# PhD Position @ ARAMIS Lab
# Paris, France

## Learning methods for the spatiotemporal analysis of longitudinal data

### *Applications to the diagnosis, prognosis and monitoring of Alzheimer's disease*

**Keywords:** statistical learning, spatiotemporal data, longitudinal data sets, personalization, classification, prediction, model of disease progression, biomarkers, neurological diseases

**The topic:**

Longitudinal data sets are often acquired in biological and medical sciences to capture variable temporal phenomena, which are due for instance to growth, ageing or disease progression. They consist in the observation of several individuals, each of them being observed at multiple points in time. The statistical exploitation of such data sets is notably difficult since data of each individual follow a different trajectory of changes and at its own pace. This difficulty is further increased if observations take the form of structured data like images or measurements distributed at the nodes of a mesh, and if the measurements themselves are normalized data or positive definite matrices for which usual linear operations are not defined.

Our team has contributed to the definition of a generic theoretical and algorithmic framework for learning typical trajectories from longitudinal data sets [1, 2, 3]. This framework is built on tools from the Riemannian geometry to describe trajectories of changes for any kind of data and their variability within a group. The inference is based on a stochastic EM algorithm coupled with Markov Chain simulation methods. So far, the framework has been used only to describe the dynamics of a set of biomarkers evolving in a sequential manner.

The goal of the thesis is to extend this theoretical framework to mixture models, which will allow us to estimate a family of typical trajectories indicative of clusters of individuals with similar spatiotemporal patterns. The thesis also aims to personalize the typical scenarios to data of new individuals in order to position them along a typical scenario and to predict their future evolution.

The techniques that will be developed will be used to estimate scenarios of Alzheimer's disease progression, to identify pathological sub-types in a non-supervised manner, and to use these scenarios for diagnosis and prognosis purposes. The scenarios will combine scores of neuro-psychological tests, which assess performance of various cognitive tasks like memory or language, images of brain metabolism and maps of cortical thickness and maps of deposits of neuro-toxic proteins.

Being able to robustly predict clinical symptoms only few months before their onset is a crucial public health challenge, which will open up the possibility to test treatments at the stage when they have the highest chance of success.

**ARAMIS Team**
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References:
[1] S. Durrleman, X. Pennec, A. Trouvé, J. Braga, G. Gerig, N. Ayache, ***Toward a comprehensive framework for the spatiotemporal statistical analysis of longitudinal shape data***, International journal of computer vision 103 (1), 22-59, 2013
[2] J.-B. Schiratti, S. Allassonnière, A. Routier, O. Colliot, S. Durrleman, ***A mixed-effects model with time reparametrization for longitudinal univariate manifold-valued data***, Information Processing in Medical Imaging (IPMI), Lecture Notes in Computer Science (LNCS) 9123, 564-575, 2015
[3] J.-B. Schiratti, S. Allassonnière, A. Routier, O. Colliot, S. Durrleman, ***Learning scenarios of disease progression with spatiotemporal mixed effect models for manifold-valued data***, Neural Information Processing System (NIPS), 2015

**The team:**
The PhD will take place within the ARAMIS lab (www.aramislab.fr), which is a common lab between INRIA (the national French institute dedicated to applied mathematics and computer science) and the Brain and Spine Institute (ICM). Located within an institute dedicated to basic and translational neurosciences, the ARAMIS lab develops advanced statistical and computational methods to analyze imaging and electrophysiological data.

The development of statistical tools for the exploitation of longitudinal data set is among the top priorities of the team for the forthcoming years. This research is supported by important European grants and aims to theoretical breakthroughs, the development of innovative technologies and their transfer to the clinic and pharmaceutical companies. The candidate will interact with our engineers and clinical collaborators in Europe and the United States.

The thesis will be funded in the framework of the Horizon 2020 European project EuroPOND (Progression of Neurodegenerative Disorders). The candidate will participate to progress report meetings and interact with our partner within the consortium.

**Your profile:**
You must have a strong background in statistical learning and a good knowledge of the fundamental principles of Riemannian geometry. You have a strong interest in data analysis, numerical implementation and experimentation. Good knowledge of the basic techniques for medical image computing will be a plus.

**To apply** or for further information, please send an email to Stanley.Durrleman@inria.fr
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