

## PhD offer

# Multimodal analysis for disease progression modeling and quantification in Facioscapulohumeral muscular dystrophy

### Project Description:

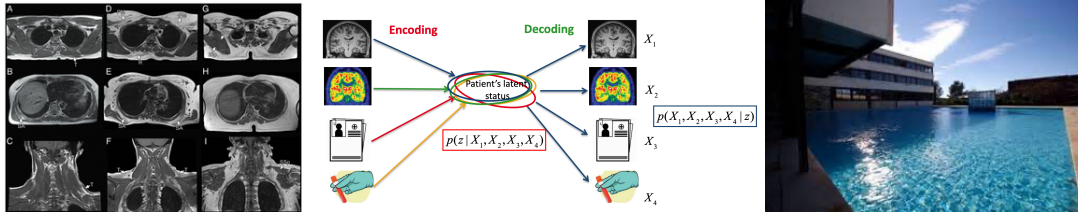
Facioscapulohumeral muscular dystrophy (FSHD) is one of the most common adult muscular dystrophies with an estimated prevalence range of 5-12 per 100,000 people. Clinically, FSHD is characterized by an important interfamilial and intrafamilial variability in term of age at onset, muscle involvement and disease progression leading to significant lifetime morbidity, with up to 20% eventually requiring full-time wheelchair use or becoming disabled. The clinical heterogeneity of FSHD mirrors the complexity of its pathophysiology, it is only partially explained by its complex genetic and epigenetic variability, and several other factors seems to play a role in modifying disease progression. The variability in FSHD progression and severity, yet unpredictable, and the limited knowledge in determinants of disease progression complicate the development of sensitive outcome measures, as well as potential biomarkers search and represent a major obstacle for new therapeutic strategies development: **there is still a gap in the understanding of the relationships between genetics, demographic features, and disease severity and progression.**

The clinical goal of this project consists in better understanding the genetic contribution to the phenotypic variability found in FSHD patients and to develop predictive models of patients' disease evolution and severity based on genetics and epigenetics, which can further evaluate pharmacological responses to a therapeutical intervention and help in the follow up of patients.

To achieve this goal, the project focuses on the development of novel machine learning approaches for predictive modelling from heterogeneous biomedical data sources. The envisaged methodology will leverage the latest advances in Bayesian learning for uncertainty estimation of predictions. The project will require to extend the state-of-the-art on multimodal data analysis, such as the multi-channel variational autoencoder (mcVAE) developed by the EPIONE team, allowing to combine heterogeneous information to characterize the FSHD progression and severity across time.

The project will also focus on the problem of model interpretability in healthcare, for instance by studying regularization constraints based on the available genetic information, including regulatory networks extracted from known ontologies. These constraints will help to identify plausible patterns of genetic variation associated with the disease status. The combined use of the unsupervised data assimilation framework and biologically inspired

regularization will potentially enable us to redefine the current classification of the disease, by investigating the ability of the latent representation in disentangle the pathological variation of the data.



### Hosting groups:

[Epione](#) team (Inria Sophia Antipolis). The group is located in the tech Park of Sophia Antipolis and in Nice, in the French Riviera. The aim of this multidisciplinary and multi-centric project is to jointly analyze medical imaging, clinical, and biological data for better diagnosis and treatment of FSHD.

### Main activities:

- Feature extraction from muscle imaging data (anatomical magnetic resonance images), by using methods based on computer vision and machine learning.
- Feature extraction and analysis from non-imaging data, such as clinical and biological data. During the project different feature extraction methods will be investigated.
- Contributing to the integration and joint analysis of these heterogeneous biomedical data. The aim is 1) the identification of discriminative traits of disease progression, and 2) the development of novel quantitative methods for assessing the severity of the disease

### During the internship the candidate will:

- Acquire skills in the advanced processing of medical images and sensors data;
- Collect/investigate datasets containing several modalities, such as medical images, clinical and genetic data;
- Develop learning methods for the analysis of heterogeneous biomedical data;
- Gather competencies on the use of novel health-care technologies in neurodegenerative disorders;
- Participate to the clinical activity within a CHU group, interact with the clinicians as well as with the clinical research assistants;
- Interact with INRIA students and researchers, and participate to scientific life of the teams.

### Required competences:

Competences in machine learning and mathematical modeling are essential, as well as knowledge in medical imaging, signal and image processing (Master 2 level). Solid programming and IT skills are necessary (Python, bash scripting, version control systems), along with strong communication abilities.

### Contact:

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