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# Splines for diffeomorphisms

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ABSTRACT

This paper develops a method for higher order parametric regression on diffeomorphisms for image regression. We present a principled way to define curves with nonzero acceleration and nonzero jerk. This work extends methods based on geodesics which have been developed during the last decade for computational anatomy in the large deformation diffeomorphic image analysis framework. In contrast to previously proposed methods to capture image changes over time, such as geodesic regression, the proposed method can capture more complex spatio-temporal deformations.

We take a variational approach that is governed by an underlying energy formulation, which respects the nonflat geometry of diffeomorphisms. Such an approach of minimal energy curve estimation also provides a physical analogy to particle motion under a varying force field. This gives rise to the notion of the quadratic, the cubic and the piecewise cubic splines on the manifold of diffeomorphisms. The variational formulation of splines also allows for the use of temporal control points to control spline behavior. This necessitates the development of a shooting formulation for splines.

The initial conditions of our proposed shooting polynomial paths in diffeomorphisms are analogous to the Euclidean polynomial coefficients. We experimentally demonstrate the effectiveness of using the parametric curves both for synthesizing polynomial paths and for regression of imaging data. The performance of the method is compared to geodesic regression.



## 1. Introduction

With the now common availability of longitudinal and time series image data, models for their analysis are critically needed. In particular, spatial correspondences need to be established through image registration for many medical image analysis tasks. While this can be accomplished by pair-wise image registration to a template image, such an approach neglects spatio-temporal data aspects. Instead, explicitly accounting for spatial *and* temporal dependencies is desirable.

A common way to describe differences in geometry of objects in images is to summarize them using transformations. Transformations are fundamental mathematical objects and have long been known to effectively represent biological changes in organisms (Amit et al., 1991; Thompson et al., 1942). The field of *computational anatomy* (Grenander and Miller, 1998; Miller, 2004; Miller et al., 1997; Thompson and Toga, 2002) provides a rich mathematical setting for statistical analysis of complex geometrical structures seen in 3D medical images. At its core, computational anatomy is based on the representation of anatomical shape and its variability using smooth and invertible transformations that are elements of the nonflat manifold of diffeomorphisms with an associated Riemannian structure. The large deformation diffeomorphic metric mapping (LDDMM) framework of computational anatomy exploits ideas from fluid mechanics and builds maps of diffeomorphisms as flows of smooth velocity fields (Younes, 2010; Younes et al., 2009).

Research in the last decade provideds several methods to represent natural biological variability by modeling them as nonlinear transformations in the manifold of diffeomorphisms. Their focus has primarily been on geodesic models. For example, methods of Fréchet mean (Davis, 2008), geodesic regression (Niethammer et al., 2011) and hierarchical geodesic models (Singh et al., 2013a) are first order models that rely on computing geodesics within the space of diffeomorphisms. While such models have proven to be effective, their use is limited to modeling only "geodesic-like" image data. However, geodesics are not always appropriate for regression modeling of time series data. In particular, nonmonotonous shape changes seen in time sequence or videos of medical images of periodic breathing, cardiac motion, or shape changes in the human brain during a long age range (10–90 years), do generally not adhere to constraints of geodesicity. This necessitates the development of higher order models of regression within the space of diffeomorphic transformations. Computational anatomy has seen very little work on

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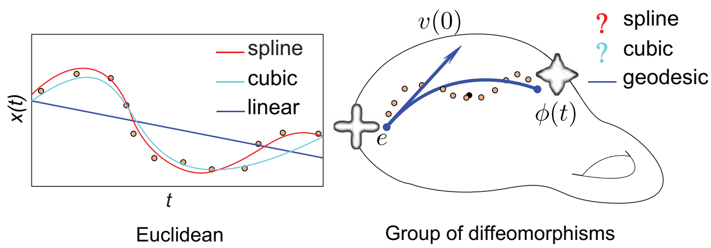


**Fig. 1.** Models of parametric regression for computational anatomy. Geodesic regression generalizes the notion of parametric linear regression in the Euclidean spaces (left) to the group of diffeomorphisms (right). The model estimate comprises of the initial velocity, $v(0)$, at the identify diffeomorphism, $e$, and completely parameterizes the best fit regression geodesic path, $\phi(t)$. However, no such generalizations of the known Euclidean models of higher order parametric regression such as the cubics or the splines (left) exist for the group of diffeomorphisms (right).

higher-order models of registrations for modeling image time series (Fig. 1).

*Contribution.* In this article we propose:

1. an acceleration-controlled model that generalizes the idea of cubic curves to manifold of diffeomorphisms and is capable of modeling nonmonotonic shape changes under the large deformation (LDDMM) setting,
2. a shooting based solution to cubic curves that enables parametrization of the full regression path using only initial conditions,
3. a method of shooting cubic splines as smooth curves to fit complex shape trends while keeping data-independent (finite and few) parameters, and
4. a numerically practical algorithm for regression of “non-geodesic” medical imaging data.

The work described in this manuscript significantly extends our work presented at MICCAI (Singh and Niethammer (2014)). In particular, (1) we make use of a new formulation directly advecting the inverse of a diffeomorphism, (2) we provide extended discussions of the approach, and (3) present a variety of new results to illustrate the behavior of the approach.

### 1.1. Related work

Methods that generalize Euclidean parametric regression models to manifolds have proven to be effective for modeling the dynamics of changes represented in time series of medical images. For instance, methods of geodesic image regression (Niethammer et al., 2011; Singh et al., 2013b) and longitudinal models on images (Singh et al., 2013a) generalize linear and hierarchical linear models, respectively. Although the idea of polynomials (Hinkle et al., 2014) and splines (Trouvé & Vialard, 2012) on the landmark representation of shapes has been proposed, higher-order extensions for image regression remain deficient. While Hinkle et al. (2014) develop an approach for general polynomial regression and demonstrate it on finite-dimensional Lie groups, infinite dimensional regression is demonstrated only for first-order geodesic image regression.

These parametric regression models are advantageous since their estimated parameters can be used for further statistical analysis. For instance, initial momenta obtained from Fréchet atlas construction of a population of images can be treated as signature representations of shape differences across the group and can be treated as features to train classification and regression models (Singh et al., 2014).

Machado et al. (2006) also discuss the notion of first order variational fitting of curves to data on Riemannian manifolds. The solution to the variational problem results in piecewise geodesics, where the number of pieces is equal to the number of manifold data points. Durrleman et al. (2013) present a method of regression analysis of population of time series of shapes based on timewarping. This model is presented for regression of shapes that do not trivially generalize to the regression of image time series data. The model also results in piecewise geodesics to summarize individual spatiotemporal trends such that the number of pieces is data dependent. Following the earliest ideas presented in Noakes et al. (1989), Camarinha et al. (1995), Crouch and Leite (1995), the work of Machado et al. (2010) further develops the notion of variational fitting to estimating piecewise higher order curves on data in general Riemannian manifolds. The solution involves estimating the Riemannian curvature tensor and is useful for finite dimensional manifolds where the tensor can be evaluated analytically. Krakowski (2003) provides a theoretical review of variational splines and explores, in particular, splines on finite-dimensional manifolds such as the space of rotations, $\mathbb{SO}(3)$, and the unit sphere, $\mathbb{S}^n$.

Other regression methods include those by Davis et al. (2010), Lorenzi et al. (2010), Vercauteren et al. (2009), Schwartz et al. (2015) and Gu et al. (2006). Davis et al. (2010) generalize the notion of kernel regression to manifolds. Kernel regression is a nonparametric approach and hence does not provide a summary representation of the regression fit in terms of a finite set of parameters for further analysis. Lorenzi et al. (2010) propose a smooth spatiotemporal modeling of image time series data using the regression of pairwise registrations under the stationary velocity field (SVF) framework of LogDemons (Vercauteren et al., 2009). More recently, Schwartz et al. (2015) extend this idea and propose locally linear regression under the SVF framework. Gu et al. (2006) develop the spline interpolation for the case when the domain of the independent variable itself is a manifold. This is useful for surface interpolation, for example, in graphics or geometric design to interpolate surfaces represented on manifold domains that give rise to shapes with arbitrary topologies.

Relevant background readings include those by Noakes et al. (1989), Camarinha et al. (1995), Crouch and Leite (1995), where the notion of splines on general Riemannian manifolds were first introduced. These series of papers discuss a theoretical characterization of the general variational cubic curves and spline interpolation. In this paper, we present a shooting based formulation of the classical variational spline formulation and derive its solution and numerical estimation procedures for the group of diffeomorphisms.

The remainder of this article is structured as follows: Section 2 reviews the variational approach to splines in Euclidean space and motivate its shooting formulation for parametric regression. Section 3 then generalizes this concept of shooting splines for diffeomorphic image regression. We discuss experimental results in Section 4, and conclude the article with a discussion of future work in Section 5.

## 2. Shooting-splines in the Euclidean case

To motivate our formulation for splines on diffeomorphisms it is instructive to first revisit the variational formulation for splines in the Euclidean case. This facilitates a more straightforward presentation