A multiscale algorithm for computing realistic image transformations in the LDDMM framework – Application to the modelling of fetal brain growth

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1. DESCRIPTION OF PURPOSE

Due to the rapidity of anatomical changes occurring during pregnancy, modelling the fetal brain growth is a challenging task. Most often, spatio-temporal atlases establish a discrete representation of the brain across gestation.[1] However, continuous models have the potential to depict these anatomical changes more accurately,[2,3] while providing a straightforward way of comparing subjects of different ages.[4] To build such a model, geodesic regression is an adequate tool that encodes in a single deformation the time-dependent changes of images acquired at different time points.[5] The Large Deformation Diffeomorphic Metric Mapping (LDDMM) framework offers a convenient mathematical setting to compute diffeomorphic changes, which are constructed by integrating time-varying vector fields.[6] Yet, estimating high-dimensional and accurate transformations remains very challenging in a clinical setting, as the risk of falling in an unrealistic local minimum increases with the number of parameters to optimize. Further, spatial regularization constrains deformations to occur at a single scale.[7] These issues are especially true in the case of modelling anatomical changes, where one seeks to estimate a template image along with the single trajectory that best fits dozens of high-dimensional images. Recently, we introduced a wavelet-based multiscale strategy to improve atlas estimation in the LDDMM setting.[7] Optimization was performed in a coarse-to-fine fashion, leading to more realistic template images and template-to-subject deformations.

Here, we extend our previous work by introducing a dual multiscale strategy whereby multiscale representations are used for both the velocity fields and the subjects images. Further, we broaden the application field of our algorithm by applying this multiscale strategy not only to atlas estimation but also to geodesic regression. Using a large dataset of fetal brain Magnetic Resonance Images (MRIs), we illustrate the efficiency of our algorithm on the challenging problem of modelling fetal brain growth within a single trajectory.

2. METHODS

2.1 Mathematical framework

In the LDDMM framework, images are deformed through a flow of diffeomorphisms, constructed by integrating time-dependant velocity fields $(v_t)_t$.[6]

We impose that the initial velocity fields belong to a Reproducing Kernel Hilbert Space (RKHS) V defined by a regularizing kernel using the following parametrization:[8] $v_0(x) = \sum_{k=1}^{k_g} K_g(x, c_k(0))\alpha_k(0)$ where K_g is a Gaussian kernel of width σ_g and the $(\alpha_k)_k$ are momentum vectors attached to control points $(c_k)_k$. The control points are set on a regular grid of spacing σ_g.

Optimization is performed by minimizing a cost function whose formulation depends on the task at hand. It is composed of a data fidelity term, i.e. the Euclidean l^2 distance between the images to be registered, plus a regularizing term. The latter constrains the $(v_t)_t$ to be geodesics, i.e. shortest paths on a Riemannian manifold according to the V norm. Importantly, the vector fields satisfying this condition keep their RKHS structure along time. A geodesic vector field v_t is fully parameterized by the initial velocity field v_0, which means only the initial momentum vectors $(\alpha_k(0))_k$ need to be optimized.

This framework can be used to compute standard anatomy tools. Here, we focus on registration, atlas estimation and geodesic regression, which differ only in the formulation of the cost function.

- Atlas estimation: given a cross-sectional dataset of N images $(I_i)_{1\leq i\leq N}$, one seeks to estimate a template image I_0 representative of the average anatomy, and N template-to-subject deformations.
- Registration is a particular case of atlas estimation whereby $N = 1$ and I_0 is frozen
- Geodesic regression: given N images $(I_i)_{1\leq i\leq N}$ acquired at times $(t_i)_{1\leq i\leq N}$, one seeks to estimate a template image T at age t_0, along with the single geodesic trajectory that deforms T and best depicts how the input images evolve with time.

In this work, parameters optimization is performed through steepest gradient descent. We use an efficient numerical scheme[8] that relies on the structural constraint imposed on the vector fields.

2.2 Multiscale optimization

Based on our previous work,[7] we perform a change of basis on v_0 from the RKHS V to vector spaces of different resolutions: $v_0(x) = \sum_s \sum_k \sum_o \Phi^o_{s,k}(x)\beta^o_{s,k}$

where $\Phi^o_{s,k}$ is a wavelet function of scale s, location k and orientation o and the β are the coordinates in this new basis. (Note that in atlas estimation, N velocity fields are optimized: the formulation above holds for the $(v_{0,i})_i$.) In this setting, gradients are still optimized with regards to the momentum vectors $(\alpha_k(0))_k$. The change of basis is used only during the parameters update step to perform optimization in a coarse-to-fine manner. All coefficients β, except those corresponding to the coarsest scale S_{max}, are set to zero so that the algorithm first optimizes smooth initial velocity fields. These vector fiels are progressively refined by adding finer scale coefficients. Importantly, this optimization scheme preserves the RKHS structure of the vector fields and the computational efficiency of the original algorithm. This strategy will be referred to as "multiscale deformations" in the following.

In addition, we introduce a multiresolution representation of the input images (I_i) based on Gaussian smoothing. No filter is applied to the initial template image to be optimized. Given a deformation scale s, we set the kernel standard deviation $\sigma(s)$ so that the image filter width is equivalent to the area over which the vector fields are constant. Starting at scales $S_{max} - 1$ and $\sigma(S_{max} - 1)$, optimization is performed using the filtered subjects images and the reparametrized velocity fields. The two scales are alternatively refined each time the algorithm is close to convergence. This dual multiscale strategy will be referred to as "multiscale" in the following. The code is available at a public Git repository[*].

3. RESULTS

We evaluate the ability of our algorithm to generate realistic deformations compared to the original version on two types of data. Using artificial images, the first experiment demonstrates the efficiency of the new multiscale strategy on an atlas estimation task. The second experiment illustrates the algorithm usefulness in a clinical setting by modelling time-dependant brain changes during pregnancy. The performance of the algorithms is evaluated with the Structural Similarity Index Measure (SSIM),[9] a classical metric to measure image similarity. The parameters of the algorithms are set as follows: trade-off between data attachment and regularity $\sigma_t = 0.1$ in the cost criterion; initial step size $h = 0.01$; convergence threshold $= 0.0001$.

3.1 Atlas estimation on artificial images

In this experiment, we compare the performance of the dual multiscale algorithm to that of the original and multiscale deformations versions. We use a dataset of 30 images of manually designed characters[7] which have the advantage of providing clear and interpretable results. Though the characters share a common anatomy, their variable postures make it difficult to estimate realistic template images and deformations. We perform 5-fold cross validation with different kernel widths $\sigma_g \in \{4, 6, 8\}$ corresponding to a number of control points $k_g \in \{49, 25, 16\}$. During training, each algorithm estimates independently a template image from the training set. Then, the template is registered to each image in the test set.

[*] https://github.com/fleurgaudfernau/Deformetrica_multiscale/

Quantitative results (not shown here) show that the two multiscale algorithms outperform the original algorithm for all values of σ_g, and that the new multiscale strategy reaches higher performance than the multiscale deformations strategy. Visual inspection of the template images and template-to-subject reconstruction shows that the multiscale algorithm produces more realistic deformations with regard to the anatomy of the characters (see an example in Figure 1).

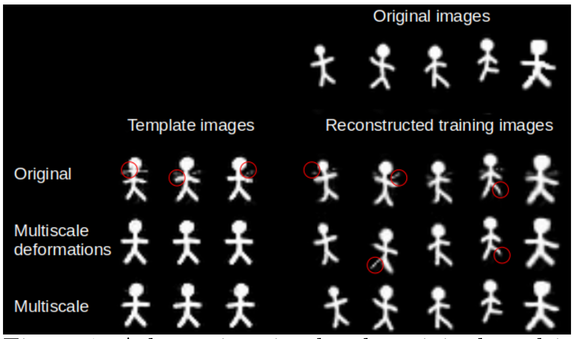

Figure 1: Atlas estimation by the original, multiscale deformations and multiscale algorithms for $\sigma_g = 4$ and $k_g = 49$. Left column: 3 estimated template images. Right column: the template image from the first training set wrapped to five training images. Red circles indicate inaccurate features.

3.2 Fetal brain geodesic regression

Here, we demonstrate the efficiency of the multiscale strategy compared to the original algorithm on a more challenging task: estimating an average trajectory from a cross-sectional dataset of subjects imaged at different ages. In order to ease the optimization, we provide the regression with a baseline image initialized by performing atlas estimation on a subset of subjects.

We use 58 volume-reconstructed brain MRIs of healthy fetuses from the open-source FeTa dataset.[10] Gestational ages range between 22 and 36 weeks (mean= 28.72 ± 3.58). Images are skull-stripped, rigidly aligned to a common coordinate space and intensity normalized. We perform several 5-fold cross validation procedures with parameters $\sigma_g \in \{8, 10, 14\}$ (i.e. $k_g \in \{8\,500, 4\,256, 1\,680\}$). Evaluation is performed as follows:

1. Using atlas estimation, each algorithm estimates a baseline image I_0 from training set subjects aged between 25 and 33 gestational weeks (35 images). A wide range of subjects are included so that the baseline image accurately represents the variability in the dataset.
2. Using the template image as a starting point at time $t_0 = 28.72$ weeks, the trajectory that best fits the images in the training set (45-46 images) is computed between 23 and 34 weeks, along with the template T to which the deformation is applied.
3. To assess the accuracy of the estimated trajectory, each image in the test set (11-12 images) is compared to the age-matched template image from regression using registration.

Quantitative results (not shown here) show that the multiscale algorithm reaches higher SSIM values than the original algorithm during training (i.e. atlas estimation and geodesic regression) and test. Figure 2 provides a visual comparison of the geodesic regression outputs for $\sigma_g = 10$. The original algorithm fails to estimate realistic brain images (exaggerated thickness of the cerebrospinal fluid, fuzzy delineation of the cortical plate). The multiscale strategy for atlas estimation and geodesic regression allows to correct these flaws, resulting in more natural template images.

4. NEW OR BREAKTHROUGH WORK TO BE PRESENTED

The novelty of our work is based on two aspects:
1-A methodological contribution intending to improve our previous work on multiscale optimization for atlas estimation in the LDDMM framework: we extend this strategy to a multiscale representation of images, and we apply it not only to atlas estimation but also to geodesic regression.
2-A clinical application: multiscale regression is applied to the difficult problem of establishing a continuous trajectory of the fetal brain growth.

A paper describing the multiscale deformations algorithm for atlas estimation has been submitted for publication.

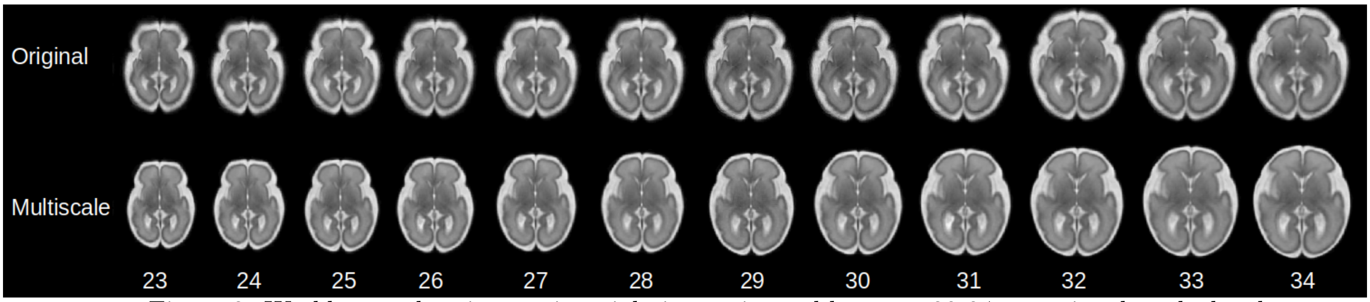

Figure 2: Weekly template images in axial view estimated between 23-34 gestational weeks by the original (top row) and dual multiscale (bottom row) algorithms with $\sigma_g = 10$ (first

5. CONCLUSIONS

We addressed the promising, yet mostly unexplored possibility of modelling fetal brain growth using geodesic regression. To promote realistic deformations, we presented a coarse-to-fine strategy based on multiscale representations of deformations and images in the LDDMM framework. This multiscale strategy brings substantial improvements in the estimated brain images. Future work will focus on embedding multiscale deformations in a Bayesian framework in order to establish more realistic spatio-temporal models.

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