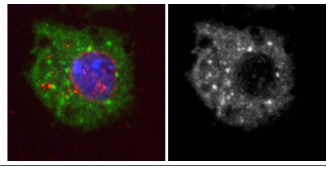

Post-Doc Position

Statistical analysis and classification of high throughput microscopy images

Supervisors: Xavier Descombes (INRIA), Eric Debreuve (I3S)

Laboratory: Morpheme, INRIA/I3S/iBV

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Location: Laboratory I3S in Sophia Antipolis

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Keywords: Spatial statistics, Classification, Cellular biology

Over the past decade, several observations have highlighted important connections between age-related degenerative diseases and the accumulation in the cell cytoplasm of large aggregates composed of RNAs and associated regulatory proteins. These pathological aggregates sequester regulatory factors, resulting in a variety of physiological changes that eventually lead to cellular dysfunction. In this context, it is thus crucial to identify the factors that trigger the aggregation of RNAs and proteins, which normally assembles into discrete particles.

To identify genes regulating the assembly and the disassembly of RNA/protein complexes, the group of F. Besse (iBV, Nice; http://ibv.unice.fr/FR/equipe/besse.php) has started a genome-wide screen relying on high throughput imaging of cultured cells. The goal of this screen is to identify mutant conditions in which the properties (number, size, distribution…) of RNA/protein particles labeled with a fluorescent protein are altered. Automatic image analysis methods are required to quantitatively and statistically analyze the millions of images generated by the screen, and to identify classes of mutants.

An image analysis pipeline consisting in three main steps has been developed. First, cell nuclei are detected and classified into alive or dead, second cytoplasm of living cells are detected, and third particles within the cytoplasm are detected. The next step is to perform a statistical analysis of the detected particles and to derive a classifier that will distinguish between different configurations among abnormal cells. We will first consider features such as the number, size and shape of the particles. In a second step, we will consider the spatial repartition of the particles within the cytoplasm (distance to the nuclei or the cell membrane, clustering property...). Therefore, the candidate will develop a statistical and classification framework to identify and characterize different populations of genes having an impact on the population of RNA/protein particles. This includes (i) the definition of a diffeomorphism that maps any individual cell into a common space (mean shape or model), (ii) the definition of a spatial statistical framework to define a notion of configuration of particles as an additional characterization of a cell (mean configuration, covariance), and (iii) the development of an unsupervised classification scheme (the control conditions are known, naturally, but the classes for the mutant conditions and their number are not known). We aim at analyzing hundreds of thousands of images. Therefore, the proposed algorithms needs to be fully automatic and to run on a cluster the team has access to.

The candidate will work under the supervision of Xavier Descombes and Eric Debreuve, in close collaboration with biologists from F. Besse's team (Fabienne de Graeve and Florence Besse). The position is funded for 12 months and should start on the 1st of March 2018 at the latest.