## Modeling and Measuring the Evolution of Alzheimer's Disease in Longitudinal Time-Series of Images

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## Résumé

Alzheimer's disease is a most common form of dementia and a neurodegenerative pathology. As such it affects the brain geometry ; the longitudinal analysis of time series of structural MRIs is fundamental to model and measure the progression of the disease. Our goal is to present a complete deformation-based framework to describe and quantify these dynamics.

First, a processing framework allows us to retrieve parametric deformations to characterize geometrical changes. The hierarchy between intra-subject changes and populations dynamics are essential and both the intra-subject and the population-wise analyses have to be robust and reproducible. In fact, the inter-subject variability might be higher than the longitudinal change we are interested in. So any bias, caused by multi-centric acquisitions or differences in examination times, could messed with further statistical detection and has to be controlled. Also our framework is based on stationary velocity fields (SVF) to efficiently describe complex deformations.

Then, using these image-based measurements we propose ways to compare, qualitatively and quantitatively, dynamics. In our framework, the analysis can be volumetric or can take directly into account the whole transformation. These comparisons validate our approach as we can reproducibly localize affected areas. But they also highlight early atrophy patterns of evolution in prodromal stages. Indeed we showed that, among healthy subjects, a with positive beta-amyloid biomarker is related to an evolution closer to the one associated with Alzheimer's disease.

We can also propose new biomarkers based on the deformations to characterize the disease progression. It is useful to spatially understand the disease ; for example a topological decomposition of the SVF gave us a new segmentation of the brain evolution.

Also, a more global components decomposition gives insights about the time dynamics. For example, the projection of every subject on a reference normal-aging trajectory show an acceleration of aging for Alzheimer's subject but also complementary evolutions which are orthogonal to aging.

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