Diffeomorphic Directly Manipulated Free-Form Deformation Image Registration via Vector Field Flows

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Abstract. Motivated by previous work [8] and recent diffeomorphic image registration developments in which the characteristic velocity field is represented by spatiotemporal B-splines [2], we present a diffeomorphic B-spline-based image registration algorithm combining and extending these techniques. The advancements of the proposed framework over previous work include analytical integration of the continuous B-spline velocity field, potential spatial weighting of the gradient permitting (among other things) enforcement of stationary boundary conditions, multiresolution in terms of the B-spline mesh, facilitating the incorporation of landmark information, and the possibility of modeling temporal periodicity. In addition to theoretical and practical discussions of our contribution, we also describe its parallelized implementation as open source in the Insight Toolkit.

Keywords: B-splines, DMFFD, diffeomorphism, ITK

1 Introduction

Significant algorithmic developments characterizing modern intensity-based image registration research include the B-spline parameterized approach (so called *free-form deformation*) with early contributions including [5, 6, 3]. Amongst the variant extensions, the *directly manipulated free-form deformation* approach addressed the hemstitching issue associated with the problematic energy topographies caused by the distribution of the uniform B-spline shape functions over the transformation domain [8].

Other important image registration research reflected increased emphasis on topological transformation considerations in modeling biological/physical systems where topology is consistent throughout the course of deformation or a homeomorphic relationship is assumed between image domains. Methods such as LDDMM [1] optimize time-varying velocity field flows to yield diffeomorphic transformations. Alternatively, the FFD variant reported in [4] enforced diffeomorphic transforms by concatenating multiple FFD transforms, each of which is constrained to describe a one-to-one mapping. Recently, the work of [2] combined these registration concepts into a single framework called *temporal free-form deformation* in which the time-varying velocity field characteristic of LDDMM-style algorithms is modeled using a 4-D B-spline object (3-D + time). Integration of the velocity field yields the mapping between parameterized time points.

In this work, we describe our extension to these methods. Similar to [2], we also use an N-D + time B-spline object to represent the characteristic velocity field. However, we use the directly manipulated free-form deformation optimization formulation to improve convergence during the course of optimization. This also facilitates modeling temporal periodicity and the enforcement of stationary boundaries consistent with diffeomorphic transforms. We also incorporate B-spline mesh multi-resolution capabilities for increased control during registration progress. Of note, whereas the previous work described in [2] discretized the velocity field before performing numerical integration (which reduces the advantages of the continuous B-spline representation including the decrease in accuracy associated with numerical integration and increased computational time) we show how the continuous B-spline representation permits analytical integration for increased accuracy. Most importantly, we also describe our parallelized algorithmic implementation as open source available through the Insight Toolkit.[3]

We first describe the methodology by laying out a mathematical description of the various algorithmic elements coupled with implementation details where appropriate. This is followed by several registration examples to provide insight into the details of our contribution.

2 Methods: Formulae and Implementation

In this section, we explain the underlying theory focusing on differences with previous work. We first explain how B-spline velocity fields can be used to produce diffeomorphisms through analytical integration involving the B-spline basis functions. We then show how our previous work involving optimization in B-spline vector spaces [8] can be used for optimization of diffeomorphisms. Additional insight is then gleaned by illustrating correspondence between theory and implementation.

2.1 B-spline velocity field transform

Briefly, as with other diffeomorphic formulations based on vector flows, we assume the diffeomorphism, ϕ, is defined on the image domain, Ω, with stationary boundaries such that $\phi(\partial\Omega) = \mathbf{Id}$. ϕ is generated as the solution of the ordinary differential equation

$$\frac{d\phi(\mathbf{x},t)}{dt} = v(\phi(\mathbf{x},t),t),\ \ \phi(\mathbf{x},0) = \mathbf{x} \qquad (1)$$

[3] http://www.itk.org/

where v is a (potentially) time-dependent smooth field, $v : \Omega \times t \rightarrow \mathrm{R}^d$ parameterized by $t \in [0,1]$. Diffeomorphic mappings between parameterized time points $\{t_a, t_b\} \in [0,1]$ are obtained from Eq. (1) through the following integration

$$\phi(\mathbf{x}, t_b) = \phi(\mathbf{x}, t_a) + \int_{t_a}^{t_b} v(\phi(\mathbf{x}), t)dt. \tag{2}$$

In the case of d-dimensional registration, we can represent the time-dependent velocity field as a $(d+1)$-dimensional B-spline object

$$v(\phi(\mathbf{x}, t), t) = \sum_{i_1=1}^{X_1} \dots \sum_{i_d=1}^{X_d} \sum_{i_t=1}^{T} v_{i_1,\dots,i_d,i_t} B_{i_t}(t) \prod_{j=1}^{d} B_{i_j}(x_j) \tag{3}$$

where $v_{i_1,\dots,i_d,i_t}$ is a $(d+1)$-dimensional control point lattice characterizing the velocity field and $B(\cdot)$ are the univariate B-spline basis functions separately modulating the solution in each parametric dimension. Combining Eqns. (1) and (2) we obtain

$$\phi(\mathbf{x}, t_b) = \phi(\mathbf{x}, t_a) + \int_{t_a}^{t_b} \left(\sum_{i_1=1}^{X_1} \dots \sum_{i_d=1}^{X_d} \sum_{i_t=1}^{T} v_{i_1,\dots,i_d,i_t} B_{i_t}(t) \prod_{j=1}^{d} B_j(x_j) \right) dt \tag{4}$$

Moving the integral inside the summations

$$\phi(\mathbf{x}, t_b) = \phi(\mathbf{x}, t_a) + \sum_{i_1=1}^{X_1} \dots \sum_{i_d=1}^{X_d} \underbrace{\left(\sum_{i_t=1}^{T} v_{i_1,\dots,i_d,i_t} \int_{t_a}^{t_b} B_{i_t}(t)dt \right)}_{\phi'_{i_1,\dots,i_d}} \prod_{j=1}^{d} B_{i_j}(x_j) \tag{5}$$

demonstrates the sole dependency on the B-spline basis functions in the temporal parametric dimension. The integral is easily calculated as the B-spline basis functions are piecewise polynomials. Also, it is seen that the quantity inside the parentheses comprises the d-dimensional control point lattice defining the diffeomorphic mapping defined between time points $[t_a, t_b]$ obtained by integration. Furthermore, supposing the initial diffeomorphism, $\phi(\mathbf{x}, t_a)$, is similarly parameterized, i.e.

$$\phi(\mathbf{x}, t_a) = \sum_{i_1=1}^{X_1} \dots \sum_{i_d=1}^{X_d} \phi_{i_1,\dots,i_d}^{t_a} \prod_{j=1}^{d} B_{i_j}(x_j), \tag{6}$$

the diffeomorphism at t_b is obtained by simple addition of the two control point lattices,

$$\phi(\mathbf{x}, t_b) = \sum_{i_1=1}^{X_1} \dots \sum_{i_d=1}^{X_d} \left(\phi^{t_a} + \phi'\right)_{i_1,\dots,i_d} \prod_{j=1}^{d} B_{i_j}(x_j). \tag{7}$$

2.2 Directly manipulated free-form deformation optimization of the B-spline velocity field

In [8] it was observed that optimization of FFD registration with gradient descent is intrinsically susceptible to problematic energy topographies. However, a well-understood preconditioned gradient was proposed based on the work described in [7] which substantially improves performance which we refer to as DMFFD image registration. Similarly, we propose the following velocity field control point lattice preconditioned gradient, $\delta v_{i_1,\ldots,i_d,i_t}$, given the similarity metric, Π,[4]

$$\begin{aligned}\delta v_{i_1,\ldots,i_d,i_t} = &\left(\sum_{c=1}^{N_\Omega \times N_t} \left(\frac{\partial \Pi}{\partial \mathbf{x}} \right)_c B_{i_t}(t^c) \prod_{j=1}^{d} B_{i_j}(x_j^c) \right.\\ &\left. \cdot \frac{B_{i_t}^2(t^c) \prod_{j=1}^{d} B_{i_j}^2(x_j^c)}{\sum_{k_1=1}^{r+1} \cdots \sum_{k_d=1}^{r+1} \sum_{k_t=1}^{r+1} B_{k_t}^2(t^c) \prod_{j=1}^{d} B_{k_j}^2(x_j^c)} \right)\\ &\cdot \left(\sum_{c=1}^{N_\Omega \times N_t} B_{i_t}^2(t^c) \prod_{j=1}^{d} B_{i_j}^2(x_j^c) \right)^{-1} \qquad (8)\end{aligned}$$

which is a slight modification of Eqn. (21) in [8] which takes into account the temporal locations of the dense gradient field sampled in $t \in [0, 1]$. N_t and N_Ω are the number of time point samples and the number of voxels in the reference image domain, respectively. r is the spline order in all dimensions[5] and c indexes the spatio-temporal dense metric gradient sample. Combining DMFFD optimization with the B-spline velocity field transform discussed in the previous subsection, we outline the iterative routine for optimizing the velocity field control in Algorithm 1.

2.3 Implementation

As mentioned previously, the registration algorithm has been implemented in the Insight Toolkit and consists of the following major classes:

- `itk::TimeVaryingBSplineVelocityFieldIntegrationImageFilter`
- `itk::TimeVaryingBSplineVelocityFieldTransform`
- `itk::TimeVaryingBSplineVelocityFieldImageRegistrationMethod`
- `itk::TimeVaryingBSplineVelocityFieldTransformParametersAdaptor`
- `itk::BSplineScatteredDataPointSetToImageFilter`

[4] Current options include neighborhood cross correlation (CC), mutual information (MI), and Demons-style sum of squared differences (Demons).

[5] Spline orders can be specified separately for each dimension but, for simplicity, we only specify a single spline order. However, the framework can easily accommodate different spline orders.

Algorithm 1 Gradient descent optimization of the B-spline velocity field

Input: images $\mathcal{I}$ and $\mathcal{J}$
Input: user-specified similarity metric Π
Input: velocity field mesh size and multiresolution schedule, R
Input: number of time point samples, N_t (default: 4)
Input: spline order (default: 3)
Input: gradient step size, λ (default: 0.25)
Output: velocity field control point lattice, v
1: $v \leftarrow \mathbf{0}$ // Initialize velocity field
2: **for** number of resolution levels **do**
3:   **for** number of iterations for current level **do**
4:     $G \leftarrow []$ // Initialize dense gradient storage array
5:     **for** $t = 1 \rightarrow N_t$ **do**
6:       $t' \leftarrow \frac{t-1}{N_t-1}$ // Scale time point to $[0, 1]$
7:       $\mathcal{I}' \leftarrow \mathcal{I} \circ \phi(\mathbf{x}, t')$ // Warp $\mathcal{I}$ to the current time point
8:       $\mathcal{J}' \leftarrow \mathcal{J} \circ \phi^{-1}(\mathbf{x}, 1 - t')$ // Warp $\mathcal{J}$ to the current time point
9:       $G[t] \leftarrow \frac{\partial \Pi(\mathcal{I}', \mathcal{J}')}{\partial \mathbf{x}}$ // Store dense similarity metric gradient
10:     **end for**
11:     $\delta v \leftarrow B(G)$ // Calculate velocity lattice gradient (Eqn. (8))
12:     $v \leftarrow v + \lambda \delta v$ // Take a step in the gradient direction
13:   **end for**
14:   $v \leftarrow R(v)$ // Refine lattice based on schedule
15: **end for**

The `TimeVaryingBSplineVelocityFieldIntegrationImageFilter` class implements the integration described by Eqn. (5). Given a velocity field control point lattice as input and the lower and upper integration limits, integration is performed in a multi-threaded fashion (since each control point in $\phi'_{i_1,\ldots,i_d}$ can be integrated separately). The `TimeVaryingBSplineVelocityFieldTransform` is derived from the base transform class which handles the mapping of geometric primitives for warping images. The DMFFD gradient calculation is handled by the class `BSplineScatteredDataPointSetToImageFilter` (cf. Eqn. 8 and line 11 of Algorithm 1) which takes as input the dense similarity metric and an optional weighting for each gradient sample. This permits enforcement of stationary physical boundaries by specifying a zero gradient on the boundaries and a large weighting. Coordinating all the elements of image registration is the `TimeVaryingBSplineVelocityFieldImageRegistrationMethod` class which encapsulates Algorithm 1. The resolution scheduling is determined by the `TimeVaryingBSplineVelocityFieldTransformParametersAdaptor` class. We provide access to the new ITK registration framework (including the B-spline velocity field transform) through the command line module `hormigita` available both in ANTs[6] and accompanied by a technical report offered through the In-

[6] http://www.picsl.upenn.edu/ANTs

sight Journal [?].[7] The interested reader should consult [?] for further details on actual usage.

3 Registration Examples

4 Discussion and Conclusions

This work constitutes an advantageous combination of the continuous aspects of B-splines with the diffeomorphic registration framework via vector field flows. In contrast to previous work, we take advantage of the continuous aspect of the velocity field representation by analytical integration for a more accurate diffeomorphic transform derivation. We also incorporate DMFFD optimization of the B-spline velocity field which facilitates convergence and permits enforcement of stationary boundary conditions. While not discussed, further advantages include incorporation of temporal periodicity in dealing with the possibility of multiple images describing periodic motion (e.g. cardiac or pulmonary motion). Although not discussed in this work, a future publication will explore these possibilities in greater detail.

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