach uses an interleaved optimization scheme borrowed from multiobjective optimization theory constrained by an inverse-consistency criterion. The new optimization scheme provides an efficient search in the space of diffeomorphisms while solving the symmetric registration problem. Moreover, it is not bound to any specific optimizer or energy functional other than to the requirement of being well-defined. In our experiments on clinical cardiac data, superior performance compared to standard, one-directional registration is achieved. The resulting inverse-consistency and symmetry errors match previously reported values while being computed more efficiently. This general approach addresses a clinical need for consistent, highly accurate image alignment achieved in a practically accepted timeframe.

**Index Terms**— Image Registration, Optimization Methods, Magnetic Resonance, Time Series Analysis

1. INTRODUCTION

Deformable registration plays an essential role in a number of challenging medical image analysis tasks such as motion correction and analysis, template matching, segmentation, image reconstruction, and so on. Symmetry and inverse-consistency of the estimated image alignment becomes increasingly important in clinical systems and applications. For example, in the analysis of ventricular function in spatio-temporal cardiac cine Magnet Resonance (MR) data, the inverse transformation provides means to spatially connect all time points in the series. In treatment follow-up studies, symmetric deformable registration is utilized to compare before and after treatment pathologies. Moreover, due to the large variety of image content in clinical data, symmetric registration provides more accurate and consistent image alignments in applications such as perfusion MR studies where large breathing motion needs to be compensated while contrast agent is flowing in and out of the image plane.

Consequently, the area of symmetric and inverse-consistent image registration is a very active field of which we provide a brief summary here. Christensen and colleagues were the first to introduce the concept of consistent image registration in [1] by evaluation forward and backward transformation direction while using a penalty term to achieve inverse-consistency. Symmetric diffeomorphic registration following the geodesic path between the two images was described by Avants and colleagues [2]. Hernandez et al. parametrize paths of diffeomorphisms with stationary vector field flows to register images using the LDDMM (Large Deformation Diffeomorphic Metric Mapping) paradigm [3] and Tagare et al. [4] focus on achieving symmetry through the cost function without involving the inverse direction. Unfortunately, most contributions remain largely academic with few work focussing on practical aspects such as achieving similar numerical accuracy in clinically affordable time-frames. Yang et al. [5] present an inverse-consistent registration algorithm that is similar to Avants et al. diffeomorphic mapping, but focusses on simplicity and computational efficiency. Nevertheless, their reported results are still costly for clinical applications.

In this work, we use the theory of multiobjective optimization to introduce an interleaved optimization scheme subject to constraints of symmetry and inverse-consistency of the estimated image alignment. In this optimization scheme the gradient of a symmetric energy functional is descended by alternating the registration direction after each iteration. At the same time, inverse consistency is enforced through updating the inverse direction. The numerical implementation of this scheme can be done efficiently and the resulting algorithm requires little extra time per iteration when compared to a highly optimized, one-directional method. Moreover, the proposed method achieves accurate image registration while requiring significantly less time to be computed than state-of-the-art symmetric registration methods.

The paper is organized as follows. Section 2 introduces the deformable registration framework followed by the proposed interleaved optimization scheme. In the subsequent section 3 experiments on synthetic and clinical data demon-
strate the feasibility of our method. We conclude with discussions on future directions in section 4.

2. SYMMETRIC AND INVERSE-CONSISTENT REGISTRATION

Let’s consider the two images are described by the square-integrable functions \( f_1 : \mathbb{R}^n \to \mathbb{R} \) and \( f_2 : \mathbb{R}^n \to \mathbb{R} \). Deformable image registration is the search for a function \( \Phi_{12} : \Omega \to \Omega \) that transforms each location \( x \) in \( \Omega \) (\( \Omega \) is a bounded region of \( \mathbb{R}^n \), \( n = 2, 3 \)) using a displacement field \( u : \Omega \to \mathbb{R}^n \) such that both images are accurately aligned: \( \Phi_{12}(x) = x + u(x) \). This function is searched in a set of admissible functions such that it minimizes an energy functional \( \mathcal{J} \), and the minimizing function \( \hat{\Phi} \) represents the solution of the deformable registration problem:

\[
\hat{\Phi}_{12} = \arg \min \mathcal{J}(f_1, f_2, \Phi_{12}),
\]

where \( \mathcal{J} \) depends on the two images \( f_1, f_2 \) and \( \Phi_{12} \) describing the transformation from \( f_1 \) to \( f_2 \). The deformation function \( \Phi_{12} \) can be retrieved by descending the gradient of \( \mathcal{J} \) using an iterative scheme of composing incremental updates of the deformation:

\[
\Phi_{12,k+1} = \Phi_{12,k} \circ \left( \text{id} + \tau \cdot \nabla u \mathcal{J} \ast G_\sigma \right),
\]

with \( \tau \) controlling the step size along the gradient, and \( G_\sigma \) denoting a Gaussian filter. Step size parameter \( \tau \) describes a trade-off between speed and accuracy. An example of a robust energy functional in images with similar intensity profiles is the sum-of-squared differences (SSD) that can be described as a symmetric similarity measure by

\[
\mathcal{J}_{12} = \int_\Omega (f_1 - f_2 \circ \Phi_{12})^2 + \lambda \mathcal{J}_{\text{smooth}}(u) \, dx,
\]

\[
\mathcal{J}_{21} = \int_\Omega (f_1 \circ \Phi_{21} - f_2)^2 + \lambda \mathcal{J}_{\text{smooth}}(v) \, dx,
\]

where \( \mathcal{J}_{12} \) denotes \( \mathcal{J}(f_1, f_2, \Phi_{12}) \), and \( \mathcal{J}_{\text{smooth}} \) preventing fast variations of the displacements \( u \) and \( v \) respectively. There are two reasons of asymmetry in registration formulations. Firstly, asymmetry is due to the use of Euclidean volume forms [4]. Secondly, many image registration similarity criteria do not uniquely specify correspondence between the two images due to image complexity, an infinite-dimensional transformation space, and the one-sided choice of the alignment image in standard registration methods. However, a registration method is symmetric if and only if the following equality is satisfied:

\[
\mathcal{J}(f_1, f_2, \Phi_{12}) = \mathcal{J}(f_2, f_1, \Phi_{12}^{-1}),
\]

for all ordered functions \( (f_1, f_2) \) and all \( \Phi_{12} \in C^2 \), with \( \det \Phi_{12}(x) > 0 \). The inverse transformation \( \Phi_{12}^{-1} \) describes the transformation from \( f_2 \) to \( f_1 \) and satisfies

\[
\Phi_{12} \circ \Phi_{12}^{-1} = \Phi_{21} \circ \Phi_{21}^{-1} = \text{id},
\]

as proposed by Christensen and colleagues [1] provides an inverse-consistent deformable registration algorithm in its original form. In order to retrieve the minimizer of energy (7), Christensen jointly estimates forward and backward transformations while adding an inverse-consistency penalty. The computational efforts and memory footprints of current optimization approaches for (7) are, at minimum, double the efforts required for one-directional registration independent of the optimization strategy (e.g., gradient descent, line search, etc.).

We propose a deformable registration algorithm that solves a symmetric energy functional and provides forward as well as inverse deformations at little performance loss to the one-directional and asymmetric estimation. This is achieved by making use of the theory of multiobjective optimization stating that two or more conflicting objectives can be optimized simultaneously subject to certain constraints [6]. In our context, the two competing objectives are forward and backward deformation estimation, i.e., \( \mathcal{J}_{12} \) and \( \mathcal{J}_{21} \), under the constraint that both are to be inverses of each other. In order to solve the symmetric registration problem in (7), we propose an interleaved optimization scheme alternating the optimizing directions at each iteration. The inverse-consistency constraint is enforced at each iteration. The outline of the first few iterations in such an interleaved optimization scheme is

\[
\Phi_{12,0} = \Phi_{21,0} = \Phi_{21,0}^{-1} = \text{id},
\]

\[
\Phi_{12,1} = \Phi_{21,0} \circ (\text{id} + \tau \cdot \nabla u \mathcal{J}_{12} \ast G_\sigma),
\]

\[
\Phi_{21,1,\text{initial}} = \Phi_{12,1}^{-1},
\]

\[
\Phi_{21,2} = \Phi_{21,1} \circ (\text{id} + \tau \cdot \nabla v \mathcal{J}_{21} \ast G_\sigma),
\]

\[
\Phi_{12,2,\text{initial}} = \Phi_{21,2}^{-1},
\]

\[
\Phi_{12,3} = \Phi_{12,2} \circ (\text{id} + \tau \cdot \nabla u \mathcal{J}_{12} \ast G_\sigma),
\]

with an iterative inverse transformation estimation step. For-
ward $\Phi_{12,k}$ and backward $\Phi_{21,k}$ transformations at iteration $k$ are forced to be inverse by the fixed-point iteration scheme:

$$
\varphi_{i+1}^{-1}(x) = \frac{1}{2} ( - \varphi_i (\text{id} \circ \varphi_i^{-1}(x)) + \varphi_i^{-1}(x)) \quad (9)
$$

where $N$ describes how many iterations should be taken for the estimation\(^1\). Setting $\varphi = \Phi_{12,k}$ and $\varphi^{-1} = \Phi_{21,k}$ enforces the inverse condition. The correction step can be repeated after the optimization has converged in order to further decrease the inverse-consistency error. Note that our approach differs from [1] to the extent that we explicitly enforce inverse-consistency and symmetry and do not use a penalty scheme. Simultaneous estimation of forward and backward direction is achieved through generating a highly accurate inverse at each iteration that is used as the initial forward direction for the next iteration. At convergence of the interleaved optimization scheme of (9) the solution $\hat{\Phi} = \{\Phi_{12}, \Phi_{21}\}$ minimizes the symmetric energy functional (7) (e.g. see also figure 1). Note that due to performance reasons, our algorithm is terminated by several convergence criteria.

The swapping of registration direction and estimation of corresponding inverse transformation during each iteration can be implemented efficiently such that the difference in computational efforts compared to one-directional deformable registration is kept small.

Our interleaved optimization scheme is neither restricted to a particular representation of transformation nor to any specific energy functional, and can be applied to any $J$ that is differentiable and whose gradient exist and can be computed. Though several choices for $J$ are feasible, we will simply focus on the local cross-correlation (LCC) here because it is a robust and accurate similarity measure in clinical MRI. The LCC is defined as

$$
J_{12}(x) = \ldots \sum_{i,j} \sum_{n} (f_1(i,j) - \bar{f}_1)(f_2 \circ \Phi_{12}(i,j) - \bar{f}_2) \sqrt{\sum_{n} (f_1(i,j) - \bar{f}_1)^2 \sum_{n} (f_2 \circ \Phi_{12}(i,j) - \bar{f}_2)^2},
$$

where $\bar{f}_1$ and $\bar{f}_2$ are the mean values of the neighborhood $n$ around location $(i,j) \in \mathbb{R}^2$ in both images, and $N_n$ determines the number of elements in that neighborhood. The variational gradients of SSD and LCC can be computed and are well-defined as shown in [7].

3. EXPERIMENTAL RESULTS

Two types of experiments have been performed to demonstrate the symmetric and inverse-consistent deformable registration algorithm. At first, high registration accuracy of symmetric image registration is demonstrated on synthetic images. The second set of experiments is designed to report inverse-consistency (IC), and symmetric registration (Sym) errors as well as computational efforts on clinical cardiac MRI data. The errors are defined as $|\Phi|_{IC} = ||\Phi_{12} \circ \Phi_{21}^{-1} - \text{id}||^2$ and $|\Phi|_{Sym} = ||\Phi_{12} \circ \Phi_{21} - \text{id}||^2$ and presented in pixel units. We use a coarse-to-fine strategy of 4 levels to capture large deformations, a max. number of iterations of 32 per level, and terminate the registration if an iteration results in an increased energy value. All results were generated on a Windows\(^2\) system equipped with a dual core Intel Xeon\(^\circledR\) 2.33 GHz processor and 2GB RAM.

In figure 2, two images $f_1, f_2$ taken from a synthetic perfusion MR time series are shown. The images inhibit a simple diagonal translation while disk intensities change simulating in- and out-flowing contrast agent. Due to this signal change image gradients may appear, disappear, or weaken across the time series. Consequently, it will be challenging for intensity based deformable registration methods to achieve high accuracy rates in such data. Figure 2 elegantly simulates the effect of vanishing gradients and varying intensities for the disks. Registration accuracy of the dense deformation $\Phi$ is evaluated by computing $J(f_1, f_2, \Phi_{12})$ and $J(f_2, f_3, \Phi_{23})$, where $f_1 = f_3$, and measuring the accuracy error $|\Phi|_{err} = ||\Phi_{12} \circ \Phi_{23} - \text{id}||^2$. Though this experiment also evaluates symmetry (i.e. $f_1 = f_3$), it moreover measures the error accumulation of individual registrations. When comparing the accuracy of one-directional $\Phi_{one}$ and bi-directional, symmetric transformation $\Phi_{sym}$, the advantage of incorporating image information from both images is striking. Figures 2c and 2d visualize the accumulated accuracy error images scaled to the error maximum. Note that $\max(|\Phi_{one}|_{err}) = 4.08$ and $\max(|\Phi_{sym}|_{err}) = 0.80$. The mean and standard deviations of accuracy errors from the entire synthetic time series of 40 phases are $\bar{(\Phi_{one})} = 0.72 \pm 1.23$ and $\bar{(\Phi_{sym})} = 0.15 \pm 0.21$. Moreover, estimating forward and inverse deformation, i.e. $\Phi_{sym}$, required only 45% more time than estimating just forward direction, i.e. $\Phi_{one}$.

The second set of experiments demonstrates performance on three different clinical cardiac time series data sets, i.e

\(^1\)It has been shown that the averaging formulation in (9) converges.

\(^2\)One- and bi-directional registration on synthetic images simulating perfusion MRI. Maximum error accumulation (pixel), $\max(|\Phi_{one}|_{IC}) = 4.0826$ and $\max(|\Phi_{sym}|_{IC}) = 0.8036$, shows the superior consistency of symmetric registration.

![Fig. 2. One- and bi-directional registration on synthetic images simulating perfusion MRI.](image-url)
cine, perfusion, and tagged MRI. The cine MRI was acquired using a routine TrueFisp (SSFP) protocol resulting in 13 short axis slices with 25 phases (256x208px). Perfusion MRI was acquired with a TurboFlash protocol providing 1 slice of 40 phases (260x320px), and the tagged MRI data contains 1 slice of 15 images (192x156). We chose this data due to the largely different motion typical for each set. IC, Sym error, and computational efforts are computed for each entire data set. Results are computed per registration and averaged over the respective data set. Table 1 plots the IC and Sym errors per data set and table 2 presents the respective timings. For comparison purposes, we added previously reported results of symmetric, inverse-consistent techniques to table 1. Both tables report the achieved inverse-consistency and symmetry properties of our approach that are achieved in, up to our knowledge, unreported efficiency. Our approach needs, at best, less than 45% additional time than a highly optimized one-directional registration algorithm.

Symmetry and the availability of an accurate inverse deformation is beneficial to a tremendous amount of clinical applications. For example, in time-series analysis, the inverse can be used to eliminate the dependency on the chosen reference frame. Consequently, all favorable properties of the proposed approach can provide a highly accurate tracking algorithm that elegantly intertwines with a fully-automatic and robust algorithm for left-ventricular segmentation in cardiac cine data [8]. We have employed the presented approach in [8], but did not describe, measure, and validate it as it is performed here.

### 4. DISCUSSION AND CONCLUSION

We have developed an efficient interleaved update scheme for iterative gradient descent optimization and showed how to solve a symmetric registration formulation in a clinically acceptable time-frame through utilizing information from both image domains. The additional computational effort for accurate symmetric and inverse-consistent deformable registration is about 45%-75% in comparison to a highly optimized, one-directional algorithm. This amounts to a practical algorithm benefiting numerous clinical applications. In future work, we would like to investigate performance on higher dimensional medical data since the presented data is inherently 2-dimensional. It will also be interesting to transfer the proposed optimization concepts to other image processing methods in biomedical imaging to allow other sophisticated methods to enter the clinical domain.

### 5. REFERENCES


---

**Table 1.** Inverse-consistency and symmetric registration errors (in pixels) of the deformation field in cardiac MR data.

<table>
<thead>
<tr>
<th>Method</th>
<th>IC Error</th>
<th>Sym Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christensen et al. [1]</td>
<td>0.571; 0.749</td>
<td>n/a</td>
</tr>
<tr>
<td>Yang et al. [5]</td>
<td>0.0022 ± 0.018</td>
<td>n/a</td>
</tr>
<tr>
<td>Int. Opt. (synthetic)</td>
<td>0.0005 ± 0.005</td>
<td>0.1471 ± 0.205</td>
</tr>
<tr>
<td>Int. Opt. (cine)</td>
<td>0.0011 ± 0.001</td>
<td>0.0459 ± 0.040</td>
</tr>
<tr>
<td>Int. Opt. (perfusion)</td>
<td>0.0052 ± 0.011</td>
<td>0.4741 ± 0.255</td>
</tr>
<tr>
<td>Int. Opt. (tagged)</td>
<td>0.0071 ± 0.008</td>
<td>0.1384 ± 0.2066</td>
</tr>
</tbody>
</table>

**Table 2.** Computation time per registration in seconds average over data set, plus additional time needed to estimate $\Delta^{sym}$ compared to an efficient implementation of computing $\Delta^{one}$.

<table>
<thead>
<tr>
<th>Methods</th>
<th>synth.</th>
<th>cine</th>
<th>perfusion</th>
<th>tagged</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uni-Directional</td>
<td>0.85s</td>
<td>0.69s</td>
<td>1.26s</td>
<td>0.42s</td>
</tr>
<tr>
<td>Symmetric - Int.Opt.</td>
<td>1.24s</td>
<td>1.10s</td>
<td>2.16s</td>
<td>0.75s</td>
</tr>
<tr>
<td>Added Time (%)</td>
<td>45%</td>
<td>59%</td>
<td>71%</td>
<td>78%</td>
</tr>
</tbody>
</table>