



Offer #2023-06288

PhD Position F/M Modeling brain structural and functional connectivity in neurodegenerative diseases

Contract type : Fixed-term contract

Level of qualifications required : Graduate degree or equivalent

Fonction : PhD Position

About the research centre or Inria department

The Inria Rennes - Bretagne Atlantique Centre is one of Inria's eight centres and has more than thirty research teams. The Inria Center is a major and recognized player in the field of digital sciences. It is at the heart of a rich R&D and innovation ecosystem: highly innovative PMEs, large industrial groups, competitiveness clusters, research and higher education players, laboratories of excellence, technological research institute, etc.

Context

The neurodegenerative diseases like Alzheimer's (AD) and Parkinson's (PD) disease are the consequences of pathological processes that begin decades before the onset of the typical clinical symptoms [1][2]. However, current diagnosis comes quite late in the course of the disease, while evidences underline the multiple benefits that would be associated with earlier diagnosis [3]. An outstanding challenge for clinical neurosciences is therefore to provide reliable, non-invasive, affordable and easy-to-track biomarkers able to improve both the early detection and the monitoring of neurodegenerative diseases, that can be applied at an individual level. It is well acknowledged that AD and PD display a progressive multifactorial disruption of cerebral networks, all along the course of the diseases, which is highly related to the clinical phenotype [4].

In the search for those biomarkers, the introduction of non-invasive imaging techniques, such as functional magnetic resonance imaging (fMRI) and diffusion weighted imaging (DWI), prompted important discoveries to provide a comprehensive map of neural connections, known as the connectome. The field of network science for analyzing the connectome offers new insights into networks disruptions that are characteristic of specific brain disorders [5]. Mathematical modelling using graph theory, which appeared in neuroimaging at the beginning of this century, provides powerful quantitative tools and measures for the analysis of complex cerebral networks [6][7]. Undirected brain connectivity has been classified in two categories: (i) structural connectivity estimated by DWI, where links represent axons or neuronal fiber density or (ii) functional connectivity (measured for instance with fMRI) where links represent statistical dependencies between brain signals from different areas, such as correlations, coherence, or transfer entropy. However, prior studies have largely focused on the comparison between patients suffering from AD or PD versus healthy subjects. As a result, the relevance of the reported alterations in brain network may be limited due to a lack of specificity. Indeed, the extracted features that are sensitive to AD or PD may well reflect common neurodegenerative processes, therefore lacking specificity for the disease-related physiopathology at the individual level. Integrating simultaneously these modalities could yield a powerful tool, to expand the knowledge of our brain and to exhibit robust biomarkers of AD and PD, more sensitive to pathophysiological changes.

Assignment

The major scientific objective for this PhD will be to look at how the integration of these advanced MRI techniques may allow a better definition of the brain change patterns in different states of AD and PD. To do so, the PhD student will first evaluate methodologies to jointly analyze functional and structural neuroimaging data, such as a recent framework called Graph Signal Processing (GSP)[8], [9]. Indeed, this approach analyzing functional activity and the underlying structural connectome. Another approach is the multilayer networks to combine both structural and functional graphs [10].

Main activities

After that, he will develop a new multimodal and multi-stage approach using **innovative machine learning (ML) methods**, adapted for multimodal features, to provide **non-invasive, reliable and easy-to-track candidate biomarkers** for each stage of AD and PD diseases. The PhD student will apply the developed approach on two large patients' cohorts and, then, assess the effectiveness of candidate disease-specific biomarkers on a new innovative local multimodal cohort including patients with and without cognitive impairment, at various stages of the diseases. The proposed PhD project is an part of a

long-term project, funded by the French research agency (ANR).

References :

- [1] G. M. McKhannet *et al.*, « The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease », *Alzheimer's & dementia*, vol. 7, n° 3. p. 263-269, 2011.
- [2] I. Liepelt-Scarfone, A. Ophey, et E. Kalbe, « Cognition in prodromal Parkinson's disease » *Progress in brain research*, vol. 269, n° 1. p. 93-111, 2022.
- [3] R. Brookmeyer, S. Gray, et C. Kawas, « Projections of Alzheimer's disease in the United States and the public health impact of delaying disease onset », *American journal of public health*, vol. 88, n° 9. p. 1337-1342, 1998.
- [4] C. Hohenfeld, C. J. Werner, et K. Reetz, « Resting-state connectivity in neurodegenerative disorders: Is there potential for an imaging biomarker? », *NeuroImage: Clinical*, vol. 18. p. 849-870, 2018.
- [5] A. Fornito, A. Zalesky, et M. Breakspear, « The connectomics of brain disorders » *Nature Reviews Neuroscience*, vol. 16, n° 3. p. 159-172, 2015.
- [6] E. Bullmore et O. Sporns, « Complex brain networks: graph theoretical analysis of structural and functional systems », *Nature Reviews Neuroscience*, vol. 10, n° 3. p. 186-198, 2009.
- [7] A. W. Toga, K. A. Clark, P. M. Thompson, D. W. Shattuck, et J. D. Van Horn, « Mapping the human connectome », *Neurosurgery*, vol. 71, n° 1. p. 1-5, 2012.
- [8] A. Ortega, P. Frossard, J. Kovačević, J. M. Moura, et P. Vandergheynst, « Graph signal processing: Overview, challenges, and applications », *Proceedings of the IEEE*, vol. 106, n° 5. p. 808-828, 2018.
- [9] G. Lioi, V. Gripon, A. Brahim, F. Rousseau, et N. Farrugia, « Gradients of Connectivity as Graph Fourier Bases of Brain Activity », *Network Neuroscience*, n° Just Accepted. p. 1-25, 2020.
- [10] Z. Hammoud et F. Kramer, « Multilayer networks: aspects, implementations, and application in biomedicine », *Big Data Anal.*, vol. 5, n° 1, p. 2, déc. 2020, doi: 10.1186/s41044-020-00046-0.

Benefits package

- Subsidized meals
- Partial reimbursement of public transport costs
- Possibility of teleworking (90 days per year) and flexible organization of working hours
- Partial payment of insurance costs

Remuneration

Monthly gross salary amounting to :

- 2051 euros for the first and second years and
- 2158 euros for the third year

General Information

- **Theme/Domain** : Computational Neuroscience and Medicine
Biologie et santé, Sciences de la vie et de la terre (BAP A)
- **Town/city** : Rennes
- **Inria Center** : [Centre Inria de l'Université de Rennes](#)
- **Starting date** : 2023-10-01
- **Duration of contract** : 3 years
- **Deadline to apply** : 2023-07-31

Contacts

- **Inria Team** : [EMPENN](#)
- **PhD Supervisor** :
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About Inria

Inria is the French national research institute dedicated to digital science and technology. It employs 2,600 people. Its 200 agile project teams, generally run jointly with academic partners, include more than 3,500 scientists and engineers working to meet the challenges of digital technology, often at the interface with other disciplines. The Institute also employs numerous talents in over forty different professions. 900 research support staff contribute to the preparation and development of scientific and

entrepreneurial projects that have a worldwide impact.

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Instruction to apply

Please submit online : your resume, cover letter and letters of recommendation eventually

For more information, please contact julie.coloiner@inria.fr

Defence Security :

This position is likely to be situated in a restricted area (ZRR), as defined in Decree No. 2011-1425 relating to the protection of national scientific and technical potential (PPST). Authorisation to enter an area is granted by the director of the unit, following a favourable Ministerial decision, as defined in the decree of 3 July 2012 relating to the PPST. An unfavourable Ministerial decision in respect of a position situated in a ZRR would result in the cancellation of the appointment.

Recruitment Policy :

As part of its diversity policy, all Inria positions are accessible to people with disabilities.