Post-doctoral position – 12 months contract: Institut du Thorax, Inserm Nantes.

Statistics applied to multi-scale imaging in biology-health

Context:

Heart valve diseases are common pathologies and the only treatment currently available is open heart surgery. Understanding the biological mechanisms involved in the development of these diseases is therefore essential to identify possible therapeutic targets.

Correlative microscopy is a particularly interesting approach to decipher the fundamental mechanisms of heart valve dysfunction. It makes it possible to combine different scales of observations and different types of content, functional and morphological, thanks to all microscopy technologies available for the life sciences, which have grown phenomenally in recent years (e.g. Nobel Prize in 2015 and 2017). Correlative microscopies rely crucially on a step of registration of the images observed, prior to a relevant fusion of the data available.

The objective of this project, funded by the National Agency for Research (ANR), is to develop adapted methods of registration between two images observed by microscopy to study the biological mechanisms involved. We wish to develop an original approach of computer vision that takes into account the estimation of confidence in the registration to acquire and analyze the microscopy data, on an animal model developed by the team which is carrying a genetic mutation identified in the valvulopathies [1, 2]. The methods developed can be applied more widely and distributed via the software platform developed by the team [3]. This project is a collaboration between the Thorax Institute, the MicroPICell platform (SFR Santé Bonamy), and the Jean Leray Mathematics laboratory.

Objective :

Estimating the accuracy of matching data between two images of the same sample is one of the central problems in correlative microscopy, especially because the structure of interest is not visible or identified in both images. It is therefore essential to confirm that the mapping is correct and unbiased by the registration assumptions.
A common registration technique consists of using reference points (known as fiducial points) observed in the two images and estimating, by least squares, the optimal rigid deformation (a rotation combined with a translation) between these points. This technique allows, under certain assumptions notably developed by Fitzpatrick [4, 5], to estimate the error of registration and to predict with some precision the position of the structure of interest in the image where it is not visible. The uncertainties of the registration come on the one hand from the errors of observation of the fiducial points, on the other hand from the hypothesis of rigid transformation which can be questioned.

The purpose of this mission is to extend the previous statistical framework to more general transformations (notably affine) and anisotropic observation errors, by proposing an estimation of the law of the errors of registration and prediction. These characteristics will be used to propose a measure of the quality of fit and to test the validity of the assumptions made, in particular of the selected transformation model. In the situation where different transformations are tested, model selection procedures may also be developed. Many validation data will be available in the context of this project.

Administrative information :

INSERM postdoctoral contract of one year (ANR CROCOVAL), with a beginning between February and May 2019.

Salary according to the INSERM grids (from 2500 to 3000 euros according to experience).

Funding planned for presentation of the work in an international conference.

Laptop provided.

Required profile :

Statistics, Applied Mathematics.

Programming: at least one of the languages Java, R, Python, C ++ or equivalent.

A first interdisciplinary work experience, ideally in biomedical imaging, would be a plus.

English necessary.

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Keywords:

Data fusion, registration, linear model, error estimation, model selection, imaging, cell and tissue microscopy, heart disease.

References:

1. Le Tourneau, T., et al., *New insights into mitral valve dystrophy: a Filamin-A genotype-phenotype and outcome study.* Eur Heart J, 2017.
2. Dina, C., et al., *Genetic association analyses highlight biological pathways underlying mitral valve prolapse.* Nat Genet, 2015. **47**(10): p. 1206-11.
3. Paul-Gilloteaux, P., et al., *eC-CLEM: flexible multidimensional registration software for correlative microscopies.* Nat Methods, 2017. **14**(2): p. 102-103.
4. Fitzpatrick, J.M. and J.B. West, *The distribution of target registration error in rigid-body point-based registration.* IEEE Trans Med Imaging, 2001. **20**(9): p. 917-27.
5. Fitzpatrick, J.M., J.B. West, and C.R. Maurer, Jr., *Predicting error in rigid-body point-based registration.* IEEE Trans Med Imaging, 1998. **17**(5): p. 694-702.