PhD thesis subject proposal at Inria center of Université Côte d'Azur

# Geometric statistics on stratified quotient spaces: topologically constrained multi-atlases for brain diffeomorphometry

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The number of acquisition of biomedical images and associated clinical data is currently rapidly increasing. We can now study patients at the scale of a population of subjects to model the normal and pathological structural variations, and then simulate the disease evolution to forecast the medical outcome. Pivotal applications include the evolution of the brain in Alzheimer's and other neurodegenerative diseases, and analysis of the shape and contraction of the heart to simulate different pathologies. This is the core topic of the Meditwin project joining forces between Inria and 3DS.

Building generative models simulating the organs function and pathologies however requires prior models of the organs anatomy so that the simulation becomes patient-specific. Establishing representative spatial models of the anatomy at the scale of a population of subjects is the goal of computational anatomy. A classical method is to compute the mean shape (called template or atlas) and encode its variability through tangent PCA or deformation modes. Despite important successes, anatomical data tend to exhibit an extensive variability than cannot be modelled with such a unimodal Gaussian model, hampering the prediction power. Thus, the field has moved in practice towards multiple atlases.

The goal of PhD is to develop new methodological techniques for modelling the very wide variability of inter-subject image registration. The PhD student will in particular investigate:

- New stratified representations of template images / shapes;
- New representations of diffeomorphism and of their action on images or shapes;
- Innovative reduced-order image registration algorithms;
- Experimentations on real-world image databases to demonstrate the power of the developed methods.

## Objectives

In computational anatomy, a shape may be a 3D curve, a surface embedded in a 3D space, a collection of curves and surfaces or a 3D image. In this PhD project, we will mainly focus on images, but a special care will be taken to think about images as extension of the methods to curves and surfaces, encoding for instance isolevel surfaces of images using currents **?** or varifolds **?**. One of the goal is to design sparse representation of images that are computationally efficient for their diffeomorphic deformations using stationary velocity fields **??** or momenta of right-invariant metrics in LDDMM.

In diffeomorphometry, the main method is to identify a reference shape, called the template, and to encode its geometric variations by the diffeomorphic transformations that best describe the observed data shapes. In practice, though, the template has to be estimated from the data and one usually requires it to be optimally centered so that it is an unbiased representative of the population. The so-called unbiased atlas algorithm **?** used for that consists in iteratively registering the template to the data, deforming the template along the mean forward deformations to recenter it, and then updating the atlas image intensities by averaging the intensities of the data backward transformed to the template space to recenter it in intensity. Geometrically, the procedure can be summarized as the computation of the template as the "Fréchet mean" of the images projected in a quotient space.

However, it has been shown that this technique actually has a bias repulsing the estimation away from the singularities of the lower dimensional strata of the shape space **?**. In other words, even with an infinite number of brain images in the database, the template estimate may not converge to the brain anatomy it is meant to estimate. In finite dimension, this means that generic data and templates live almost surely on the principal stratum, which is dense in the stratified space. This puts a bound on the complexity of the shapes. In infinite dimension, however, there is no upper limit on the dimensionality of the strata, and adding more data will actually ever complexify the topology of the template intensities in generic conditions. This led us to investigate constraints on the topology of the template's intensity level sets, represented by its Morse–Smale (MS) complex in **?**

A first goal will be to reconsider this topologically constrained adaptation of the template computation with both a topological data analysis (TDA) and a geometric quotient space (geometric statistic) point of view. Computational feasibility will be one of the main criterion to evaluate the possibilities in order to obtain a computable optimization of a template with limited Morse-Smale complexity. One will consider extending Morse-Smale structure with more geometric features to better represent the important image information. In particular, it will be important to consider non generic Morse singularities to correctly account for uniform areas in medical images such as the cortical ribbon for instance in brain images. A potential idea will be to revisit image representations with isolevel surfaces along with their gradient information, and to leverage on recent robustness results with complexes similar to Morse-Smale, such as Mapper complexes and Reeb spaces **???**.

In order to model the huge variability of the anatomies at the population level, which will not be able to fit under a single topologically constrained model, a second goal will be to adapt ideas from the $k$-means algorithm and multi-atlas image segmentation to estimate multiple templates with different topologies. A framework for this could be the barycentric subspace analysis approach of **?**, exemplified in the image registration context with cardiac sequence in **?**. Experiments on real-world medical image databases like ADNI and BraTS for the brain will be performed to exemplify the power of the developed methods.

## Working environment

The PhD project will take place at Inria Center of Université Côte d'Azur in the Epione team[1] under the supervision of Xavier Pennec, in close collaboration with Mathieu Carrière in the Datashape team. This PhD is funded for 3 years as part of the project Meditwin where many teams from Inria, 3DS (Dassault Systemes), 7 IHUs (University Research Hospitals) and other partners contribute to build personalized virtual twins of organs, metabolism and cancer, for better diagnosis and treatment.

[1]This may evolve with the creation of the GeoTopIA team.

## Required skills

- Master 2 degree with strong competences in mathematics, notably geometry and topology. Some knowledge in signal and image processing is necessary, some knowledge of medical imaging would be an important asset.
- Solid programming and IT skills are necessary (Python or C++, bash scripting, version control systems).
- Strong communication abilities with fluent English (written and spoken)

## Required documents for candidates

- Detailed Curriculum vitae;
- Motivation letter;
- Academic transcripts of a master's degree(s) or equivalent (with grades and courses followed);
- Two reference contacts willing to provide a letter of recommendation;
- Internship report.

## Contact Person / Application

Interested candidates are invited to submit their CV along with a cover letter detailing their relevant experience and interest in the position to Xavier Pennec (xavier.pennec@inria.fr) and Mathieu Carrière (mathieu.carriere@inria.fr).

## References

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