RESEARCH CENTRE

Inria Paris Centre
at Sorbonne University

IN PARTNERSHIP WITH:

CNRS, INSERM, Sorbonne Université

2023
ACTIVITY REPORT

Project-Team
ARAMIS

Algorithms, models and methods for images and signals of the human brain

IN COLLABORATION WITH: Institut du Cerveau et de la Moelle Epinière

DOMAIN

Digital Health, Biology and Earth

THEME

Computational Neuroscience and Medicine

Inria

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Project-Team ARAMIS

Creation of the Project-Team: 2014 July 01

Keywords

Computer sciences and digital sciences

A3.4. – Machine learning and statistics

A3.4.1. – Supervised learning

A3.4.2. – Unsupervised learning

A3.4.4. – Optimization and learning

A3.4.6. – Neural networks

A3.4.8. – Deep learning

A5.3. – Image processing and analysis

A5.4. – Computer vision

A5.9. – Signal processing

A9. – Artificial intelligence

A9.2. – Machine learning

A9.3. – Signal analysis

A9.6. – Decision support

Other research topics and application domains

B2. – Health

B2.2.6. – Neurodegenerative diseases

B2.6. – Biological and medical imaging

B2.6.1. – Brain imaging

1 Team members, visitors, external collaborators

Research Scientists

- Olivier Colliot [Team leader, CNRS, Senior Researcher, HDR]
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Administrative Assistant

- Helene Milome [INRIA]

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- Marc Dibling [INSERM, from Jul 2023 until Sep 2023]

2 Overall objectives

2.1 Context

ARAMIS is an Inria project-team within the Paris Brain Institute (ICM) at the Pitié-Salpêtrière hospital (AP-HP) in Paris. ARAMIS was created as a team of the Inria Paris Center in 2012 and became a project-team in 2014. ARAMIS has a joint affiliation to Inria, CNRS, Inserm and Sorbonne University.

The **Pitié-Salpêtrière hospital** is the largest adult hospital in Europe. It is a leading center for neurological diseases: in terms of size (around 20,000 neurological patients each year), level of clinical expertise and quality of the technical facilities. Created in 2010, the **Paris Brain Institute (ICM)** gathers all research activities in neuroscience and neurology of the Pitié-Salpêtrière hospital. The ICM is both a private foundation and a public research unit (affiliated to CNRS, Inserm and Sorbonne University). It hosts about 25 research teams as well as various high level technical facilities (neuroimaging, genotyping/sequencing, cell culture, cellular imaging, bioinformatics ...), and gathers over 800 personnel. In addition, the ICM hosts one of the six IHU (*Instituts Hospitalo-Universitaires*).

ARAMIS is thus located both within a leading neuroscience institute and within a large hospital. This unique position has several advantages: direct contact with neuroscientists and clinicians allows us to foresee the emergence of new problems and opportunities for new methodological developments, provides access to unique datasets, and eases the transfer of our results to clinical research and clinical practice.

2.2 General aim

The ARAMIS team is devoted to the design of **computational, mathematical and statistical approaches for the analysis of multimodal patient data**, with an emphasis on neuroimaging data. The core methodological domains of our team are: machine learning, statistical modeling of complex geometric data, connectivity and network analysis. These new approaches are applied to clinical research in neurological diseases in collaboration with other teams of the ICM, clinical departments of the Pitié-Salpêtrière hospital and external partners.

We develop various clinical applications of our research, in particular in neurodegenerative disorders (Alzheimer's disease and other dementias, Parkinson's disease…), multiple sclerosis, developmental disorders, stroke and to design brain-computer interfaces for rehabilitation.

3 Research program

3.1 Neuroimaging-based biomarkers and decision support systems

Neuroimaging provides critical information on anatomical and functional alterations as well as on specific molecular and cellular processes. Our work is focused on the development of computational approaches to extract biomarkers and build computer-aided diagnosis (CAD) systems from MRI and PET data. More specifically, we developed: i) image translation models that can generate biomarkers of specific pathological processes from unspecific routine imaging data; ii) approaches for detecting local abnormalities; iii) frameworks for reproducible and reliable evaluation of CAD systems; iv) methods for training and validating from large-scale hospital data warehouses.

3.2 Models of brain networks

Functional imaging techniques (EEG, MEG and fMRI) allow characterizing the statistical interactions between the activities of different brain areas, i.e. functional connectivity. Functional integration of spatially distributed brain regions is a well-known mechanism underlying various cognitive tasks, and is disrupted in brain disorders. Our team develops mathematical frameworks to analyze and model brain networks, or graphs, estimated from experimental data via network-science approaches. More specifically, we proposed analytical tools to infer brain networks, characterize their structure and dynamics, over multiple spatial and temporal scales.

3.3 Disease progression modeling with longitudinal data

Longitudinal data sets contain observations of multiple subjects observed at multiple time-points. They offer a unique opportunity to understand temporal processes such as ageing or disease progression. We aim here to develop a new generation of statistical methods to infer the dynamics of changes of a series of data such as biomarkers, images or clinical endpoints, together with the variability of such multivariate trajectories within a population of reference. We apply these new models across an array of neurodegenerative diseases to i) understand the heterogeneity in disease progression, in particular how genetic factors may control variations in disease progression, ii) forecast the progression of a new patient at entry of a clinical trial for stratification purposes and iii) the design of new clinical scales for use as outcomes in trials.

3.4 High-dimensional and multimodal data

We then aim to develop tools to assist clinical decisions such as diagnosis, prognosis or inclusion in therapeutic trials. To that purpose, we leverage the tools developed by the team, such as multimodal representations, network indices and spatio-temporal models which are combined with advanced classification and regression approaches. We also dedicate strong efforts to rigorous, transparent and reproducible validation of the decision support systems on large clinical datasets.

3.5 Clinical research studies

Finally, we aim to apply advanced computational and statistical tools to clinical research studies. These studies are often performed in collaboration with other researchers of the ICM, clinicians of the Pitié-Salpêtrière hospital or external partners. Our aim is to better understand brain disorders by characterizing alterations and their progression, and to validate new tools to assist clinical decisions. While a large part of these clinical studies were in the field of dementia (Alzheimer's disease, fronto-temporal dementia), we have developed successful collaborations in other fields including multiple sclerosis, Parkinson's disease and related disorders, Huntington's disease or spino-cerebellar ataxia.

4 Application domains

4.1 Introduction

We develop different applications of our new methodologies to brain pathologies, mainly neurodegenerative diseases. These applications aim at:

- better understanding the pathophysiology of brain disorders;
- designing systems to support clinical decisions such as diagnosis, prognosis and design of clinical trials;
- developing brain computer interfaces for clinical applications.

4.2 Understanding brain disorders

Computational and statistical approaches have the potential to help understand the pathophysiology of brain disorders. We first aim to contribute to better understand the relationships between pathological processes, anatomical and functional alterations, and symptoms. Moreover, within a single disease, there is an important variability between patients. The models that we develop have the potential to identify more homogeneous disease subtypes, that would constitute more adequate targets for new treatments. Finally, we aim to establish the chronology of the different types of alterations. We focus these activities on neurodegeneratives diseases: dementia (Alzheimer's disease, fronto-temporal dementia), Parkinson's disease, multiple sclerosis.

4.3 Supporting clinical decisions

We aim to design computational tools to support clinical decisions, including diagnosis, prognosis and the design of clinical trials. We design new approaches for extracting biomarkers from different types of data. Our tools have the potential to help clinicians in their diagnosis by providing automated classification that can integrate multiple types of data (clinical/cognitive tests, imaging, biomarkers). Predicting the evolution of disease in individual patients is even more difficult. We aim to develop approaches that can predict which alterations and symptoms will occur and when. Finally, new approaches are needed to select participants in clinical trials. Indeed, it is widely recognized that, to have a chance to be successful, treatments should be administered at a very early stage.

4.4 Brain computer interfaces for clinical applications

A brain computer interface (BCI) is a device aiming to decode brain activity, thus creating an alternate communication channel between a person and the external environment. BCI systems can be categorized on the basis of the classification of an induced or evoked brain activity. The central tenet of a BCI is the capability to distinguish different patterns of brain activity, each being associated to a particular intention or mental task. Hence adaptation, as well as learning, is a key component of a BCI because users must learn to modulate their brainwaves to generate distinct brain patterns. Usually, a BCI is considered a technology for people to substitute some lost functions. However, a BCI could also help in clinical rehabilitation to recover motor functions. Indeed, in current neuroscience-based rehabilitation it

is recognized that protocols based on mental rehearsal of movements (like motor imagery practicing) are a way to access the motor system because they can induce an activation of sensorimotor networks that were affected by lesions. Hence, a BCI based on movement imagery can objectively monitor patients' progress and their compliance with the protocol, monitoring that they are actually imagining movements. It also follows that feedback from such a BCI can provide patients with an early reinforcement in the critical phase when there is not yet an overt sign of movement recovery.

5 Highlights of the year

- Olivier Colliot has edited the Open Access book Machine Learning for Brain Disorders (Springer, 2023, 1047 pages) which is the most comprehensive resource on this topic.
- Olivier Colliot is Conference Chair of the SPIE Medical Imaging: Image Processing conference for the period 2022-2025.
- Baptiste Couvy-Duchesne is PI of an INRIA associate team Brainetics, which started in 2023 to foster the collaboration between ARAMIS and the University of Queensland (Australia).
- Fabrizio De Vico Fallani created a new INRIA team-project called NERV devoted to complex systems and neuroengineering.

5.1 Awards

- Ravi Hassanaly received the best poster runner-up award at SPIE Medical Imaging 2023: Image processing for his paper 'Simulation-based evaluation framework for deep learning unsupervised anomaly detection on brain FDG PET' [68].

6 New software, platforms, open data

6.1 New software

6.1.1 Clinica

Name: Clinica

Keywords: Neuroimaging, Brain MRI, MRI, Clinical analysis, Image analysis, Machine learning

Scientific Description: Clinica is a software platform for multimodal brain image analysis in clinical research studies. It makes it easy to apply advanced analysis tools to large scale clinical studies. For that purpose, it integrates a comprehensive set of processing tools for the main neuroimaging modalities: currently anatomical MRI, diffusion MRI, PET. For each modality, Clinica allows to easily extract various types of features (regional measures, parametric maps, surfaces, curves, networks). Such features are then subsequently used as input of machine learning, statistical modeling, morphometry or network analysis methods. Processing pipelines are based on combinations of freely available tools developed by the community. It provides an integrated data management specification to store raw and processing data. Clinica is written in Python. It uses the Nipype system for pipelining. It combines widely-used software for neuroimaging data analysis (SPM, Freesurfer, FSL, MRtrix...), morphometry (Deformetrica), machine learning (Scikit-learn) and the BIDS standard for data organization.

Functional Description: Clinica is a software platform for multimodal brain image analysis in clinical research studies. It makes it easy to apply advanced analysis tools to large scale clinical studies. For that purpose, it integrates a comprehensive set of processing tools for the main neuroimaging modalities: currently anatomical MRI, diffusion MRI, PET. For each modality, Clinica allows to easily extract various types of features (regional measures, parametric maps, surfaces, curves, networks). Such features are then subsequently used as input of machine learning, statistical modeling, morphometry or network analysis methods. Clinica also provides an integrated data

management specification to store raw and processing data. Overall, Clinica helps to: i) apply advanced analysis tools to clinical research studies, ii) easily share data and results, iii) make research more reproducible.

URL: http://www.clinica.run

Publications: hal-04278898, hal-03728243, hal-03513920, hal-02549242, hal-02132147, hal-02308126, hal-02562504, hal-01518785, hal-01578479, hal-01858384, hal-01907482, hal-01654000, hal-02566361, hal-01950933

Contact: Olivier Colliot

Participants: Olivier Colliot, Ninon Burgos, Stanley Durrleman, Nicolas Gensollen, Mauricio Diaz, Ghislain Vaillant, Matthieu Joulot, Ravi Hassanaly, Michael Bacci, Simona Bottani, Sabrina Fontanella, Pietro Gori, Jeremy Guillon, Thomas Jacquemont, Pascal Lu, Arnaud Marcoux, Tristan Moreau, Alexandre Routier, Omar El Rifai, Jorge Samper Gonzalez, Elina Thibeau-sutre, Junhao Wen

Partners: Institut du Cerveau et de la Moelle épinière (ICM), CNRS, INSERM, Sorbonne Université

6.1.2 ClinicaDL

Keywords: Deep learning, Neuroimaging, Reproducibility

Scientific Description: As deep learning faces a reproducibility crisis and studies on deep learning applied to neuroimaging are contaminated by methodological flaws, there is an urgent need to provide a safe environment for deep learning users to help them avoid common pitfalls that will bias and discredit their results. Several tools have been proposed to help deep learning users design their framework for neuroimaging data sets. ClinicaDL has been developed to bring answers to three common issues encountered by deep learning users who are not always familiar with neuroimaging data: (1) the format and preprocessing of neuroimaging data sets, (2) the contamination of the evaluation procedure by data leakage and (3) a lack of reproducibility. The combination of ClinicaDL and its companion project Clinica allows performing an end-to-end neuroimaging analysis, from the download of raw data sets to the interpretation of trained networks, including neuroimaging preprocessing, quality check, label definition, architecture search, and network training and evaluation.

Functional Description: ClinicaDL is a Python open-source software for neuroimaging data processing with deep learning. This software includes many functionalities, such as neuroimaging preprocessing, synthetic dataset generation, label definition, data split with similar demographics, architecture search, network training, performance evaluation and trained network interpretation. The three main objectives of ClinicaDL are to (1) help manipulate neuroimaging data sets, (2) prevent data leakage from biasing results and (3) reproduce deep learning experiments.

URL: https://clinicadl.readthedocs.io

Publications: hal-03351976, hal-04279014, hal-02562504

Contact: Ninon Burgos

Participants: Ninon Burgos, Olivier Colliot, Mauricio Diaz, Elina Thibeau-sutre, Ravi Hassanaly, Camille Brianceau, Alexandre Routier, Maelys Solal

Partners: Institut du Cerveau et de la Moelle épinière (ICM), CNRS, INSERM, Sorbonne Université

6.1.3 Deformetrica

Keywords: Anatomy, Mesh, Automatic Learning, C++, 3D modeling, Image analysis

Scientific Description: Deformetrica is a software for the statistical analysis of 2D and 3D shape data. It essentially computes deformations of the 2D or 3D ambient space, which, in turn, warp any object embedded in this space, whether this object is a curve, a surface, a structured or unstructured set of points, or any combination of them.

Deformetrica comes with two applications:

registration, which computes the best possible deformation between two sets of objects, atlas construction, which computes an average object configuration from a collection of object sets, and the deformations from this average to each sample in the collection.

Deformetrica has very little requirements about the data it can deal with. In particular, it does not require point correspondence between objects!

Functional Description: Deformetrica is a software for the statistical analysis of 2D and 3D shape data. It essentially computes deformations of the 2D or 3D ambient space, which, in turn, warp any object embedded in this space, whether this object is a curve, a surface, a structured or unstructured set of points, or any combination of them.

Deformetrica comes with two applications:

- Registration, which computes the optimal deformation between two sets of objects,

- Atlas construction, which computes an average object configuration from a collection of object sets, and the deformations from this average to each sample in the collection.

Deformetrica has very little requirements about the data it can deal with. In particular, it does not require point correspondence between objects!

URL: http://www.deformetrica.org/

Contact: Stanley Durrleman

Participants: Alexandre Routier, Ana Fouquier, Barbara Gris, Benjamin Charlier, Cedric Doucet, Joan Alexis Glaunès, Marcel Prastawa, Michael Bacci, Pietro Gori, Stanley Durrleman

Partners: University of Utah, Université de Montpellier 2, Université Paris-Descartes

6.1.4 leaspy

Name: Learning spatiotemporal patterns in python

Keywords: Clinical analysis, Medical applications, Personalized medicine

Functional Description: Leaspy, standing for LEArning Spatiotemporal Patterns in Python, has been developed to analyze longitudinal (or sequential) data that correspond to the measurements of a long-term progression. Said differently, each sequence of repeated observations derives from a portion of the global process, with a certain variability between sequence.

Contact: Stanley Durrleman

6.1.5 Brain Networks Toolbox

Keywords: Neuroimaging, Medical imaging

Functional Description: Brain Networks Toolbox is an open-source package of documented routines implementing new graph algorithms for brain network analysis. It mainly contains Matlab code of new methods developed by the team and associated to publications (e.g., brain network thresholding, extraction of the information redundancy, node accessibility, etc). It requires, as input, adjacency matrices representing brain connectivity networks. Thus, it is independent on the specific approach used to construct brain networks and it can be used to extract network properties from any neuroimaging modality in healthy and diseased subjects.

URL: https://github.com/brain-network/bnt

Contact: Fabrizio De Vico Fallani

Participants: Fabrizio De Vico Fallani, Jeremy Guillon, Mario Chavez

6.1.6 OpenVIBE

Keywords: Neurosciences, Interaction, Virtual reality, Health, Real time, Neurofeedback, Brain-Computer Interface, EEG, 3D interaction

Functional Description: OpenViBE is a free and open-source software platform devoted to the design, test and use of Brain-Computer Interfaces (BCI). The platform consists of a set of software modules that can be integrated easily and efficiently to design BCI applications. The key features of OpenViBE software are its modularity, its high performance, its portability, its multiple-user facilities and its connection with high-end/VR displays. The designer of the platform enables users to build complete scenarios based on existing software modules using a dedicated graphical language and a simple Graphical User Interface (GUI). This software is available on the Inria Forge under the terms of the AGPL licence, and it was officially released in June 2009. Since then, the OpenViBE software has already been downloaded more than 60000 times, and it is used by numerous laboratories, projects, or individuals worldwide. More information, downloads, tutorials, videos, documentations are available on the OpenViBE website.

Release Contributions: Added: - Metabox to perform log of signal power - Artifacted files for algorithm tests

Changed: - Refactoring of CMake build process - Update wildcards in gitignore - Update CSV File Writer/Reader - Stimulations only

Removed: - Ogre games and dependencies - Mensia distribution

Fixed: - Intermittent compiler bug

News of the Year: Python2 support dropped in favour of Python3 New feature boxes: - Riemannian geometry - Multimodal Graz visualisation - Artefact detection - Features selection - Stimulation validator

Support for Ubuntu 18.04 Support for Fedora 31

URL: http://openvibe.inria.fr

Contact: Anatole Lecuyer

Participants: Cedric Riou, Thierry Gaugry, Anatole Lecuyer, Fabien Lotte, Jussi Lindgren, Laurent Bougrain, Maureen Clerc Gallagher, Théodore Papadopoulo, Thomas Prampart

Partners: INSERM, GIPSA-Lab

6.1.7 brainMapR

Keywords: 3D rendering, Brain MRI, Clustering

Functional Description: brainMapR is an R package to analyse and plot brain association maps (results of brain-wide association studies). It is tailored for brain MRI vertex-wise analyses, and requires brain MRI to be processed with FreeSurfer (for cortical vertices) and/or ENIGMA-shape package (for subcortical vertices). Functions include annotation of the association maps to describe and locate associated brain regions, Manhattan plots for brain, high quality plots of cortical and subcortical meshes, and GIFs generation.

Publication: hal-03118366

Author: Baptiste Couvy-Duchesne

Contact: Baptiste Couvy-Duchesne

6.2 New platforms

Platform Brain-computer interface

Participants: Marie-Constance Corsi, Arthur Desbois, Fabrizio De Vico Fallani *(Correspondant)*.

Our team coordinates the developments of the Brain-Computer Interface (BCI) platform at the Centre EEG/MEG of the neuroimaging core facility of the ICM. Several projects, including our NETBCI NNIH/ANR and ATTACK Big-brain theory funded projects, as well as experiments by different researchers of the Institute (ANR BETAPARK Project), and the BCINET ERC Consolidator grant are currently being run. To reinforce the impact of the platform we have extended the contract of our Inria ADT engineer, who is significantly contributing to the extension of the Inria software OpenVibe allowing for new functionalities based on our methodological development on brain connectivity and develop new sofwtare for the individual calibration (A. Desbois)

7 New results

7.1 Book: Machine Learning for Brain Disorders

Participants: Ninon Burgos, Baptiste Couvy-Duchesne, Marie-Constance Corsi, Johann Faouzi, Federica Cacciamani, Gabriel Jimenez, Daniel Racoceanu, Olivier Colliot *(Correspondant)*.

This book provides readers with an up-to-date and comprehensive guide to both methodological and applicative aspects of machine learning (ML) for brain disorders. The chapters in this book are organized into five parts. Part One presents the fundamentals of ML. Part Two looks at the main types of data used to characterize brain disorders, including clinical assessments, neuroimaging, electro- and magnetoencephalography, genetics and omics data, electronic health records, mobile devices, connected objects and sensors. Part Three covers the core methodologies of ML in brain disorders and the latest techniques used to study them. Part Four is dedicated to validation and datasets, and Part Five discusses applications of ML to various neurological and psychiatric disorders.

More details in [83].

7.2 Evaluation of MRI-based machine learning approaches for computer-aided diagnosis of dementia in a clinical data warehouse

Participants: Simona Bottani, Didier Dormont, Ninon Burgos, Olivier Colliot *(Correspondant)*.

A variety of algorithms have been proposed for computer-aided diagnosis of dementia from anatomical brain MRI. These approaches achieve high accuracy when applied to research data sets but their performance on real-life clinical routine data has not been evaluated yet. The aim of this work was to study the performance of such approaches on clinical routine data, based on a hospital data warehouse, and to compare the results to those obtained on a research data set. The clinical data set was extracted from the hospital data warehouse of the Greater Paris area, which includes 39 different hospitals. The research set was composed of data from the Alzheimer's Disease Neuroimaging Initiative data set. In the clinical set, the population of interest was identified by exploiting the diagnostic codes from the 10th revision of the International Classification of Diseases that are assigned to each patient. We studied how the imbalance of the training sets, in terms of contrast agent injection and image quality, may bias the results. We demonstrated that computer-aided diagnosis performance was strongly biased upwards

(over 17 percent points of balanced accuracy) by the confounders of image quality and contrast agent injection, a phenomenon known as the Clever Hans effect or shortcut learning. When these biases were removed, the performance was very poor. In any case, the performance was considerably lower than on the research data set. Our study highlights that there are still considerable challenges for translating dementia computer-aided diagnosis systems to clinical routine.

More details in [39].

7.3 Automatic segmentation of the choroid plexuses: Method and validation in controls and patients with multiple sclerosis

Participants: Arya Yazdan-Panah, Olivier Colliot *(Correspondant)*.

Choroid Plexuses (ChP) are structures located in the ventricles that produce the cerebrospinal fluid (CSF) in the central nervous system. They are also a key component of the blood-CSF barrier. Recent studies have described clinically relevant ChP volumetric changes in several neurological diseases including Alzheimer's, Parkinson's disease, and multiple sclerosis (MS). Therefore, a reliable and automated tool for ChP segmentation on images derived from magnetic resonance imaging (MRI) is a crucial need for large studies attempting to elucidate their role in neurological disorders. Here, we propose a novel automatic method for ChP segmentation in large imaging datasets. The approach is based on a 2-step 3D U-Net to keep preprocessing steps to a minimum for ease of use and to lower memory requirements. The models are trained and validated on a first research cohort including people with MS and healthy subjects. A second validation is also performed on a cohort of pre-symptomatic MS patients having acquired MRIs in routine clinical practice. Our method reaches an average Dice coefficient of 0.72 with the ground truth and a volume correlation of 0.86 on the first cohort while outperforming FreeSurfer and FastSurfer-based ChP segmentations. On the dataset originating from clinical practice, the method reaches a Dice coefficient of 0.67 (being close to the inter-rater agreement of 0.64) and a volume correlation of 0.84. These results demonstrate that this is a suitable and robust method for the segmentation of the ChP both on research and clinical datasets.

More details in [61].

7.4 How precise are performance estimates for typical medical image segmentation tasks?

Participants: Rosana El Jurdi, Olivier Colliot *(Correspondant)*.

An important issue in medical image processing is to be able to estimate not only the performances of algorithms but also the precision of the estimation of these performances. Reporting precision typically amounts to reporting standard-error of the mean (SEM) or equivalently confidence intervals. However, this is rarely done in medical image segmentation studies. In this paper, we aim to estimate what is the typical confidence that can be expected in such studies. To that end, we first perform experiments for Dice metric estimation using a standard deep learning model (U-net) and a classical task from the Medical Segmentation Decathlon. We extensively study precision estimation using both Gaussian assumption and bootstrapping (which does not require any assumption on the distribution). We then perform simulations for other test set sizes and performance spreads. Overall, our work shows that small test sets lead to wide confidence intervals (e.g. 8 points of Dice for 20 samples with $\sigma \approx 10$).

More details in [71].

7.5 Introducing Soft Topology Constraints in Deep Learning-based Segmentation using Projected Pooling Loss

Participants: Guanghui Fu, Rosana El Jurdi, Lydia Chougar, Didier Dormont, Olivier Colliot *(Correspondant)*.

Deep learning methods have achieved impressive results for 3D medical image segmentation. However, when the network is only guided by voxel-level information, it may provide anatomically aberrant segmentations. When performing manual segmentations, experts heavily rely on prior anatomical knowledge. Topology is an important prior information due to its stability across patients. Recently, several losses based on persistent homology were proposed to constrain topology. Persistent homology offers a principled way to control topology. However, it is computationally expensive and complex to implement, in particular in 3D. In this paper, we propose a novel loss function to introduce topological priors in deep learning-based segmentation, which is fast to compute and easy to implement. The loss performs a projected pooling within two steps. We first focus on errors from a global perspective by using 3D MaxPooling to obtain projections of 3D data onto three planes: axial, coronal and sagittal. Then, 2D MaxPooling layers with different kernel sizes are used to extract topological features from the multi-view projections. These two steps are combined using only MaxPooling, thus ensuring the efficiency of the loss function. Our approach was evaluated in several medical image datasets (spleen, heart, hippocampus, red nucleus). It allowed reducing topological errors and, in some cases, improving voxel-level accuracy.

More details in [66].

7.6 Interpretable automatic detection of incomplete hippocampal inversions using anatomical criteria

Participants: Lisa Hemforth, Claire Cury, Baptiste Couvy-Duchesne, Olivier Colliot *(Correspondant)*.

Incomplete Hippocampal Inversion (IHI) is an atypical anatomical pattern of the hippocampus that has been associated with several brain disorders (epilepsy, schizophrenia). IHI can be visually detected on coronal T1 weighted MRI images. IHI can be absent, partial or complete (no IHI, partial IHI, IHI). However, visual evaluation can be long and tedious, justifying the need for an automatic method. In this paper, we propose, to the best of our knowledge, the first automatic IHI detection method from T1-weighted MRI. The originality of our approach is that, instead of directly detecting IHI, we propose to predict several anatomical criteria, which each characterize a particular anatomical feature of IHI, and that can ultimately be combined for IHI detection. Such individual criteria have the advantage of providing interpretable anatomical information regarding the morphological aspect of a given hippocampus. We relied on a large population of 2,008 participants from the IMAGEN study. The approach is general and can be used with different machine learning models. In this paper, we explored two different backbone models for the prediction: a linear method (ridge regression) and a deep convolutional neural network. We demonstrated that the interpretable, anatomical based prediction was at least as good as when predicting directly the presence of IHI, while providing interpretable information to the clinician or neuroscientist. This approach may be applied to other diagnostic tasks which can be characterized radiologically by several anatomical features.

More details in [69].

7.7 Interpretability of Machine Learning Methods Applied to Neuroimaging

Participants: Elina Thibeau-Sutre, Ninon Burgos, Olivier Colliot *(Correspondant)*.

Deep learning methods have become very popular for the processing of natural images, and were then successfully adapted to the neuroimaging field. As these methods are non-transparent, interpretability methods are needed to validate them and ensure their reliability. Indeed, it has been shown that deep

learning models may obtain high performance even when using irrelevant features, by exploiting biases in the training set. Such undesirable situations can potentially be detected by using interpretability methods. Recently, many methods have been proposed to interpret neural networks. However, this domain is not mature yet. Machine learning users face two major issues when aiming to interpret their models: which method to choose, and how to assess its reliability? Here, we aim at providing answers to these questions by presenting the most common interpretability methods and metrics developed to assess their reliability, as well as their applications and benchmarks in the neuroimaging context. Note that this is not an exhaustive survey: we aimed to focus on the studies which we found to be the most representative and relevant.

More details in [91].

7.8 Evaluating machine learning models and their diagnostic value

Participants: Gaël Varoquaux, Olivier Colliot *(Correspondant)*.

This chapter describes model validation, a crucial part of machine learning whether it is to select the best model or to assess risk of a given model. We start by detailing the main performance metrics for different tasks (classification, regression), and how they may be interpreted, including in the face of class imbalance, varying prevalence, or asymmetric cost-benefit trade-offs. We then explain how to estimate these metrics in a unbiased manner using training, validation, and test sets. We describe cross-validation procedures –to use a larger part of the data for both training and testing– and the dangers of data leakage –optimism bias due to training data contaminating the test set. Finally, we discuss how to obtain confidence intervals of performance metrics, distinguishing two situations: internal validation or evaluation of learning algorithms, and external validation or evaluation of resulting prediction models.

More details in [93].

7.9 Reproducibility in machine learning for medical imaging

Participants: Olivier Colliot, Elina Thibeau-Sutre, Ninon Burgos *(Correspondant)*.

Reproducibility is a cornerstone of science, as the replication of findings is the process through which they become knowledge. It is widely considered that many fields of science are undergoing a reproducibility crisis. This has led to the publications of various guidelines in order to improve research reproducibility. This didactic chapter intends at being an introduction to reproducibility for researchers in the field of machine learning for medical imaging. We first distinguish between different types of reproducibility. For each of them, we aim at defining it, at describing the requirements to achieve it and at discussing its utility. The chapter ends with a discussion on the benefits of reproducibility and with a plea for a non-dogmatic approach to this concept and its implementation in research practice.

More details in [85].

7.10 Association Between Diseases and Symptoms Diagnosed in Primary Care and the Subsequent Specific Risk of Multiple Sclerosis

Participants: Octave Guinebretiere, Thomas Nédelec, Laurène Gantzer, Béranger Lekens, Stanley Durrleman, Céline Louapre *(Correspondant)*.

Previous studies have reported a possible prodrome in multiple sclerosis (MS) defined by non-specific symptoms including mood disorder or genito-urinary symptoms and increased health care use detected several years before diagnosis. This study aimed to evaluate agnostically the associations between

diseases and symptoms diagnosed in primary care and the risk of multiple sclerosis (MS) relative to controls and two other autoimmune inflammatory diseases with similar population characteristics, namely lupus and Crohn's disease.

A case-control study was conducted using electronic health records from the Health Improvement Network database in the UK and France. We agnostically assessed the associations between 113 diseases and symptoms in the five years before and after diagnosis in patients with subsequent diagnosis of MS. Individuals with a diagnosis of MS were compared to individuals without MS, and individuals with two other auto-immune diseases, Crohn's disease and lupus

The study population consisted of patients with MS (n= 20,174), patients without MS (n=54,790), patients with Crohn's disease (n=30,477) or patients with lupus (n=7,337). Twelve ICD-10 codes were significantly positively associated with the risk of MS compared to controls without MS. After considering ICD-10 codes suggestive of neurological symptoms as the first diagnosis of MS, five ICD-10 codes remained significantly associated with MS: depression (UK OR 1.22 [95%CI 1.11-1.34]), sexual dysfunction (1.47 [1.11-1.95]), constipation (1.5 [1.27-1.78]), cystitis (1.21 [1.05-1.39]), and urinary tract infections of unspecified site (1.38 [1.18-1.61]). However, none of these conditions was selectively associated with MS in comparisons with both lupus and Crohn's disease. All five ICD-10 codes identified were still associated with MS during the five years after diagnosis.

This study identified 5 health conditions associated with subsequent MS diagnosis, which may be considered not only prodromal but also early-stage symptoms. However, these health conditions overlap with prodrome of two other autoimmune diseases, hence lacking specificity to MS.

More details in [46].

7.11 Charting Disease Trajectories from Isolated REM Sleep Behavior Disorder to Parkinson's Disease

Participants: Cécile di Folco, Raphael Couronné, Isabelle Arnulf, Graziella Mangone, Smaranda Leu-Semenescu, Pauline Dodet, Marie Vidailhet, Jean-Christophe Corvol, Stéphane Lehéricy, Stanley Durrleman *(Correspondant)*.

Clinical presentation and progression dynamics are variable in patients with Parkinson's disease (PD). Disease course mapping is an innovative disease modelling technique that summarizes the range of possible disease trajectories and estimates dimensions related to onset, sequence, and speed of progression of disease markers. Objective To propose a disease course map for PD and investigate progression profiles in patients with or without rapid eye movement sleep behavioral disorders (RBD).

Data of 919 PD patients and 88 isolated RBD patients from three independent longitudinal cohorts were analyzed (follow-up duration: 5.1; 95% confidence interval, 1.1-8.1] years). Disease course map was estimated by using eight clinical markers (motor and non-motor symptoms) and four imaging markers (dopaminergic denervation).

PD course map showed that the first changes occurred in the contralateral putamen 13 years before diagnosis, followed by changes in motor symptoms, dysautonomia, sleep—all before diagnosis—and finally cognitive decline at the time of diagnosis. The model showed earlier disease onset, earlier non-motor and later motor symptoms, more rapid progression of cognitive decline in PD patients with RBD than PD patients without RBD. This pattern was even more pronounced in patients with isolated RBD with early changes in sleep, followed by cognition and non-motor symptoms and later changes in motor symptoms.

These findings are consistent with the presence of distinct patterns of progression between patients with and without RBD. Understanding heterogeneity of PD progression is key to decipher the underlying pathophysiology and select homogeneous subgroups of patients for precision medicine.

More details in [43].

7.12 A Multimodal Disease Progression Model for Genetic Associations with Disease Dynamics

Participants: Némo Fournier *(Correspondant)*, Stanley Durrleman.

This article introduced a disease progression model suited for neurodegenerative pathologies that allows to model associations between covariates and dynamic features of the disease course. It established a statistical framework and implemented an algorithm for its estimation. It showed that the model is reliable and can provide uncertainty estimates of the discovered associations thanks to its Bayesian formulation. The model's interest was showcased by shining a new light on genetic associations.

More details in [65].

7.13 Interaction of sex and onset site on the disease trajectory of amyotrophic lateral sclerosis

Participants: Juliette Ortholand *(Correspondant)*, Pierre-François Pradat, Sophie Tezenas du Montcel, Stanley Durrleman.

Studies showed the impact of sex and onset site (spinal or bulbar) on disease onset and survival in ALS. However, they mainly result from cross-sectional or survival analysis, and the interaction of sex and onset site on the different proxies of disease trajectory has not been fully investigated.

We selected all patients with repeated observations in the PRO-ACT database. We divided them into four groups depending on their sex and onset site. We estimated a multivariate disease progression model, named ALS Course Map, to investigate the combined temporal changes of the four sub-scores of the revised ALS Functional Rating Scale (ALSFRSr), the forced vital capacity (FVC), and the body mass index (BMI). We then compared the progression rate, the estimated age at onset, and the relative progression of the outcomes across each group.

We included 1,438 patients from the PRO-ACT database. They were 51% men with spinal onset, 12% men with bulbar onset, 26% women with spinal onset, and 11% women with bulbar onset. We showed a significant influence of both sex and onset site on the ALSFRSr progression. The BMI decreased 8.9 months earlier (95% CI = [3.9, 13.8]) in women than men, after correction for the onset site. Among patients with bulbar onset, FVC was impaired 2.6 months earlier (95% CI = [0.6, 4.6]) in women. Conclusion: Using a multivariable disease modelling approach, we showed that sex and onset site are important drivers of the progression of motor function, BMI, and FVC decline.

More details in [52].

7.14 Impact of sex and APOE-e4 genotype on regional brain metabolism in Alzheimer's Disease

Participants: Benoît Sauty *(Correspondant)*, Stanley Durrleman.

Age, sex and APOE-e4 genotype have been identified as the strongest predictors of the risk of developing Alzheimer's Disease (AD). This work models the pathological progression of regional brain hypometabolism, using mixed-effect models with latent time variable and longitudinal FDG-PET data. Statistical comparisons then disentangle the effects of sex and APOE-e4 genotype on the onset age and pace of progression of hympometabolism in each brain region, while correcting for education level. They provide a brain map of the regions with earlier and/or faster alterations of the metabolism. We show that females are associated with faster hypometabolism in the caudate nuclei, the thalamus and right temporal and medial-occipital lobes, while APOE-e4 is associated with earlier hypometabolism in the limbic system (hippocampus, parahippocampus and amygdala) and temporal lobe.

More details in [74].

7.15 Forecasting individual progression trajectories in Alzheimer's disease

The anticipation of progression of Alzheimer's disease (AD) is crucial for evaluations of secondary prevention measures thought to modify the disease trajectory. However, it is difficult to forecast the natural progression of AD, notably because several functions decline at different ages and different rates in different patients. We evaluate here AD Course Map, a statistical model predicting the progression of neuropsychological assessments and imaging biomarkers for a patient from current medical and radiological data at early disease stages. We tested the method on more than 96,000 cases, with a pool of more than 4,600 patients from four continents. We measured the accuracy of the method for selecting participants displaying a progression of clinical endpoints during a hypothetical trial. We show that enriching the population with the predicted progressors decreases the required sample size by 38% to 50%, depending on trial duration, outcome, and targeted disease stage, from asymptomatic individuals at risk of AD to subjects with early and mild AD. We show that the method introduces no biases regarding sex or geographic locations and is robust to missing data. It performs best at the earliest stages of disease and is therefore highly suitable for use in prevention trials.

Participants: Etienne Maheux *(Correspondant)*, Igor Koval, Juliette Ortholand, Colin Birkenbihl, Damanio Archetti, Vincent Bouteloup, Stéphane Epelbaum, Carole Dufouil, Martin Hofmann-Apitius, Stanley Durrleman.

More details in [48].

7.16 Measuring Neuronal Avalanches to inform Brain-Computer Interfaces

Participants: Marie-Constance Corsi *(Correspondant)*, Fabrizio De Vico Fallani.

Large-scale interactions among multiple brain regions manifest as bursts of activations called neuronal avalanches, which reconfigure according to the task at hand and, hence, might constitute natural candidates to design brain-computer interfaces (BCI). To test this hypothesis, we used source-reconstructed magneto/electroencephalography, during resting state and a motor imagery task performed within a BCI protocol. To track the probability that an avalanche would spread across any two regions we built an avalanche transition matrix (ATM) and demonstrated that the edges whose transition probabilities significantly differed between conditions hinged selectively on premotor regions in all subjects. Furthermore, we showed that the topology of the ATMs allows task-decoding above the current gold standard. Hence, our results suggest that Neuronal Avalanches might capture interpretable differences between tasks that can be used to inform brain-computer interfaces.

More details in [41].

7.17 Automatic motion artefact detection in brain T1-weighted magnetic resonance images from a clinical data warehouse using synthetic data

Participants: Sophie Loizillon, Simona Bottani, Didier Dormont, Olivier Colliot, Ninon Burgos *(Correspondant)*.

Containing the medical data of millions of patients, clinical data warehouses (CDWs) represent a great opportunity to develop computational tools. Magnetic resonance images (MRIs) are particularly sensitive to patient movements during image acquisition, which will result in artefacts (blurring, ghosting and ringing) in the reconstructed image. As a result, a significant number of MRIs in CDWs are corrupted by these artefacts and may be unusable. Since their manual detection is impossible due to the large number of scans, it is necessary to develop tools to automatically exclude (or at least identify) images

with motion in order to fully exploit CDWs. In this paper, we propose a novel transfer learning method for the automatic detection of motion in 3D T1-weighted brain MRI. The method consists of two steps: a pre-training on research data using synthetic motion, followed by a fine-tuning step to generalise our pre-trained model to clinical data, relying on the labelling of 4045 images. The objectives were both (1) to be able to exclude images with severe motion, (2) to detect mild motion artefacts. Our approach achieved excellent accuracy for the first objective with a balanced accuracy nearly similar to that of the annotators (balanced accuracy>80%). However, for the second objective, the performance was weaker and substantially lower than that of human raters. Overall, our framework will be useful to take advantage of CDWs in medical imaging and highlight the importance of a clinical validation of models trained on research data.

More details in [47].

7.18 How can data augmentation improve attribution maps for disease subtype explainability?

Participants: Elina Thibeau-Sutre, Olivier Colliot, Ninon Burgos *(Correspondant)*.

As deep learning has been widely used for computer aided-diagnosis, we wished to know whether attribution maps obtained using gradient back-propagation could correctly highlight the patterns of disease subtypes discovered by a deep learning classifier. As the correctness of attribution maps is difficult to evaluate directly on medical images, we used synthetic data mimicking the difference between brain MRI of controls and demented patients to design more reliable evaluation criteria of attribution maps. We demonstrated that attribution maps may mix the regions associated with different subtypes for small data sets while they could accurately characterize both subtypes using a large data set. We then proposed simple data augmentation techniques and showed that they could improve the coherence of the explanations for a small data set.

More details in [77].

7.19 Transfer learning from synthetic to routine clinical data for motion artefact detection in brain T1-weighted MRI

Participants: Sophie Loizillon, Simona Bottani, Didier Dormont, Olivier Colliot, Ninon Burgos *(Correspondant)*.

Clinical data warehouses (CDWs) contain the medical data of millions of patients and represent a great opportunity to develop computational tools. MRIs are particularly sensitive to patient movements during image acquisition, which will result in artefacts (blurring, ghosting and ringing) in the reconstructed image. As a result, a significant number of MRIs in CDWs are unusable because corrupted by these artefacts. Since their manual detection is impossible due to the number of scans, it is necessary to develop a tool to automatically exclude images with motion in order to fully exploit CDWs. In this paper, we propose a CNN for the automatic detection of motion in 3D T1-weighted brain MRI. Our transfer learning approach, based on synthetic motion generation, consists of two steps: a pre-training on research data using synthetic motion, followed by a fine-tuning step to generalise our pre-trained model to clinical data, relying on the manual labelling of 5500 images. The objectives were both (1) to be able to exclude images with severe motion, (2) to detect mild motion artefacts. Our approach achieved excellent accuracy for the first objective with a balanced accuracy nearly similar to that of the annotators (balanced accuracy>80%). However, for the second objective, the performance was weaker and substantially lower than that of human raters. Overall, our framework will be useful to take advantage of CDWs in medical imaging and to highlight the importance of a clinical validation of models trained on research data.

More details in [72].

7.20 Simulation-based evaluation framework for deep learning unsupervised anomaly detection on brain FDG PET

Participants: Ravi Hassanaly, Simona Bottani, Benoît Sauty, Olivier Colliot, Ninon Burgos *(Correspondant)*.

Unsupervised anomaly detection using deep learning models is a popular computer-aided diagnosis approach because it does not need annotated data and is not restricted to the diagnosis of a disease seen during training. Such approach consists in first learning the distribution of anomaly free images. Images presenting anomalies are then detected as outliers of this distribution. These approaches have been widely applied in neuroimaging to detect sharp and localized anomalies such as tumors or white matter hyper-intensities from structural MRI. In this work, we aim to detect anomalies from FDG PET images of patients with Alzheimer's disease. In this context, the anomalies can be subtle and difficult to delineate, making the task more difficult and meaning that no ground truth exists to evaluate the approaches. We thus propose a framework to evaluate unsupervised anomaly detection approaches that consists in simulating realistic anomalies from images of healthy subjects. We demonstrate the use of this framework by evaluating an approach based on a 3D variational autoencoder.

More details in [68].

7.21 Unsupervised anomaly detection in 3D brain FDG PET: A benchmark of 17 VAE-based approaches

Participants: Ravi Hassanaly, Camille Brianceau, Olivier Colliot, Ninon Burgos *(Correspondant)*.

The use of deep generative models for unsupervised anomaly detection is an area of research that has gained interest in recent years in the field of medical imaging. Among all the existing models, the variational autoencoder (VAE) has proven to be efficient while remaining simple to use. Much research to improve the original method has been achieved in the computer vision literature, but rarely translated to medical imaging applications. To fill this gap, we propose a benchmark of fifteen variants of VAE that we compare with a vanilla autoencoder and VAE for a neuroimaging use case relying on a simulation-based evaluation framework. The use case is the detection of anomalies related to Alzheimer's disease and other dementias in 3D FDG PET. We show that among the fifteen VAE variants tested, nine lead to a good reconstruction accuracy and are able to generate healthy-looking images. This indicates that many approaches developed for computer vision applications can generalize to the unsupervised detection of anomalies of various shapes, intensities and locations in 3D FDG PET. However, these models do not outperform the vanilla autoencoder and VAE. More details in [81].

7.22 Semi-supervised domain adaptation for automatic quality control of FLAIR MRIs in a clinical data warehouse

Participants: Sophie Loizillon, Olivier Colliot, Lydia Chougar, Didier Dormont, Ninon Burgos *(Correspondant)*.

Domain adaptation is a very useful approach to exploit the potential of clinical data warehouses, which gather a vast amount of medical imaging encompassing various modalities, sequences, manufacturers and machines. In this study, we propose a semi-supervised domain adaptation (SSDA) framework for automatically detecting poor quality FLAIR MRIs within a clinical data warehouse. Leveraging a limited number of labelled FLAIR and a large number of labelled T1-weighted MRIs, we introduce a novel architecture based on the well known Domain Adversarial Neural Network (DANN) that incorporates a specific classifier for the target domain. Our method effectively addresses the covariate shift and class

distribution shift between T1-weighted and FLAIR MRIs, surpassing existing SSDA approaches by more than 10 percent points.

More details in [73].

7.23 A2V: A Semi-Supervised Domain Adaptation Framework for Brain Vessel Segmentation via Two-Phase Training Angiography-to-Venography Translation

Participants: Francesco Galati, Ninon Burgos, Maria A. Zualuaga *(Correspondant)*.

We present a semi-supervised domain adaptation framework for brain vessel segmentation from different image modalities. Existing state-of-the-art methods focus on a single modality, despite the wide range of available cerebrovascular imaging techniques. This can lead to significant distribution shifts that negatively impact the generalization across modalities. By relying on annotated angiographies and a limited number of annotated venographies, our framework accomplishes image-to-image translation and semantic segmentation, leveraging a disentangled and semantically rich latent space to represent heterogeneous data and perform image-level adaptation from source to target domains. Moreover, we reduce the typical complexity of cycle-based architectures and minimize the use of adversarial training, which allows us to build an efficient and intuitive model with stable training. We evaluate our method on magnetic resonance angiographies and venographies. While achieving state-of-the-art performance in the source domain, our method attains a Dice score coefficient in the target domain that is only 8.9% lower, highlighting its promising potential for robust cerebrovascular image segmentation across different modalities.

More details in [67].

7.24 Temporal dynamics of the Scale for the Assessment and Rating of Ataxia in Spinocerebellar ataxias

Participants: Paul Moulaire, Pierre Emmanuel Poulet, Emilien Petit, Thomas Klockgether, Alexandra Durr, Tetsuo Ashisawa, Sophie Tezenas Du Montcel *(Correspondant)*.

Background The Scale for the Assessment and Rating of Ataxia (SARA) is the reference clinical scale to assess the severity of cerebellar ataxia. In the context of upcoming therapeutic trials, a reliable clinical outcome is needed to assess the efficiency of treatments. Objective The aim is to precisely assess and compare temporal dynamics of SARA and a new f-SARA. Methods We analyzed data from four cohorts (EUROSCA, RISCA, CRC-SCA, and SPATAX) comprising 1210 participants and 4092 visits. The linearity of the progression and the variability were assessed using an ordinal Bayesian mixed-effect model (Leaspy). We performed sample size calculations for therapeutic trials with different scenarios to improve the responsiveness of the scale. Results Seven of the eight different items had a nonlinear progression. The speed of progression was different between most of the items, with an average time for a one-point increase from 3.5 years [3.4; 3.6] (median, 95% credible interval) for the fastest item to 11.4 [10.9; 12.0] years. The total SARA score had a linear progression with an average time for a one-point increase of 0.95 [0.92; 0.98] years. After removing the four last items and rescaling all items from 0 to 4, variability increased and progression was slower and thus would require a larger sample size in a future therapeutic trial. Conclusion Despite a heterogeneous temporal dynamics at the item level, the global progression of SARA was linear. Changing the initial scale deteriorates the responsiveness. This new information about the temporal dynamics of the scale should help design the outcome of future clinical trials.

More details in [50].

7.25 Baseline Clinical and Blood Biomarker in Patients With Preataxic and Early-Stage Disease Spinocerebellar Ataxia 1 and 3

Participants: Sophie Tezenas Du Montcel *(Correspondant)*, Emilien Petit, Titilayo Olubajo, Jennifer Faber, Pauline Lallemant-Dudek, Khalaf Bushara, Susan Perlman, Sub Subramony, David Morgan, Brianna Jackman, Henry Lauris Paulson, Gülin Öz, Thomas Klockgether, Alexandra Durr, Tetsuo Ashisawa.

Background and Objective: In spinocerebellar ataxia, ataxia onset can be preceded by mild clinical manifestation, cerebellar and/or brainstem alterations or biomarkers modifications. READISCA is a prospective, longitudinal observational study of patients with spinocerebellar ataxias type 1 and 3 to provide essential markers for therapeutic interventions. We looked for clinical, imaging or biological markers that are present at an early-stage of the disease. Methods: We enrolled carriers of a pathological ATXN1 or ATXN3 expansion and controls from 18 US and two European ataxia referral centers. Clinical, cognitive, quantitative motor, neuropsychological measures and plasma neurofilament light chain (NfL) measurements were compared between mutation carriers with and without ataxia and controls. Results: We enrolled 200 participants: 45 carriers of a pathological ATXN1 expansion (31 patients with ataxia (median SARA: 9 [7;10]), 14 mutation carriers without ataxia (1 [0;2])) and 116 carriers of a pathological ATXN3 expansion (80 patients with ataxia (7 [6;9]), 36 mutation carriers without ataxia (1 [0;2])). In addition, we enrolled 39 controls who did not carry a pathological expansion in ATXN1 or ATXN3 . Plasma NfL levels were significantly higher in mutation carriers without ataxia than controls, despite similar mean age (controls: 5.7 pg/mL, SCA1: 18.0 pg/mL (P <0.0001), SCA3: 19.8 pg/mL (P<0.0001). Mutation carriers without ataxia differed from controls by significantly more upper motor signs (SCA1 P=0.0003, SCA3 P=0.003) and by the presence of sensor impairment and diplopia in SCA3 (P=0.0448, and 0.0445 respectively). Functional scales, fatigue and depression scores, swallowing difficulties, and cognitive impairment were worse in mutation carriers with ataxia than those without ataxia. Ataxic SCA3 subjects showed extrapyramidal signs, urinary dysfunction and lower motor neuron signs significantly more often than mutation carriers without ataxia. Discussion: READISCA showed the feasibility of harmonized data acquisition in a multi-national network. NfL alterations, early sensory ataxia and corticospinal signs were quantifiable between preataxic participants and controls. Patients with ataxia differed in many parameters from controls and mutation carriers without ataxia, with a graded increase of abnormal measures from control to preataxic to ataxic cohorts.

More details in [59].

7.26 A meta-graph approach for analyzing whole slide histopathological images of human brain tissue with Alzheimer's disease biomarkers

Participants: Gabriel Jimenez, Pablo Mas, Anuradha Kar, Lea Ingrassia, Suzana Boluda, Benoit Delatour, Lev Stimmer, Daniel Racoceanu *(Correspondant)*.

Recently, high performance deep learning models have allowed automatic and precise analysis of high-content medical images. In digital histopathology, a typical challenge lies in analyzing whole slide images (WSI) due to their large dimensions which most often requires splitting them into small patches for feeding deep learning models. This leads to loss in global tissue level information and is particularly limiting to classification or clustering of patients based on tissue characteristics. In this study, a meta-graph approach is developed for a semantic spatial analysis of histopathological WSIs of human brain tissue containing biomarkers of Alzheimer's disease (AD) such as tau protein aggregates in brain gray matter. We propose a pipeline that extracts morphological features of tau aggregates like neuritic plaques or neurofibrillary tangles using a pre-trained U-Net model and uses these to build a graph based on Delaunay triangulation at the WSI level in order to extract topological features from them. This pipeline is generating morphological and topological tabular data from WSI for classification and clustering patients using boosted trees, SVM or K-means algorithms. Further, combining locally extracted morphological features - at the neuritic plaques or neurofibrillary tangle level - with the constructed Delaunay graph, allows constructing a meta-graph that can be efficiently fed to graph neural network models, instead of

the voluminous WSIs. This pipeline is developed and tested on a dataset of 60 WSIs from various cohorts of patients having normal and rapidly advancing AD. The purpose of this pipeline is to identify novel insights into AD evolution, as well as to provide a generic framework for creating knowledge-rich graphs for WSI characterization and analysis.

More details in [70].

7.27 Efficient 3D reconstruction of Whole Slide Images in Melanoma

Participants: Janan Arslan, Mehdi Ounissi, Haocheng Luo, Matthieu Lacroix, Pierrick Dupré, Pawan Kumar, Arran Hodgkinson, Sarah Dandou, Romain Larive, Christine Pignodel, Laurent Le Cam, Ovidiu Radulescu, Daniel Racoceanu *(Correspondant)*.

Cutaneous melanoma is an invasive cancer with a worldwide annual death toll of 57,000 (Arnold *et al.*, JAMA Dermatol 2022). In a metastatic state, surgical interventions are not curative and must be coupled with targeted therapy, or immunotherapy. However, resistance appears almost systematically and late-stage prognosis can remain poor. The complexity to eradicate melanoma stems from its plasticity; these cancer cells continually adapt to the tumor microenvironment, which leads to treatment resistance. Our primary assumption is that therapeutic resistance relies in part on a series of non-genetic transitions including changes in the metabolic states of these cancer cells. The 3D spatial distribution of blood vessels that are sources of nutrition and oxygen that drive this metabolic status is an important variable for understanding zoning aspects of this adaptation process. Using Whole Slide Images (WSI) of melanoma tumors from Patient-Derived Xenograft (PDX) mouse models, we build 3D vascular models to help predict and understand the metabolic states of cancer cells within the tumor. Our 3D reconstruction pipeline was based on PDX tumor samples sectioned over 2mm depth and stained with Hematoxylin and Eosin (H&E). The pipeline involves three primary steps, including 2D vessel segmentation using Deep Learning, intensity- and affine-based image registration, and 3D reconstruction using interpolation and 3D rendering (allowing for better interaction with biologists, pathologists, and clinicians). The originality of our computer-assisted pipeline is its capability to (a) deal with sparse data (i.e., not all tissue sections were readily available), and (b) adapt to a multitude of WSI-related challenges (e.g., epistemic uncertainty, extended processing times due to WSI scale, etc.). We posit both our 3D reconstruction pipeline, quantitative results of the major stages of the process, and a detailed illustration of the challenges faced, presenting resolutions to improve the pipeline's efficiency.

More details in [63].

7.28 Computational Pathology for Brain Disorders

Participants: Gabriel Jimenez, Daniel Racoceanu *(Correspondant)*.

Non-invasive brain imaging techniques allow understanding the behavior and macro changes in the brain to determine the progress of a disease. However, computational pathology provides a deeper understanding of brain disorders at cellular level, able to consolidate a diagnosis and make the bridge between the medical image and the omics analysis. In traditional histopathology, histology slides are visually inspected, under the microscope, by trained pathologists. This process is time-consuming and labor-intensive; therefore, the emergence of Computational Pathology has triggered great hope to ease this tedious task and make it more robust. This chapter focuses on understanding the state-of-the-art machine learning techniques used to analyze whole slide images within the context of brain disorders. We present a selective set of remarkable machine learning algorithms providing discriminative approaches and quality results on brain disorders. These methodologies are applied to different tasks, such as monitoring mechanisms contributing to disease progression and patient survival rates, analyzing morphological phenotypes for classification and quantitative assessment of disease, improving clinical care, diagnosing tumor specimens, and intraoperative interpretation. Thanks to the recent progress in

machine learning algorithms for high-content image processing, computational pathology marks the rise of a new generation of medical discoveries and clinical protocols, including in brain disorders.

More details in [90].

7.29 Phagocytosis Unveiled: A Scalable and Interpretable Deep learning Framework for Neurodegenerative Disease Analysis

Participants: Mehdi Ounissi, Daniel Racoceanu *(Correspondant)*.

Quantifying the phagocytosis of dynamic, unstained cells is essential for evaluating neurodegenerative diseases. However, measuring rapid cell interactions and distinguishing cells from backgrounds make this task challenging when processing time-lapse phase-contrast video microscopy. In this study, we introduce a fully automated, scalable, and versatile realtime framework for quantifying and analyzing phagocytic activity. Our proposed pipeline can process large data-sets and includes a data quality verification module to counteract potential perturbations such as microscope movements and frame blurring. We also propose an explainable cell segmentation module to improve the interpretability of deep learning methods compared to black-box algorithms. This includes two interpretable deep learning capabilities: visual explanation and model simplification. We demonstrate that interpretability in deep learning is not the opposite of high performance, but rather provides essential deep learning algorithm optimization insights and solutions. Incorporating interpretable modules results in an efficient architecture design and optimized execution time. We apply this pipeline to quantify and analyze microglial cell phagocytosis in frontotemporal dementia (FTD) and obtain statistically reliable results showing that FTD mutant cells are larger and more aggressive than control cells. To stimulate translational approaches and future research, we release an open-source pipeline and a unique microglial cells phagocytosis dataset for immune system characterization in neurodegenerative diseases research. This pipeline and dataset will consistently crystallize future advances in this field, promoting the development of efficient and effective interpretable algorithms dedicated to this critical domain.

More details in [99].

7.30 HappyFeat—An interactive and efficient BCI framework for clinical applications

Participants: Arthur Desbois *(Correspondant)*, Fabrizio De Vico Fallani, Marie Constance Corsi *(Correspondant)*.

Brain–Computer Interface (BCI) systems allow to perform actions by translating brain activity into commands. Such systems require training a classification algorithm to discriminate between mental states, using specific features from the brain signals. This step is crucial and presents specific constraints in clinical contexts. HappyFeat is an open-source software making BCI experiments easier in such contexts: effortlessly extracting and selecting adequate features for training, in a single GUI. Novel features based on Functional Connectivity can be used, allowing graph-oriented approaches. We describe HappyFeat's mechanisms, showing its performances in typical use cases, and showcasing how to compare different types of features.

More details in [42].

7.31 Vizaj—A free online interactive software for visualizing spatial networks

Participants: Thibault Rolland *(Correspondant)*, Fabrizio De Vico Fallani *(Correspondant)*.

In many fields of science and technology we are confronted with complex networks. Making sense of these networks often require the ability to visualize and explore their intermingled structure consisting of nodes and links. To facilitate the identification of significant connectivity patterns, many methods have been developed based on the rearrangement of the nodes so as to avoid link criss-cross. However, real networks are often embedded in a geometrical space and the nodes code for an intrinsic physical feature of the system that one might want to preserve. For these spatial networks, it is therefore crucial to find alternative strategies operating on the links and not on the nodes. Here, we introduce Vizaj a javascript web application to render spatial networks based on optimized geometrical criteria that reshape the link profiles. While optimized for 3D networks, Vizaj can also be used for 2D networks and offers the possibility to interactively customize the visualization via several controlling parameters, including network filtering and the effect of internode distance on the link trajectories. Vizaj is further equipped with additional options allowing to improve the final aesthetics, such as the color/size of both nodes and links, zooming/rotating/translating, and superimposing external objects. Vizaj is an open-source software which can be freely downloaded and updated via a github repository. Here, we provide a detailed description of its main features and algorithms together with a guide on how to use it. Finally, we validate its potential on several synthetic and real spatial networks from infrastructural to biological systems. We hope that Vizaj will help scientists and practitioners to make sense of complex networks and provide aesthetic while informative visualizations.

More details in [55].

8 Bilateral contracts and grants with industry

8.1 Bilateral grants with industry

8.1.1 Sanofi

Participants: Stanley Durrleman *(Correspondant)*.

- This project aims at modeling Parkinson disease progression for patients with mutations in the GBA genes, selecting potential good responders in clinical trials based on their progression profile, and evaluating new measures of drug efficacy.
- Coordinator: Stanley Durrleman
- Started in 2020

8.1.2 Biogen

Participants: Stanley Durrleman *(Correspondant)*.

- This project aims at analysing clinical trial data in neurodegenerative diseases.
- Coordinator: Stanley Durrleman
- Started in 2022

8.1.3 VICO

Participants: Sophie Tezenas du Montcel *(Correspondant)*.

- VO659 Strategic Advisory Board.

- Coordinator: Sophie Tezenas du Montcel
- Started in 2023

9 Partnerships and cooperations

9.1 International initiatives

9.1.1 Inria associate team not involved in an IIL or an international program

Brainetics

Participants: Baptiste Couvy-Duchesne, Olivier Colliot, Arya Yazdan-Panah, Elise Delzant, Camille Brianceau, Lisa Hemforth, Guanghui Fu.

- Project acronym: Brainetics
- Website
- Project title: Leveraging brain magnetic resonance images and genetics for neurodegenerative and psychiatric disorders
- Duration: 3 years (started 2023)
- Coordinator: Baptiste Couvy-Duchesne
- Other partner: Progam in Complex Trait Genomics (PCTG), The University of Queensland, Brisbane, Australia
- Abstract: The general objective of the associate team is to develop multi-modal methods and analyses, that combine genetics and neuroimaging data. Each member of the associate team is specialized in a data modality (genetics for PCTG, neuroimaging for ARAMIS) and both teams have a strong track record in method and software development.

9.2 European initiatives

9.2.1 Horizon Europe

BCINET BCINET project on cordis.europa.eu

Title: Non-invasive decoding of brain communication patterns to ease motor restoration after stroke

Duration: From October 1, 2020 to September 30, 2026

Partners:

- INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET AUTOMATIQUE (INRIA), France
- INSTITUT DU CERVEAU ET DE LA MOELLE EPINIERE (ICM), France

Inria contact: Fabrizio De Vico Fallani

Coordinator:

Summary: Human-computer interfaces are increasingly explored to facilitate interaction with the external world. Brain-computer interfaces (BCIs), bypassing the skeletomuscular system, are particularly promising for assisting paralyzed people in control and communication, but also for boosting neuromotor rehabilitation.

Despite their potential, the societal impact of BCIs is dramatically limited by the poor usability in real-life applications. While many solutions have been proposed - from the identification of the best classification algorithm to the type of sensory feedback - the accuracy is still highly variable across subjects and BCIs cannot be used by everyone. Critically, these approaches have implicitly assumed that the user's intent could be decoded by examining the activity of single brain areas. Today, we know that this is not true as the brain functioning essentially depends on a complex network of interactions between differently specialized areas.

The grand challenge of this project is to develop a novel generation of BCIs that integrate the user's brain network information for enhancing accuracy and usability. Based on this approach, we will experiment innovative BCI prototypes to restore the lost motor functions in patients suffering from stroke.

This project relies on a unifying framework that analyses and models brain networks by means of analytical tools derived from graph theory and complex systems science. By recruiting diverse neuroimaging and experimental methods, within a modern computational framework, we aim to i) identify new control features for enhancing BCI accuracy, ii) study the brain dynamics of human learning for improving adaptive BCI architectures, and iii) optimize brain stimulation techniques for boosting BCI skill acquisition.

This project can significantly improve BCI usability as well as determining how brain lesions compromise brain functioning and which solutions are most effective to unlock motor restoration after stroke.

VirtualBrainCloud VirtualBrainCloud project on cordis.europa.eu

Title: Personalized Recommendations for Neurodegenerative Disease

Duration: From December 1, 2018 to May 31, 2023

Partners:

- INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET AUTOMATIQUE (INRIA), France
- HELSINGIN YLIOPISTO, Finland
- INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE, France
- FORSCHUNGSZENTRUM JULICH GMBH (FZJ), Germany
- UNIVERSITAT WIEN (UNIVIE), Austria
- FRAUNHOFER GESELLSCHAFT ZUR FORDERUNG DER ANGEWANDTEN FORSCHUNG EV (Fraunhofer), Germany
- TP21 GMBH (TP21), Germany
- FUNDACIO INSTITUT DE BIOENGINYERIA DE CATALUNYA (IBEC-CERCA), Spain
- INSTITUT DU CERVEAU ET DE LA MOELLE EPINIERE (ICM), France
- EODYNE SYSTEMS SL, Spain
- UNIVERSIDAD COMPLUTENSE DE MADRID (UCM), Spain
- CHARITE - UNIVERSITAETSMEDIZIN BERLIN, Germany
- THE CHANCELLOR, MASTERS AND SCHOLARS OF THE UNIVERSITY OF OXFORD (UOXF), United Kingdom
- UNIVERSITE D'AIX MARSEILLE (AMU), France
- UNIVERSITA DEGLI STUDI DI GENOVA (UNIGE), Italy
- CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS (CNRS), France
- CODEMART SRL (CODEMART), Romania
- CODEBOX GMBH, Germany

- ALZHEIMER EUROPE (AE), Luxembourg

Inria contact: Bertrand Thirion

Coordinator:

Summary: The annual worldwide cost of Alzheimer's dementia was 777.81 billion Euro in 2015. This number will rise to 7.41 trillion Euro in 2050. Early diagnosis would save up to $7.9 trillion in medical and care costs by 2050 in the US alone. However, the emergent pathology is highly variable across people, necehighly variable across people, necessitating individualized diagnostics and interventions. The VirtualBrainCloud addresses this by bridging the gap between computational neuroscience and subcellular systems biology, integrating both research streams into a unifying computational model that supports personalized diagnostics and treatments in NDD. TheVirtualBrainCloud not only integrates existing software tools, it also merges the efforts of two big EU initiatives, namely The Virtual Brain large scale simulation platform of the EU Flagship Human Brain Project and IMI-EPAD initiative (European prevention of Alzheimer's dementia consortium). VirtualBrainCloud will develop and validate a decision support system that provides access to high quality multi-disciplinary data for clinical practice. The result will be a cloud-based brain simulation platform to support personalized diagnostics and treatments in NDD. The EU PRACE (Partnership for Advanced Computing in Europe) initiative, will provide the required computing infrastructure. The VirtualBrainCloud will develop robust solutions for legal and ethical matters by interacting with EU projects such as European Open Science Cloud (EOSC), 'cloud4health', Alzheimer's Europe patient organizations and ELIXIR, an organization that manages and safeguards EU research data. Our software developers have already produced highly successful brain simulation and clinical decision support tools. The resulting software will be a cloud based computational modeling system that is tailored to the individual, and bridges multiple scales to identify key mechanisms that predict NDD progression and serves as Precision Decision Support System.

9.3 National initiatives

Health Data Hub

Participants: Stanley Durrleman.

- Project acronym: Precise-PD-HDH
- Project title: Modélisation et prédiction de la progression de la maladie de Parkinson
- Duration: 1 year (pilot project)
- Coordinator: Jean-Christophe Corvol
- Other partners: Inserm, réseau NS-PARK, ICM

AVIESAN - ITMO Cancer

Participants: Ovidiu Radulescu, Daniel Racoceanu, Laurent Le Cam, Janan Arslan, Mehdi Ounissi, Ayse Gungor.

- Project acronym: MALMO
- Project title: Mathematical Approaches to Modelling Metabolic Plasticity and Heterogeneity in Melanoma
- Duration: 3 years (2021-2023)

- Coordinator: Ovidiu Radulescu
- Other partners: University of Montpellier (LPHI - UMR CNRS 5235, LIRMM - UMR CNRS 5506) and the Institut de Recherche en Cancérologie de Montpellier (IRCM – Inserm U1194), Paris Brain Institute (CNRS UMR 7225 – Inserm U 1127).
- Abstract: Cutaneous melanoma is a highly invasive tumor and despite recent therapeutic advances, most patients with advanced melanoma have a poor clinical outcome. At the molecular level, the most frequent mutations in melanoma affect the BRAF oncogene, a protein kinase of the MAPK pathway. Therapies targeting BRAF/MEK are effective for only 50% of the patients and almost systematically generate resistance. Some non-genetic mechanisms of drug resistance are associated with the strong heterogeneity and the plasticity and melanoma cells that still remain poorly understood. In the proposed project, we will address the importance of metabolic plasticity in melanoma cells in the context of drug resistance. In order to understand the mechanistic origin of the resistance to targeted therapies, we will build a predictive multiscale mathematical model. This model describes intracellular dynamics of the metabolic pathways and the dynamics of the melanoma cell sub- populations in interaction with their micro-environment. The model has spatial extension and takes into account cellular heterogeneity. Model initial conditions and parameters describing the microenvironment are learned from image analysis of tumour sections using deep learning as segmentation approach. In order to validate the model, we use a multiplexed imaging technique applied to the detection of metabolic markers in samples prepared from murine xenografted tumours submitted to treatment. Using the mathematical model and the in situ imaging data, we expect to prove the role of the metabolic reprogramming in generating melanoma heterogeneity and its contribution to resistance to targeted therapies. Our predictive mathematical model will also allow us to investigate in silico the relationship between micro-environment, metabolic/cellular plasticity and drug resistance, as well as the potential of combining several therapies simultaneously or with optimized scheduling.

9.3.1 ANR

ANR-PRC BETPARK

Participants: Fabrizio De Vico Fallani *(Correspondant)*.

- Project acronym: BETPARK
- Project title: Neurofeedback for Parkinson's disease
- Duration: Apr 2021 - Mar 2025
- Amount: 712k€
- Coordinator: Nathalie George
- Other partners: CNRS CCLE; ICM
- Abstract: Parkinson's disease (PD) is a complex neurodegenerative disease caused by death of midbrain dopaminergic neurons. This calls for better understanding the pathophysiology of PD in order to pave the way to new non-pharmacological and non-invasive treatment options for PD. We propose to use neurofeedback (NF) to test whether PD patients can learn to self-regulate their brain activity to reduce pathological neural activity and thereby motor symptoms. We will leverage NF to target regulation of pathological beta band (8-35 Hz) oscillations, and we will characterize training-induced changes in cortical network activity and their relationship with symptom severity. Our goal is to provide direct evidence of the functional role of beta rhythms in the pathophysiology of PD while assessing NF as a new non-pharmacological and non-invasive tool for ameliorating PD motor symptoms.

ANR-PRC BRANDY

Participants: Fabrizio De Vico Fallani *(Correspondant)*.

- Project acronym: BRANDY
- Project title: Brain attention network's dynamics
- Duration: Apr 2019 - Mar 2023
- Amount: 650k€
- Coordinator: Paolo Bartolomeo
- Other partners: ICM
- Abstract: Attention allows us to explore the environment and to effectively respond to external events. Attention sets priorities on the basis of our goals and of the salience of external stimuli. Human visual attention relies on distinct dorsal and ventral fronto-parietal networks, but little is known about their dynamics, because hitherto our knowledge mostly depends on fMRI, which has limited temporal resolution. BRANDY aims at building an anatomo-functional model of human visual attention. Specifically, BRANDY has three main objectives: Work Package (WP) 1 will determine the precise dynamics of normal visual attention on a fine-scale; WP2 will provide important evidence on neurotypical and impaired attention in neglect patients using a network-perspective. WP3 will build comprehensive anatomical and functional models of neurotypical and pathological human visual attention.

ANR-NIH-NSF CANDT

Participants: Fabrizio De Vico Fallani *(Correspondant)*.

- Project acronym: CANDT
- Project title: Advancing neuroscientific discovery and training by lowering the barrier of entry to network neuroscience via open science
- Duration: Oct 2019 - Sep 2023
- Amount: 137k€
- Coordinator: Fabrizio De Vico Fallani
- Other partners: Indiana Univ., US; UPenn, US
- Abstract: This project will use open science methods and cloud-computing, effectively lowering the barrier of entry to network neuroscience and increase the widespread availability of well-maintained and reproducible network neuroscience tools. We will use the platform brainlife.io as a digital marketplace for network neuroscience analysis methods; network neuroscience tools and software will be packaged into self-contained, standardized, reproducible Apps, shared with and modified by a burgeoning community of users, and seamlessly integrated into existing brainlife.io processing and analysis pipelines. This approach will engage both experts in network science, scientists from other domains, and users of the proposed methods. In addition, it will ensure correct implementation, a high level of reproducibility, and maximal reusability of network neuroscience methods. As a requirement, Apps will also be accompanied by links to primary sources, in-depth tutorials, and documentation, and worked-through examples, highlighting their correct usage and offering solutions for mitigating possible pitfalls. This proposed research lowers the barrier of entry to network neuroscience, standardizes the software sharing process, and provides a cloud-based repository of expertly-maintained network neuroscientific tools and software that is made available to the broader neuroscientific community.

JPND project E-DADS

Participants: Stanley Durrleman *(Correspondant)*, Nemo Fournier.

- Project acronym: E-DADS
- Project title: Early Detection of Alzheimer's Disease Subtypes
- Duration: 2019 - 2023
- Amount: 170k€
- Coordinator: Daniel Alexander (UCL)
- Other partners: University College London, Stichting VU University Medical Center, IRCCS Fatebenefratelli Brescia,Commonwealth Scientific and Industrial Research Organisation
- Abstract: Alzheimer's disease (AD) is a global health and economic burden with currently about 47 million affected individuals worldwide. No provably disease-modifying treatments exist. Delaying disease onset in dementia patients by five years can reduce care costs by 36% about €88B per year across the EU. A key confound preventing successful outcomes in most treatment trials to date has been AD's high variation in onset, mechanism, and clinical expression. E-DADS aims to untangle this heterogeneity by defining data-driven subtypes of the clinical manifestation of AD based on brain imaging, cognitive markers, and fluid biomarkers that are robustly identifiable from predictive risk factors (genetics, co-morbidities, physiological and lifestyle factors) years before disease onset. To achieve this we develop a novel multi-view learning strategies that relates end-stage disease manifestations observable in clinical cohorts to features of early-stage or at-risk individuals in preclinical cohorts and the general pre-affected population from population or aging studies. This approach is only possible now due to the availability of large population data, richly phenotyped AD cohorts and advances in machine learning. E-DADS uniquely assembles the necessary data and expertise. The ability to identify AD subtypes and predict them years before onset will significantly advance AD research and clinical management via precision medicine. First, it identifies distinct homogeneous groups, shedding new light on that nature and variability of disease mechanisms ultimately pinpointing effective drug targets. Second, it enables enrichment of future clinical trials for specific groups of patients likely to benefit from a particular intervention. Third, it highlights potential lifestyle interventions that may affect or delay disease onset at very early stages. E-DADS delivers the underpinning technology to achieve this through machine learning and big-data analytics together with a prototype software tool enabling future translation and uptake.

JPND project Lemerend

Participants: Stanley Durrleman *(Correspondant)*, Octave Guinebretière, Thomas Nedelec, Baptiste Couvy-Duchesne, Karim Zaidi.

- Project acronym: Lemerend
- Project title: Leveraging medical records to identify patients at risk of neurodegenerative disease
- Duration: 2022 - 2025
- Amount: 260k€
- Coordinator: Stanley Durrleman
- Other partners: Aix-Marseille université, Karolinska Institute, University of Queensland

- Abstract: Neurodegenerative diseases represent one of the main public health issues in our western societies and one of the greatest challenges in drug development. Prevention policies have become essential to address these issues: primary prevention to prevent disease onset by acting on actionable risk factors, or secondary prevention to slow disease progression with very early therapeutic interventions, ideally at pre-symptomatic stages. Key to the implementation of such prevention measures is the identification of at-risk patients, at the point of care, and preferably long before disease onset. Our project, LeMeReND, proposes to use electronic health records (EHR) to identify biomedical risk factors through studying previous diagnoses (pre-clinical comorbidities), drug prescription, clinical care usage, and biological test results. This analysis will use longitudinal data in EHR registries including millions of patients who have been followed for at least 10 years before diagnosis in 4 different healthcare systems: Australia, France, the UK and Sweden and across 4 therapeutic areas: Alzheimer's disease, Parkinson's disease, dementia with Lewy bodies and motor neuron diseases. We will identify the biomedical risk factors that are common to these diseases and the ones differentiating them. We will stratify patients based on the progression profile of their exposure to the set of risk factors, in order to design tailored primary prevention measures. We will also design a screening tool which will give each patient a propensity score to develop one of these neurodegenerative diseases. Such a tool could be deployed at the point of care to prioritise at-risk individuals for further inclusion in secondary prevention trials. We will evaluate the economic and social benefits of this new generation of precision prevention measures. We will study the public acceptability of a secondary-prevention effort, among the French population, and the feasibility of its implementation in primary care practices in France, Australia, and Sweden. Eventually, we will progress our understanding of the genetic and imaging markers of the disorders by studying the identified prodromal biomedical factors, using the UK BioBank and GWAS summary statistics. This will progress our understanding of the pathological processes which result in an increased risk to develop a specific neurodegenerative disease. LeMeReND gathers a multidisciplinary research group with a leading expertise in epidemiology, statistics and machine learning, in particular for the analysis of longitudinal EHR data. Partners have demonstrated a strong track record on neurodegenerative diseases (Sweden, France, Australia), analyses of large-scale data including neuroimaging (France), genetics (Australia), longitudinal modelling (Sweden, France), and machine learning (Australia, France). An expert team in health economics and health policy complements the consortium. LeMeReND will therefore provide invaluable insights to inform health policies and highlight possible new therapeutic targets. It will provide unique screening tools to facilitate the large-scale recruitment of patients in secondary prevention trials.

PEPR project REWIND

Participants: Stanley Durrleman *(Correspondant)*, Sophie Tezenas du Montcel.

- Project acronym: REWIND
- Project title: Médecine de précision avec données longitudinales
- Duration: 2023 - 2028
- Amount: k€
- Coordinator: Stéphanie Allassonnière
- Other partners: Universite de Paris Cité, Universite Grenoble-Alpes, Universite Claude Bernard Lyon 1, Sorbonne Universite, CNRS, INRIA, INSERM,CHU Pitie-Salpêtrière, Hospices Civils de Lyon
- Abstract: Longitudinal data are essential for understanding the progression of chronic diseases. They consist in the repeated observations of patients over time. Their analysis opens up new perspectives, not only for the better understanding of the natural history of the disease but it also allows earlier diagnosis, more precise prognosis, prediction of response to treatments or of the onset

of adverse events. Modeling longitudinal data means designing models to improve patients' medical care. These models have to take into account that the data have very different modalities (from organ images to patient pathways), time dependencies, they exhibit different paces of acquisition. This project aims to address these challenges. To this end, we will focus on the development of new mathematical and statistical approaches for the analysis of multimodal multiscale longitudinal data. These models will be designed, implemented as prototypes and then transferred to an easy-used-well-documented platform where researchers from diverse communities, in particular physicians, will be able to analyze their own data set. A first work-package (WP1) will be devoted to models for time-to-event data. Existing methods often face with one or more of the following limitations: numerical challenges, lack of scalability, requirement of strong assumptions of the influence of the feature on the risk or intensity of events. This WP aims to propose new prediction models for personalized medicine. These prediction models will integrate repeated (possibly intensive) measurements of multiple exposures and/or (bio)markers, to predict complex health events. Longitudinal models may also include spatial dependence or more generally multimodal information with complex structures. The second work-package (WP2) will aim at developing advanced spatio-temporal (ST) models and AI tools to extract, if it exists, a set of ST features which characterize effects of different nature that may be associated either to post-treatment side-effects, to treatment responses or to natural disease progression.This could also help in improving our knowledge about the sensitivity of patients at an individual level. All the proposed models may suffer from two issues: the high dimensionality of the data and their relevance with respect to a clinical question. Work-package 3 (WP3) will propose new model selection criteria for longitudinal models. A second aspect of this WP will be to work in the Bayesian framework to enable the integrate expert knowledge. All the previous models belong to classical machine learning and statistical models where one aims at proposing equations to mimic the generation of the observations. Work-package 4 (WP4) will look at interpretable Deep-learning models to combine data-driven and model-based approaches in order to learn mechanistic parameters allowing the interpretable description of the disease progression. Particular focus will be given to the use of auto-encoder architectures for learning compact representations of the dynamics governing spatio-temporal relationship. The resulting models and their careful implementation will allow the development of a new generation of decision support systems, which will help clinicians at the bedside to make more informed decisions for the patient. They will contribute to the development of precision medicine in several key areas.

9.3.2 IHU

General program

Participants: Olivier Colliot, Stanley Durrleman, Didier Dormont, Ninon Burgos, Fabrizio De Vico Fallani, Marie-Constance Corsi, Sophie Tezenas du Montcel, Baptiste Couvy-Duchesne, Daniel Racoceanu.

- Project acronym: IHU-A-ICM
- Project title: Institute of Translational Neuroscience
- Since 2011
- The IHU-A-ICM program was selected, in 2011, in a highly competitive national call for projects. A 10-year, 55M€ program, has been implemented by a recently created foundation for scientific cooperation. Based on the clinical and scientific strenghts of the ICM and the hospital Department of Nervous System Diseases, it mainly supports neuroscience research, but is also invested in improving care and teaching. ARAMIS is strongly involved in the IHU-A-ICM project, in particular in WP6 (neuroimaging and electrophysiology), WP7 (biostatistics), WP2 (Alzheimer) and WP5 (epilepsy). We have started collaborations with the new bioinformatics/biostatistics platform (IHU WP7, head: Ivan Moszer), in particular through a joint project on the integration of imaging and genomics data.

ICM BBT Program - project ImagingDealInMS

Participants: Olivier Colliot *(Correspondant)*, Bruno Stankoff *(Correspondant)*, Arya Yazdan-Panah.

- Project title: Translating the biological mechanisms underlying neurodegeneration into multimodal imaging signatures using deep learning in Multiple Sclerosis (ImagingDealInMS)
- Started in 2021
- Coordinators: Olivier Colliot and Bruno Stankoff (ICM)
- Following the impressive advancements in the treatment of the relapsing phase of multiple sclerosis (MS), the major challenge remaining ahead is the development of treatments effective for preventing or delaying the irreversible accumulation of disability in this disease. A deep understanding of the mechanisms underlying neuro-axonal degeneration, which is the substrate of clinical progression, together with the development of reliable biomarkers, are pre-conditions for the advent and the evaluation of breakthrough therapies. The Stankoff group has pioneered an innovative imaging approach combining positron emission tomography and MRI, and succeeded in generating individual maps or key biological processes such as endogenous remyelination, neuroinflammation, or early damage preceding lesion formation. We further showed that these mechanisms were influencing disability worsening over the disease course, and recently obtained preliminary results suggesting that a multimodal combination of advanced MRI sequences may have the potential to identify these mechanisms and reproduce the PET results. In this project we propose a totally novel imaging approach that will capture remyelination of lesions, ongoing inflammation invisible on T1 and T2 MRI sequences (subacute/chronic active lesions) and to predict short-term future disease activity (identify prelesional areas), from a single multimodal MRI acquisition in patients with MS. Using PET results as a reference, multimodal signatures of these processes will be identified, and a deep learning approach integrating the whole MRI information in the training procedure will be applied to generate masks for each of them. The accuracy of the discovered algorithms will be validated on independent datasets acquired on a PET-MR system, and their long-term clinical relevance will be tested in a clinical study evaluating patients around 10 years following their enrolment in pilot PET studies. As a result, novel tools assessing key biological processes driving neurodegeneration and disability worsening in MS will become largely available for the medical community, allowing an improved patients' stratification and prognostication, and opening the perspective of tailored care. These tools could also be use as novel endpoints in clinical trials, and may serve to capture similar processes in other neurological diseases.

ICM BBT3 Program - project StratifIAD

Participants: Daniel Racoceanu *(Correspondant)*, Benoit Delatour *(Correspondant)*, Stanley Durrleman, Lev Stimmer, Anuradha Kar, Gabriel Jimenez, Mehdi Ounissi, Leopold Herbert-Steven.

- Project title: STRATIFIAD - Refining Alzheimer Disease Patients' stratification using effective, traceable and explicable artificial intelligence approaches in computational histopathology.
- Duration: 2 years (2021-2023)
- Coordinators: Daniel Racoceanu and Benoit Delatour (ICM)
- Other partners: Histology Core plateform (HYSTOMICS) and the Data Analysis Core plateform (DAC), IHU/ICM

- Alzheimer's Disease (AD), the most frequent neurodegenerative disease, is defined by the misfolding and accumulation of Aß peptides and of tau proteins in the brain. Sporadic AD is most commonly present in later life as an amnestic syndrome. However, the clinical presentation of the patients is heterogeneous and different subtypes of the disease have been described, including a rapidly progressive subtype of AD (rAD). Until now, neuropathological assessment of rAD cases was not able to identify specific neuropathological traits for this clinico-pathological entity, despite its unusual fast progression and clinical presentation leading to frequent misdiagnosis as Creutzfeldt-Jakob disease. Our hypothesis is that rAD brains, as well as other atypical variants of AD, display subtle histological changes that would be undercovered by high-throughput automated microscopic analysis. The topography and morphology of the tau and Aß aggregates, the two main brain lesions characterizing the disease are heterogeneous. Aß accumulation takes the form of focal deposits or diffuse plaques; tau lesions form the so-called neurofibrillary tangles but also present different morphologies in dendrites or axons. We propose to study the topography and morphology of these aggregates to better understand the morphological substratum of AD heterogeneity. To address this question at a large scale, one needs to develop software systems for the automatic segmentation, annotation and quantitation of brain lesions in histo-pathological whole slide images (WSI). Therefore, the goal of the STRATIFIAD project is twofold:

  1. to develop fully automated, traceable and explainable artificial intelligence (AI) approaches for the histological location and characterization of the tau and Aß aggregates in whole slide brain images, and to deploy it for routine use on the Histomics core facility of the Paris Brain Institute,
  2. to use the previous analytics tool to study to which extent the topography and morphology of the different peptide aggregates present in the brain can be associated with the diversity of symptoms observed in various AD variants.

  We propose to design, test and implement a modern supervised (initial stratification) and semi-supervised (advance refined stratification) deep reinforcement learning pipeline, combining methods able to generate high performances (quality and speed), high traceability / explicability and facilitate its usability in biomedical research and discovery. Our pathologists have started to acquire and to extensively annotate a unique set of histological images of postmortem brains from the rare form of rpAD and from other identified AD variants. Preliminary results of the consortium suggests that morphological features analysis is eligible for the first level of stratification. We believe that combining these features with topology and semantic-driven image exploration approaches (see MICO TecSan project's references) would be able to guide our research toward a refined stratification. Therefore, causal knowledge-based elements, together with semantic-driven WSI exploration will be likely to create a reusable pipeline, able to structure our experience plan, as to justify the numeric results. The tools within this project will contribute to open-source initiatives, and would be therefore available to the scientific community for replicable massive data analysis. STRATIFIAD will therefore contribute to advance the knowledge in AD and push forward the technological development in this area.

ICM BBT3 Program - project HUMMAP

Participants: Fabrizio De Vico Fallani.

- Project title : HUman Mutations to uncover human Macrophages Activation Pattern
- Started in 2020, Ended 2023
- Coordinator: Violetta Zujovic, Fanny Mochel
- Multiple sclerosis (MS) is an inflammatory demyelinating disease in which peripheral immune cells infiltrate the central nervous system (CNS) and destroy myelin, a neuroprotective and conduction-enhancing substance. Our previous work demonstrates that MAC from MS patients exhibit a

preferential differentiation toward a pro-inflammatory state and present a mitochondrial energy metabolism blockage resulting in a shift from oxidative phosphorylation to glycolysis. Recent studies report that MAC are also implicated in two hereditary demyelinating diseases, X-linked adrenoleukodystrophy (X-ALD) and Adult-onset Leukoencephalopathy with axonal Spheroids and Pigmented glia (ALSP). In both X-ALD and ALSP, key components of MAC differentiation pattern are affected that may be reversed by hematopoietic stem cell transplantation stressing that acting on peripheral MAC has an important impact on CNS inflammation. Importantly, MAC differentiation into the pro-regenerative M2 phenotype is dependent on both CSF1 receptor activation, a pathway primarily affected in ALSP, and the oxidation of fatty acids, which accumulate in X-ALD. Therefore, deep characterization of MAC activation pattern in X-ALD and ALSP can enlighten key aspects of the innate immune response in health and disease. HUM-MAP will apply a cross-disease strategy to decipher MAC activation pattern in response to extreme stimuli (neutral/ pro-inflammatory/ pro-regenerative) in normal and disease context using state of the art molecular profiling. HUM-MAP proposes to apply mathematical algorithms to model MAC activation and determine which networks of shared or disease-specific pathways contribute to pathophysiology. By exploring how disease specific perturbations affect key components of MAC activation, we will build virtually MAC molecular machinery and identify the master genes essential to gear macrophage towards regenerative states.

9.3.3 3IA Institutes - PRAIRIE

Participants: Ninon Burgos, Olivier Colliot, Stanley Durrleman.

- Project acronym: PRAIRIE
- Project title: Paris Artificial Intelligence Research Institute
- Since 2019
- Director: Isabelle Ryl
- Website: PRAIRIE
- PRAIRIE is one of the four selected French Institutes of AI. It was selected within a call for creation of interdisciplinary AI research institutes (or “3IAs” for “Instituts Interdisciplinaires d’Intelligence Artificielle”), as part of the national French initiative on Artificial Intelligence (AI). PRAIRIE aspires to become within five years a world leader in AI research and higher education, with an undeniable impact on economy and technology at the French, European and global levels. ARAMIS team members N. Burgos, O. Colliot and S. Durrleman hold a chair at PRAIRIE.

9.3.4 National Networks

- GdR Statistics and Medicine
- GdR (MaDICS) Masses de Données, Informations et Connaissances en Sciences Big Data - Data Science, Statistics and Medicine
- F. De Vico Fallani participated to the GdR (HANDICAP) in the framework of the future strategy of Inria
- F. De Vico Fallani was founding member of the CORTICO national network for brain-computer interfaces
- M.-C. Corsi serves as Secretary General of the CORTICO national network for brain-computer interfaces
- GdR ISIS (Signal and Image Processing)

9.3.5 Other National Programs

France Parkinson

Participants: Jean-Christophe Corvol, Olivier Colliot, Stanley Durrleman
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- Project title: PRECISE-PD - From pathophysiology to precision medicine for Parkinson's disease
- 2019-2024
- Amount: 3M€
- Coordinator: Jean-Christophe Corvol
- Other partners: Inserm CIC-1436, Inserm CIC-P1421, Inserm U1171, Université de Bordeaux (IMN), University of Glasgow, University of Calgary,
- Abstract: Parkinson's disease (PD) is a complex neurodegenerative disease characterized by the progression of motor and non-motor symptoms resulting from the spreading of the disease into dopaminergic and non-dopaminergic areas. Clinical trials have failed to demonstrate efficacy to slow PD progression because the relationships between progression profiles and their underlying molecular mechanisms remain to be identified. The objective of PRECISE-PD is to propose a mechanismsbased progression model of PD by combining genetic and longitudinal clinical data from a large cohort of patients. We will implement a biobank to the NS-PARK/FCRIN cohort collecting motor and non-motor symptoms from >22,000 PD patients followed in the 24 expert centers in France. Genomic data will be generated by using a microarray platform developed for neurodegenerative diseases studies, and brain imaging will be obtained from a subgroup of patients. Computational and machine learning approaches will be developed to address the challenges of analyzing the high dimensionality and the mixture of data necessary to move beyond empirical stratification of patients. Replication will be performed in independent cohorts, and biological validation will combine biomarkers and preclinical research. PRECISE-PD is an unpreceded opportunity to open the path to the new era of precision and personalized medicine for PD.

10 Dissemination

10.1 Promoting scientific activities

10.1.1 Scientific events: organisation

- Olivier Colliot has co-organized the First French Congress on Artificial Intelligence for Biomedical Imaging, Paris, France, 2023. This event was co-organized by the 3IA Institutes PRAIRIE, MIAI and 3IA Côte d'Azur.
- Marie-Constance Corsi has co-organized the annual meeting of the French BCI Society, CORTICO, Paris, France; 2023.
- Fabrizio De Vico Fallani has co-organized the annual Network Neuroscience workshop at NETSCI, Wien, Austria; 2023.
- Fabrizio De Vico Fallani has co-organized the workshop on Challenges in BCI-based Neurofeedback Applications for Neurological Disorders workshop at BCI meeting, Bruxelles, Belgium; 2023.
- Stanley Durrleman and Ninon Burgos have co-organized the AI4Health 2023 summer school with the Health Data Hub, held at Paris Santé Campus.
- Ninon Burgos has co-organized the Tutorial on Reproductibility during MICCAI 2023 (Vancouver, Canada).
- Ninon Burgos has co-organized the Neuro OpenScience Workshop held at the Paris Brain Institute.

General chair, scientific chair

- Olivier Colliot is Conference Chair of the SPIE Medical Imaging: Image Processing conference for the period 2022-2025.

10.1.2 Scientific events: selection

Member of the conference program committees

- Olivier Colliot was Program Committee member SPIE Medical Imaging: Image Processing conference 2023
- Olivier Colliot was Meta-Reviewer, IEEE International Symposium on Biomedical ISBI 2023
- Ninon Burgos was Program Committee member of the SPIE Medical Imaging: Image Processing conference 2023
- Ninon Burgos was Program Committee member of the Medical Imaging with Deep Learning conference 2023
- Daniel Racoceanu was Meta-Reviewer / Area-Chair, 26th International Conference on Medical Image Computing and Computer Assisted Intervention, MICCAI 2023
- Fabrizio De Vico Fallani was Program Committee member for the conferences NETSCI 2023, Complenet 2023, Complex Networks 2023, CCS 2023

Reviewer

- Olivier Colliot acted as a reviewer for the international conferences IEEE International Symposium on Biomedical Imaging (IEEE ISBI), Medical Image Computing and Computer-Assisted Intervention (MICCAI), International Conference on Learning Representations (ICLR) and IEEE/CVF Computer Vision and Pattern Recognition (IEEE/CVF CVPR).
- Baptiste Couvy-Duchesne acted as a reviewer for the international conferences IEEE International Symposium on Biomedical Imaging (IEEE ISBI).
- Ninon Burgos acted as a reviewer for the international conferences IEEE International Symposium on Biomedical Imaging (IEEE ISBI), Medical Image Computing and Computer-Assisted Intervention (MICCAI), Organisation for Human Brain Mapping (OHBM), the international workshop on Simulation and Synthesis in Medical Imaging (SASHIMI)
- Daniel Racoceanu acted as a reviewer for the Medical Image Computing and Computer-Assisted Intervention (MICCAI).
- Fabrizio De Vico Fallani acted as a reviewer for the conferences NETSCI 2023, Complenet 2023, Complex Networks 2023, CCS 2023

10.1.3 Journal

Member of the editorial boards

- Olivier Colliot is an Associate Editor and a member of the Editorial Board of the journal Medical Image Analysis.
- Fabrizio De Vico Fallani is an Associate Editor and a member of the Editorial Board of PLoS One and Brain Topography

Reviewer - reviewing activities

- Olivier Colliot acted as a reviewer for the IEEE Journal of Biomedical and Health Informations, for Human Brain Mapping, for the SPIE Journal of Medical Imaging and for Neuroradiology.
- Baptiste Couvy-Duchesne acted as a reviewer for Medical Image Analysis, Developmental Cognitive Neuroscience, Communications Biology, Genome Research, Nature Communications.
- Marie-Constance Corsi acted as a reviewer for eNeuro, NeuroImage: Clinical, Brain Topography, Brain Connectivity, Journal of Neural Engineering, Frontiers
- Ninon Burgos acted as reviewer for Medical Image Analysis; MELBA; Computer Methods and Programs in Biomedicine; Nature Communications; Communications Biology; NeuroImage; Imaging Neuroscience; Journal of Nuclear Medicine
- Sophie Tezenas du Montcel acted as a reviewer for Annals of Neurology, Movement Disorders, Annals of Clinical and Translational Neurology, IEEE Journal of Biomedical and Health Informatics, The Cerebellum
- Fabrizio De Vico Fallani acted as a reviewer for Nature Communications, IEEE reviews in Biomedical Engineering, Plos One

10.1.4 Invited talks

- Ninon Burgos gave an invited talk at the SPIE Medical Imaging: Image Processing Conference (San Diego, USA)
- Ninon Burgos gave an invited talk at the Neuro OpenScience Workshop (Paris Brain Institute, France)
- Ninon Burgos gave an invited talk at the AI in Biology and Health Symposium (Institut Pasteur, Paris, France)
- Ninon Burgos gave an invited talk for the Réunion régionale des ingénieurs biomédicaux (Grand Est) (virtual)
- Ninon Burgos gave an invited talk at the ED3C Scientific Days (Paris, France)
- Ninon Burgos gave an invited talk at the Colloque Français d'Intelligence Artificielle en Imagerie Biomédicale (IABM 2023) (Paris, France)
- Baptiste Couvy-Duchesne was invited to give a talk at the Australian Dementia Research Forum 2023
- Sophie Tezenas du Montcel was invited to give a talk at the AGI's Tools & Methods studio series 2023 (virtual)
- Fabrizio De Vico Fallani gave an inaugural invited talk at the Euromov center in Montpellier
- Fabrizio De Vico Fallani gave an invited talk at Summer school of Groningen university, Neitherlands

10.1.5 Leadership within the scientific community

- Olivier Colliot is a member of the steering committee of the European infrastructure EBRAINS.
- Fabrizio De Vico Fallani is a member of the Executive Committee of the Complex Systems Society.

10.1.6 Scientific expertise

- Olivier Colliot acts as an expert for GENCI (the national facility for high-performance computing).
- Stanley Durrleman is member of the Conseil scientifique consultatif du Health Data Hub.
- Baptiste Couvy-Duchesne reviewed grant applications for the INSERM (MESSIDORE [Méthodologie des ESSais cliniques Innovants, Dispositifs, Outils et Recherches Exploitant les données de santé et biobanques]) and the UK Research and Innovation.
- Ninon Burgos reviewed grant applications for the Fonds de recherche du Québec (FRQ) NOVA programme and the Netherlands Organisation for Scientific Research Vidi programme.
- Daniel Racoceanu has been elected as a member of the Inria Evaluation Committee (period 2024-2027).
- Sophie Tezenas Du Montcel is member of the Conseil scientifique de la Banque Nationale de Données Maladies Rares (BNDMR).

10.1.7 Research administration

- Olivier Colliot is a member of the "Bureau du Comité des Projets" of the Inria Paris Center.

10.2 Teaching - Supervision - Juries

10.2.1 Teaching

- Master: Olivier Colliotcoordinates the course "Deep Learning for Medical Imaging" of the Master 2 MVA (Mathematics, Vision, Learning) of ENS Paris-Saclay, University of Paris, Centrale-Supelec and teaches 15 hours (CM).
- Master: Olivier Colliotcoordinates the course "Artificial Intelligence" of the Master 2 Bioentrepreneur of Paris-Descartes University and teaches 20 hours (CM).
- Master: Daniel Racoceanu coordinates the teaching module (UE) "Introduction to Artificial Intelligence" of the Master 1 : Control Sciences and Robotics (AR - Automatique, Robotique) and Electronics, Electrical Energy, Control Sciences (E3A - Électronique, Énergie Électrique, Automatique) at Sorbonne University, Faculty of Science and Engineering (110 students / 3 ECTS) and teaches 30 hours (CM/courses and TP/labs).
- Master: Daniel Racoceanu coordinates the teaching module (UE) "Computer Vision for Biomedical" of the Master 1 : Electronics, Electrical Energy, Control Sciences (E3A - Électronique, Énergie Électrique, Automatique) at Sorbonne University, Faculty of Science and Engineering (50 students / 3 ECTS) and teaches 32 hours (CM/courses and TP/labs).
- Master: Daniel Racoceanu coordinates the teaching module (UE) "Image Processing" of the Master 1 : Control Sciences and Robotics (AR - Automatique, Robotique) at Sorbonne University, Faculty of Science and Engineering (80 students / 3 ECTS) and teaches 36 hours (CM/courses and TP/labs) - courses in English.
- Master: Daniel Racoceanu coordinates the teaching module (UE) "3D Computer Graphics" of the Master 1 : Computer Sciences (Informatique) at Sorbonne University, Faculty of Science and Engineering (20 students / 3 ECTS) and teaches 24 hours (CM/courses and TP/labs) - courses in English (within the european programme EIT Health).
- Engineering school: Olivier Colliot, 5 hours (eqTD), Mines ParisTech
- Medical school: Didier Dormont is the Director of the University Diploma (DIU) “Diagnostic and Therapeutic Neuroradiology", Sorbonne University
- Medical school: Didier Dormont, Courses for Medical Students, Sorbonne University

- Medical school: Didier Dormont organizes and participates in the practical teaching of Neuroradiology for Medical Students in the Department of Diagnostic Neuroradiology of Pitié Salpêtrière University Hospital

- Medical school: Didier Dormont organizes and participates in the practical teaching of Neuroradiology for Radiology Specializing Residents in the Department of Diagnostic Neuroradiology of Pitié Salpêtrière University Hospital

- Master: Fabrizio De Vico Fallani gave a lecture at UE Closed-loop Neuroscience, CentraleSupelec)

- Master: Daniel Racoceanu gives lectures / labs (14 hours) in "Visual Perception for Robotics" - Master 2 : Control Science and Robotics (AR - Automatique, Robotique) at Sorbonne University, Faculty of Science and Engineering.

- Master: Daniel Racoceanu gives lectures / labs (14 hours) in "Machine Learning" - Master 1 : Control Science and Robotics (AR - Automatique, Robotique) at Sorbonne University, Faculty of Science and Engineering.

- Master: Daniel Racoceanu gives lectures / labs (20 hours) in "Object-Oriented Programming" - Master 1 : Control Science and Robotics (AR - Automatique, Robotique) at Sorbonne University, Faculty of Science and Engineering.

- Licence: Daniel Racoceanu gives seminars (TD) and labs (TP) in "Programming" - Licence 1 : all Licences - option Control Sciences at Sorbonne University, Faculty of Science and Engineering.

- Master : Stanley Durrleman gave 4hrs lecture for the Master bio-entrepreneur of the University of Paris.

- Fabrizio De Vico Fallani was invited to give a teaching lesson at School on Complex Networks, Lake Como School Advanced Studies, Italy.

- Daniel Racoceanu was invited to give a teaching lesson about explainable and interpretable artificial intelligence in front of master students from Mines, Dauphine, ENS and ESPCI, at Paris Sciences et Lettres (PSL), Paris, France.

- Baptiste Couvy-Duchesne gave a lecture at the Genetics and Genomics Winter School, held in Brisbane Australia.

- Marie-Constance Corsi gave lectures on Brain-Computer Interfaces as part of the DU IA Santé, M2 Computational Neuroscience and Neuroengineering, the Master MVA and the CENIR courses.

- Master: Sophie Tezenas du Montcel coordinates the Master 1 of Public Health of Sorbonne University.

- Master: Sophie Tezenas du Montcel coordinates the course of Biostatistics of the Master 1 of Health of Sorbonne University and teaches 18 hours (CM).

- Master: Sophie Tezenas du Montcel coordinates the course of "Bases de données médico-administratives: aspects épidémiologiques" of the Master 2 of Public Health of Sorbonne University and teaches 9 hours (CM).

- Medical school: Sophie Tezenas du Montcel gives courses for Medical students (First year, 32 hours TD).

- Ninon Burgos gave lectures on deep learning for medical imaging as part of the DU IA appliquée en santé (Paris and Lille), the CENIR courses, the European Course on Advanced Imaging Techniques in Neuroradiology and the École Saisonnière en Intelligence Artificielle.

10.2.2 Supervision

- PhD in progress: Élise Delzant, “Methods for big-data neuroimaging analyses”, started in 2022, advisors: Baptiste Couvy-Duchesne and Olivier Colliot
- PhD in progress: Ravi Hassanaly, “Deep generative models for the detection of anomalies in the brain”, started in 2020, advisors: Olivier Colliot and Ninon Burgos
- PhD in progress: Guanghui Fu, “Segmentation, classification and generative models for computer-aided diagnosis of neurological diseases from neuroimaging data”, started in 2021, advisors: Olivier Colliot and Didier Dormont
- PhD in progress: Sophie Loizillon, “Deep learning for assisting diagnosis of neurological diseases using a very large-scale clinical data warehouse”, started in 2021, advisors: Olivier Colliot, Ninon Burgos and Didier Dormont
- PhD in progress: Lisa Hemforth, “Deep learning for rating of atypical anatomical patterns on MRI data”, started in 2021, advisors: Olivier Colliot, Baptiste Couvy-Duchesne and C. Cury
- PhD in progress: Arya Yazdan-Panah, “Deep learning for multimodal image analysis in multiple sclerosis”, started in 2021, advisors: Olivier Colliot and B. Stankoff
- PhD in progress: Maëlys Solal, “Robust anomaly detection in multimodal neuroimaging”, started in 2023, advisor: Ninon Burgos
- PhD in progress: Camilla Mannino, “Neuronal avalanches as a tool to improve Brain-Computer Interfaces”, started in Nov 2023, advisors: Marie-Constance Corsi, and Mario Chavez
- PhD in progress: Marc Dibling, “Parcours de soin des patients atteints de maladies neurodégénératives rares”, started in 2023, advisor: Sophie Tezenas Du Montcel
- PhD in progress: Sofia Kaisaridi, “Modélisation multimarqueurs de l’évolution clinique et en imagerie cérébrale de patients CADASIL et de son influence sur un évènement censure”, started in 2022, advisor: Sophie Tezenas Du Montcel
- PhD in progress: Juliette Ortholand, “Modeling changes of dynamics with longitudinal data sets”, started in 2021, advisor: Stanley Durrleman and Sophie Tezenas Du Montcel
- PhD in progress: Mehdi Ounissi, “Decoding the Black Box: Unraveling explainability in deep learning for responsible biomedical and healthcare solutions”, started in 2021, supervisor: Daniel Racoceanu
- PhD in progress: Gabriel Jimenez, “Interpretable deep learning in computational histopathology for Alzheimer’s disease patients’ stratification refinement”, started in 2021, supervisor: Daniel Racoceanu
- PhD in progress: Ayse Gungor, “Correlation between eye and brain pathologies”, started in 2023, supervisors: D. Milea and Daniel Racoceanu
- PhD in progress: Ilias Sarbout, “Artificial Vision using XAI”, started in 2023, supervisors: D. Milea and Daniel Racoceanu
- PhD in progress: Esther Kozlowski, “A responsible artificial intelligence framework for modeling the progression of Parkinson’s disease”, started in 2023, supervisors: M. Vidailhet and Daniel Racoceanu
- PhD completed: Charley Presigny, “Characterization of multilayer networks: theory and applications to the brain”, started in 2020, supervisor: Fabrizio De Vico Fallani
- PhD completed: Vito Dichio, “The exploration-exploitation paradigm”, started in 2020, supervisor: Fabrizio De Vico Fallani

- PhD completed: Tristan Venot, “Design and evaluation of a multimodal control of a robotic arm with a brain-computer interface”, started in 2020, co-supervisor: Fabrizio De Vico Fallani
- PhD completed: Remy Ben Messaoud, “Low-dimensional controllability of complex networks and applications to the human brain”, started in 2020, co-supervisor: Fabrizio De Vico Fallani

10.2.3 Juries

- Olivier Colliot participated, as reviewer, to the PhD committee of Huy-Dung Nguyen, University of Bordeaux.
- Stanley Durrleman participated, as examiner, to the PhD committee of Mathieu Pont, Sorbonne Université.
- Ninon Burgos participated, as reviewer, to the PhD committee of Hugo Schmutz, Université Côte d’Azur.
- Ninon Burgos participated, as reviewer, to the PhD committee of Hilda Chourak, Université de Rennes.
- Ninon Burgos participated, as examiner, to the PhD committee of Camille Ruppli, Institut Polytechnique de Paris.
- Ninon Burgos participated, as examiner, to the PhD committee of Clément Chadebec, Université Paris Cité.
- Ninon Burgos participated, as examiner, to the PhD committee of Louise Guillon, Université Paris Saclay.
- Daniel Racoceanu participated, as reviewer, to the PhD committee of Fahad Khalid, Université Paris Saclay.
- Daniel Racoceanu participated, as reviewer, to the PhD committee of Tristan Lazard, Université Paris Sciences et Lettres (PSL).
- Daniel Racoceanu participated, as reviewer, to the PhD committee of Antonin Deschemps, Université de Rennes.
- Sophie Tezenas du Montcel participated, as reviewer, to the PhD committee of Yue Zhai, Université de Lyon 1.
- Fabrizio De Vico Fallani participated, as president, to the PhD committee of Mahede Khalilian , Université Jules Verne Picardie

10.3 Popularization

10.3.1 Articles and contents

- Ninon Burgos was interviewed by the radio France Alzheimer (‘Le rôle de l’intelligence artificielle dans la détection de la maladie d’Alzheimer’, link)
- Ninon Burgos was interviewed by Europe 1 (‘Santé : et si l’intelligence artificielle pouvait permettre de détecter plus rapidement la maladie d’Alzheimer ?’, link)
- Ninon Burgos participated to an article and video by Le Figaro (‘L’intelligence artificielle pour détecter la maladie d’Alzheimer’, link)
- Ninon Burgos participated to a TV report on LCP (‘État de santé - La santé numérique tiendra-t-elle ses promesses ?’, link)

10.3.2 Interventions

- Olivier Colliot gave a presentation for ICM founding members on artificial intelligence.
- Ninon Burgos gave a presentation for ICM founding members on artificial intelligence and neuroimage.
- Ninon Burgos gave a presentation for the Cérémonie des Olympiades de Mathématiques.

11 Scientific production

11.1 Major publications

[1] M. Ansart, S. Epelbaum, G. Bassignana, A. Bône, S. Bottani, T. Cattai, R. Couronné, J. Faouzi, I. Koval, M. Louis, E. Thibeau-Sutre, J. Wen, A. Wild, N. Burgos, D. Dormont, O. Colliot and S. Durrleman. 'Predicting the Progression of Mild Cognitive Impairment Using Machine Learning: A Systematic, Quantitative and Critical Review'. In: *Medical Image Analysis* 67 (Jan. 2021), p. 101848. DOI: 10.1016/j.media.2020.101848. URL: https://hal.archives-ouvertes.fr/hal-02337815.

[2] M. Ansart, S. Epelbaum, G. Gagliardi, O. Colliot, D. Dormont, B. Dubois, H. Hampel and S. Durrleman. 'Reduction of recruitment costs in preclinical AD trials. Validation of automatic pre-screening algorithm for brain amyloidosis'. In: *Statistical Methods in Medical Research* (Jan. 2019), p. 096228021882303. DOI: 10.1177/0962280218823036. URL: https://hal.archives-ouvertes.fr/hal-01964942.

[3] J. Arslan, H. Luo, M. Lacroix, P. Dupré, P. Kumar, A. Hodgkinson, S. Dandou, R. M. Larive, C. Pignodel, L. Le cam, O. Radulescu and D. Racoceanu. '3D Reconstruction of H&E Whole Slide Images in Melanoma'. In: *SPIE Medical Imaging*. SPIE Medical Imaging 2023. San Diego, California, United States, 22nd Feb. 2023. URL: https://hal.science/hal-03834014.

[4] F. Battiston, J. Guillon, M. Chavez, V. Latora and F. De Vico Fallani. 'Multiplex core–periphery organization of the human connectome'. In: *Journal of the Royal Society Interface* 15.146 (Sept. 2018). DOI: 10.1098/rsif.2018.0514. URL: https://hal.archives-ouvertes.fr/hal-01874871.

[5] A. Bône, O. Colliot and S. Durrleman. 'Learning the spatiotemporal variability in longitudinal shape data sets'. In: *International Journal of Computer Vision* (July 2020). DOI: 10.1007/s11263-020-01343-w. URL: https://hal.inria.fr/hal-02091549.

[6] S. Bottani, N. Burgos, A. Maire, D. Saracino, S. Stroer, D. Dormont and O. Colliot. 'Evaluation of MRI-based machine learning approaches for computer-aided diagnosis of dementia in a clinical data warehouse'. In: *Medical Image Analysis* 89 (Oct. 2023), p. 102903. URL: https://hal.science/hal-03656136.

[7] S. Bottani, N. Burgos, A. Maire, A. Wild, S. Ströer, D. Dormont and O. Colliot. 'Automatic quality control of brain T1-weighted magnetic resonance images for a clinical data warehouse'. In: *Medical Image Analysis* Volume 75 (2021). DOI: 10.1016/j.media.2021.102219. URL: https://hal.inria.fr/hal-03154792.

[8] S. Brice, S. Reyes, A. Jabouley, C. Machado, C. Rogan, N. Gastellier, N. Alili, S. Guey, E. Jouvent, D. Hervé, S. Tezenas Du Montcel and H. Chabriat. 'Trajectory Pattern of Cognitive Decline in Cerebral Autosomal Dominant Arteriopathy With Subcortical Infarcts and Leukoencephalopathy'. In: *Neurology* 99.10 (5th Sept. 2022), e1019–e1031. DOI: 10.1212/WNL.0000000000200805. URL: https://hal.inria.fr/hal-03774149.

[9] N. Burgos, S. Bottani, J. Faouzi, E. Thibeau-Sutre and O. Colliot. 'Deep learning for brain disorders: from data processing to disease treatment'. In: *Briefings in Bioinformatics* (Dec. 2020). DOI: 10.1093/bib/bbaa310. URL: https://hal.archives-ouvertes.fr/hal-03070554.

[10] N. Burgos, J. M. Cardoso, J. Samper-González, M.-O. Habert, S. Durrleman, S. Ourselin and O. Colliot. 'Anomaly detection for the individual analysis of brain PET images'. In: *Journal of Medical Imaging* 8.02 (5th Apr. 2021), p. 024003. DOI: 10.1117/1.JMI.8.2.024003. URL: https://hal.inria.fr/hal-03193306.

[11] N. Burgos and O. Colliot. 'Machine learning for classification and prediction of brain diseases: recent advances and upcoming challenges'. In: *Current Opinion in Neurology* 33.4 (2020), pp. 439–450. DOI: 10.1097/WCO.0000000000000838. URL: https://hal.inria.fr/hal-02902586.

[12] G. Coarelli, A. Heinzmann, C. Ewenczyk, C. Fischer, M. Chupin, M.-L. Monin, H. Hurmic, F. Calvas, P. Calvas, C. Goizet, S. Thobois, M. Anheim, K. Nguyen, D. Devos, C. Verny, V. a. G. Ricigliano, J.-F. Mangin, A. Brice, S. Tezenas Du Montcel and A. Durr. 'Safety and efficacy of riluzole in spinocerebellar ataxia type 2 in France (ATRIL): a multicentre, randomised, double-blind, placebo-controlled trial'. In: *The Lancet Neurology* 21 (18th Jan. 2022), pp. 225–233. DOI: 10.1016/s1474-4422(21)00457-9. URL: https://hal.science/hal-03852287.

[13] O. Colliot. *Machine Learning for Brain Disorders*. Vol. 197. Neuromethods. Springer, 2023. DOI: 10.1007/978-1-0716-3195-9. URL: https://hal.science/hal-04225627.

[14] O. Colliot, E. Thibeau-Sutre and N. Burgos. 'Reproducibility in machine learning for medical imaging'. In: *Machine Learning for Brain Disorders*. Springer, 2023. URL: https://hal.science/hal-03957240.

[15] M.-C. Corsi, M. Chavez, D. Schwartz, N. George, L. Hugueville, A. E. Kahn, S. Dupont, D. Bassett and F. De Vico Fallani. 'Functional disconnection of associative cortical areas predicts performance during BCI training'. In: *NeuroImage* (Jan. 2020), p. 116500. DOI: 10.1016/j.neuroimage.2019.116500. URL: https://hal.inria.fr/hal-02438794.

[16] B. Couvy-Duchesne, F. Zhang, K. Kemper, J. Sidorenko, N. Wray, P. Visscher, O. Colliot and J. Yang. 'Parsimonious model for mass-univariate vertexwise analysis'. In: *Journal of Medical Imaging* 9.05 (1st Sept. 2022). DOI: 10.1117/1.JMI.9.5.052404. URL: https://hal.inria.fr/hal-03675041.

[17] B. Couvy-duchesne, L. T. Strike, F. Zhang, Y. Holtz, Z. Zheng, K. E. Kemper, L. Yengo, O. Colliot, M. Wright, N. Wray, J. Yang and P. M. Visscher. 'A unified framework for association and prediction from vertex-wise grey-matter structure'. In: *Human Brain Mapping* (20th July 2020). DOI: 10.1002/hbm.25109. URL: https://hal.archives-ouvertes.fr/hal-02904458.

[18] F. De Vico Fallani and D. Bassett. 'Network neuroscience for optimizing brain–computer interfaces'. In: *Physics of Life Reviews* 31 (Dec. 2019), pp. 304–309. DOI: 10.1016/j.plrev.2018.10.001. URL: https://hal.archives-ouvertes.fr/hal-02428684.

[19] F. De Vico Fallani, V. Latora and M. Chavez. 'A Topological Criterion for Filtering Information in Complex Brain Networks'. In: *PLoS Computational Biology* 13.1 (Jan. 2017), pp. 1–18. DOI: 10.1371/journal.pcbi.1005305. URL: https://hal.inria.fr/hal-01443254.

[20] S. Diao, Y. Tian, W. Hu, J. Hou, R. Lambo, Z. Zhang, Y. Xie, X. Nie, F. Zhang, D. Racoceanu and W. Qin. 'Weakly Supervised Framework for Cancer Region Detection of Hepatocellular Carcinoma in Whole-Slide Pathologic Images Based on Multiscale Attention Convolutional Neural Network'. In: *American Journal of Pathology* 192.3 (Mar. 2022), pp. 553–563. DOI: 10.1016/j.ajpath.2021.11.009. URL: https://hal.archives-ouvertes.fr/hal-03677649.

[21] A. Guyot, A. B. Graciano Fouquier, E. Gerardin, M. Chupin, J. Glaunès, L. Marrakchi-Kacem, J. Germain, C. Boutet, C. Cury, L. Hertz-Pannier, A. Vignaud, S. Durrleman, T. Henry, P.-F. Van De Moortele, A. Trouvé and O. Colliot. 'A Diffeomorphic Vector Field Approach to Analyze the Thickness of the Hippocampus from 7T MRI'. In: *IEEE Transactions on Biomedical Engineering* 68.2 (Feb. 2021), pp. 393–403. DOI: 10.1109/TBME.2020.2999941. URL: https://hal.inria.fr/hal-02359660.

[22] G. Jimenez and D. Racoceanu. 'Computational Pathology for Brain Disorders'. In: *Machine Learning for Brain Disorders*. Vol. 197. Part of the Neuromethods book series (NM,volume 197). Springer; Humana, New York, NY, 23rd July 2023, pp. 533–572. DOI: 10.1007/978-1-0716-3195-9_18. URL: https://hal.science/hal-03936550.

[23] G. Jiménez, A. Kar, M. Ounissi, L. Ingrassia, S. Boluda, B. Delatour, L. Stimmer and D. Racoceanu. 'Visual deep learning-based explanation for neuritic plaques segmentation in Alzheimer's Disease using weakly annotated whole slide histopathological images'. In: *Lecture Notes in Computer Science*. MICCAI 2022 - 25th International Conference on Medical Image Computing and Computer Assisted Intervention. Vol. LNCS-13432. Medical Image Computing and Computer Assisted Intervention Part VIII. Singapore, Singapore: Springer Nature Switzerland, 16th Sept. 2022, pp. 336–344. DOI: 10.1007/978-3-031-16434-7_33. URL: https://hal.science/hal-03810578.

[24] I. Koval, A. Bône, M. Louis, T. Lartigue, S. Bottani, A. Marcoux, J. Samper-Gonzalez, N. Burgos, B. Charlier, A. Bertrand, S. Epelbaum, O. Colliot, S. Allassonnière and S. Durrleman. 'AD Course Map charts Alzheimer's disease progression'. In: *Scientific Reports* 11.1 (13th Apr. 2021). DOI: 10.1038/s41598-021-87434-1. URL: https://hal.inria.fr/hal-01964821.

[25] I. Koval, T. Dighiero-Brecht, A. J. Tobin, S. J. Tabrizi, R. I. Scahill, S. Tezenas Du Montcel, S. Durrleman and A. Durr. 'Forecasting individual progression trajectories in Huntington disease enables more powered clinical trials'. In: *Scientific Reports* 12.1 (Dec. 2022), p. 18928. DOI: 10.1038/s41598-022-18848-8. URL: https://hal.inria.fr/hal-03877293.

[26] K. de Matos, C. Cury, L. Chougar, L. T. Strike, T. Rolland, M. Riche, L. Hemforth, A. Martin, T. Banaschewski, A. L. W. Bokde, S. Desrivières, H. Flor, A. Grigis, H. Garavan, P. Gowland, A. Heinz, R. Brühl, J.-L. Martinot, M.-L. Paillère Martinot, E. Artiges, F. Nees, J. H. Fröhner, H. Lemaitre, D. Papadopoulos Orfanos, T. Paus, L. Poustka, S. Hohmann, S. Millenet, J. H. Fröhner, M. N. Smolka, N. Vaidya, H. Walter, R. Whelan, G. Schumann, V. Frouin, M. Bach Cuadra, O. Colliot and B. Couvy-Duchesne. 'Temporo-basal sulcal connections: a manual annotation protocol and an investigation of sexual dimorphism and heritability'. In: *Brain Structure and Function* 228.6 (June 2023), pp. 1459–1478. DOI: 10.1007/s00429-023-02663-6. URL: https://hal.science/hal-04132176.

[27] P. Moulaire, P.-E. Poulet, E. Petit, T. Klockgether, A. Durr, T. Ashizawa and S. Tezenas Du Montcel. 'Temporal Dynamics of the Scale for the Assessment and Rating of Ataxia in Spinocerebellar Ataxias'. In: *Movement Disorders* (23rd Oct. 2022). DOI: 10.1002/mds.29255. URL: https://hal.science/hal-03831598.

[28] T. Nedelec, B. Couvy-Duchesne, F. Monnet, T. Daly, M. Ansart, L. Gantzer, B. Lekens, S. Epelbaum, C. Dufouil and S. Durrleman. 'Identifying health conditions associated with Alzheimer's disease up to 15 years before diagnosis: an agnostic study of French and British health records'. In: *The Lancet Digital Health* (1st Mar. 2022). DOI: 10.1016/S2589-7500(21)00275-2. URL: https://hal.archives-ouvertes.fr/hal-03628268.

[29] M. Ounissi, M. Latouche and D. Racoceanu. *Phagocytosis Unveiled: A Scalable and Interpretable Deep learning Framework for Neurodegenerative Disease Analysis*. 26th Apr. 2023. URL: https://hal.science/hal-04067345.

[30] D. Racoceanu, M. Ounissi and Y. L. Kergosien. 'Explainability in Artificial Intelligence; towards Responsible AI: Instanciation dans le domaine de la santé'. In: *Techniques de l'Ingenieur* (10th Dec. 2022). DOI: 10.51257/a-v1-h5030. URL: https://hal.science/hal-03936135.

[31] A. Routier, N. Burgos, M. Diaz, M. Bacci, S. Bottani, O. El-Rifai, S. Fontanella, P. Gori, J. Guillon, A. Guyot, R. Hassanaly, T. Jacquemont, P. Lu, A. Marcoux, T. Moreau, J. Samper-González, M. Teichmann, E. Thibeau-Sutre, G. Vaillant, J. Wen, A. Wild, M.-O. Habert, S. Durrleman and O. Colliot. 'Clinica: an open source software platform for reproducible clinical neuroscience studies'. In: *Frontiers in Neuroinformatics* 15 (13th Aug. 2021), p. 689675. DOI: 10.3389/fninf.2021.689675. URL: https://hal.inria.fr/hal-02308126.

[32] J. Samper-González, N. Burgos, S. Bottani, S. Fontanella, P. Lu, A. Marcoux, A. Routier, J. Guillon, M. Bacci, J. Wen, A. Bertrand, H. Bertin, M.-O. Habert, S. Durrleman, T. Evgeniou and O. Colliot. 'Reproducible evaluation of classification methods in Alzheimer's disease: Framework and application to MRI and PET data'. In: *NeuroImage* 183 (Dec. 2018), pp. 504–521. DOI: 10.1016/j.neuroimage.2018.08.042. URL: https://hal.inria.fr/hal-01858384.

[33] J.-B. Schiratti, S. Allassonniere, O. Colliot and S. Durrleman. 'A Bayesian mixed-effects model to learn trajectories of changes from repeated manifold-valued observations'. In: *Journal of Machine Learning Research* 18 (Dec. 2017), pp. 1–33. URL: https://hal.archives-ouvertes.fr/hal-01540367.

[34] S. Tezenas Du Montcel, E. Petit, T. Olubajo, J. Faber, P. Lallemant-Dudek, K. Bushara, S. Perlman, S. Subramony, D. Morgan, B. Jackman, H. L. Paulson, G. Öz, T. Klockgether, A. Durr and T. Ashizawa. 'Baseline Clinical and Blood Biomarker in Patients With Preataxic and Early-Stage Disease Spinocerebellar Ataxia 1 and 3'. In: *Neurology* (16th Feb. 2023), 10.1212/WNL.0000000000207088. DOI: 10.1212/WNL.0000000000207088. URL: https://hal.science/hal-03996914.

[35] E. Thibeau-Sutre, M. Diaz, R. Hassanaly, A. M. Routier, D. Dormont, O. Colliot and N. Burgos. 'ClinicaDL: an open-source deep learning software for reproducible neuroimaging processing'. In: *Computer Methods and Programs in Biomedicine* 220 (June 2022), p. 106818. DOI: 10.1016/j.cmpb.2022.106818. URL: https://hal.archives-ouvertes.fr/hal-03351976.

[36] Q. Vanderbecq, E. Xu, S. Stroër, B. Couvy-Duchesne, M. Diaz-Melo, D. Dormont and O. Colliot. 'Comparison and validation of seven white matter hyperintensities segmentation software in elderly patients'. In: *Neuroimage-Clinical* 27 (2020), p. 102357. DOI: 10.1016/j.nicl.2020.102357. URL: https://hal.archives-ouvertes.fr/hal-02926474.

[37] W. Wei, E. Poirion, B. Bodini, S. Durrleman, N. Ayache, B. Stankoff and O. Colliot. 'Predicting PET-derived Demyelination from Multimodal MRI using Sketcher-Refiner Adversarial Training for Multiple Sclerosis'. In: *Medical Image Analysis* 58.101546 (Dec. 2019). DOI: 10.1016/j.media.2019.101546. URL: https://hal.archives-ouvertes.fr/hal-02276634.

[38] J. Wen, E. Thibeau-Sutre, M. Diaz-Melo, J. Samper-González, A. Routier, S. Bottani, D. Dormont, S. Durrleman, N. Burgos and O. Colliot. 'Convolutional Neural Networks for Classification of Alzheimer's Disease: Overview and Reproducible Evaluation'. In: *Medical Image Analysis* 63 (July 2020), p. 101694. DOI: 10.1016/j.media.2020.101694. URL: https://hal.archives-ouvertes.fr/hal-02562504.

11.2 Publications of the year

International journals

[39] S. Bottani, N. Burgos, A. Maire, D. Saracino, S. Stroer, D. Dormont and O. Colliot. 'Evaluation of MRI-based machine learning approaches for computer-aided diagnosis of dementia in a clinical data warehouse'. In: *Medical Image Analysis* 89 (Oct. 2023), p. 102903. URL: https://hal.science/hal-03656136.

[40] W. Coath, M. Modat, M. J. Cardoso, P. Markiewicz, C. Lane, T. Parker, A. Keshavan, S. Buchanan, S. Keuss, M. Harris, N. Burgos, J. Dickson, A. Barnes, D. Thomas, D. Beasley, I. Malone, A. Wong, K. Erlandsson, B. Thomas, M. Schöll, S. Ourselin, M. Richards, N. Fox, J. Schott and D. Cash. 'Operationalizing the centiloid scale for [18 F]florbetapir PET studies on PET/MRI'. In: *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring* 15.2 (Apr. 2023). DOI: 10.1002/dad2.12434. URL: https://inria.hal.science/hal-04099627.

[41] M.-C. Corsi, P. Sorrentino, D. P. Schwartz, N. George, L. L. Gollo, S. Chevallier, L. Hugueville, A. E. Kahn, S. Dupont, D. S. Bassett, V. Jirsa and F. de Vico Fallani. 'Measuring Neuronal Avalanches to inform Brain-Computer Interfaces'. In: *iScience* (13th Dec. 2023). DOI: 10.1016/j.isci.2023.108734. URL: https://inria.hal.science/hal-04345847.

[42] A. Desbois, T. Venot, F. de Vico Fallani and M.-C. Corsi. 'HappyFeat—An interactive and efficient BCI framework for clinical applications'. In: *Software Impacts* 19 (2024), p. 100610. DOI: 10.1016/j.simpa.2023.100610. URL: https://hal.science/hal-04343247.

[43] C. Di Folco, R. Couronné, I. Arnulf, G. Mangone, S. Leu-Semenescu, P. Dodet, M. Vidailhet, J.-c. Corvol, S. Lehéricy and S. Durrleman. 'Charting Disease Trajectories from Isolated REM Sleep Behavior Disorder to Parkinson's Disease'. In: *Movement Disorders* (25th Nov. 2023). DOI: 10.1002/mds.29662. URL: https://inria.hal.science/hal-04319442.

[44] V. Dichio and F. De Vico Fallani. 'Statistical models of complex brain networks: a maximum entropy approach'. In: *Reports on Progress in Physics* 86.10 (22nd Aug. 2023), p. 102601. DOI: 10.1088/1361-6633/ace6bc. URL: https://inria.hal.science/hal-03781966.

[45] A. Fürtjes, J. Cole, B. Couvy-Duchesne and S. Ritchie. 'A quantified comparison of cortical atlases on the basis of trait morphometricity'. In: *Cortex* 158 (Jan. 2023), pp. 110–126. DOI: 10.1016/j.cortex.2022.11.001. URL: https://hal.science/hal-03918221.

[46] O. Guinebretiere, T. Nedelec, L. Gantzer, B. Lekens, S. Durrleman and C. Louapre. 'Association Between Diseases and Symptoms Diagnosed in Primary Care and the Subsequent Specific Risk of Multiple Sclerosis'. In: *Neurology* 101.24 (12th Dec. 2023). DOI: 10.1212/WNL.0000000000207981. URL: https://hal.science/hal-04330030.

[47] S. Loizillon, S. Bottani, A. Maire, S. Ströer, D. Dormont, O. Colliot and N. Burgos. 'Automatic motion artefact detection in brain T1-weighted magnetic resonance images from a clinical data warehouse using synthetic data'. In: *Medical Image Analysis* 93 (Apr. 2024), p. 103073. DOI: 10.1016/j.media.2023.103073. URL: https://inria.hal.science/hal-03910451.

[48] E. Maheux, I. Koval, J. Ortholand, C. Birkenbihl, D. Archetti, V. Bouteloup, S. Epelbaum, C. Dufouil, M. Hofmann-Apitius and S. Durrleman. 'Forecasting individual progression trajectories in Alzheimer's disease'. In: *Nature Communications* 14.1 (10th Feb. 2023), p. 761. DOI: 10.1038/s41467-022-35712-5. URL: https://inria.hal.science/hal-04023781.

[49] K. de Matos, C. Cury, L. Chougar, L. T. Strike, T. Rolland, M. Riche, L. Hemforth, A. Martin, T. Banaschewski, A. L. W. Bokde, S. Desrivières, H. Flor, A. Grigis, H. Garavan, P. Gowland, A. Heinz, R. Brühl, J.-L. Martinot, M.-L. Paillère Martinot, E. Artiges, F. Nees, J. H. Fröhner, H. Lemaitre, D. Papadopoulos Orfanos, T. Paus, L. Poustka, S. Hohmann, S. Millenet, J. H. Fröhner, M. N. Smolka, N. Vaidya, H. Walter, R. Whelan, G. Schumann, V. Frouin, M. Bach Cuadra, O. Colliot and B. Couvy-Duchesne. 'Temporo-basal sulcal connections: a manual annotation protocol and an investigation of sexual dimorphism and heritability'. In: *Brain Structure and Function* 228.6 (June 2023), pp. 1459–1478. DOI: 10.1007/s00429-023-02663-6. URL: https://hal.science/hal-04132176.

[50] P. Moulaire, P. E. Poulet, E. Petit, T. Klockgether, A. Durr, T. Ashisawa and S. Tezenas Du Montcel. 'Temporal Dynamics of the Scale for the Assessment and Rating of Ataxia in Spinocerebellar Ataxias'. In: *Movement Disorders* 38.1 (19th Jan. 2023), pp. 35–44. DOI: 10.1002/mds.29255. URL: https://hal.science/hal-03831598.

[51] T. Nedelec, B. Couvy-Duchesne, A. Darves-bornoz, R. Couronné, F. Monnet, L. Gantzer, B. Lekens, Y. Wu, N. Villain, A. Schrag, S. Durrleman and J.-C. Corvol. 'A Comparison Between Early Presentation of Dementia with Lewy Bodies, Alzheimer's Disease, and Parkinson's Disease: Evidence from Routine Primary Care and UK Biobank Data'. In: *Annals of Neurology* 94.2 (Aug. 2023), pp. 259–270. DOI: 10.1002/ana.26670. URL: https://hal.science/hal-04389605.

[52] J. Ortholand, P.-F. Pradat, S. Tezenas Du Montcel and S. Durrleman. 'Interaction of sex and onset site on the disease trajectory of amyotrophic lateral sclerosis'. In: *Journal of Neurology* (23rd Aug. 2023). DOI: 10.1007/s00415-023-11932-7. URL: https://inria.hal.science/hal-04216957.

[53] P.-e. Poulet and S. Durrleman. 'Multivariate disease progression modelling with longitudinal ordinal data'. In: *Statistics in Medicine* (25th May 2023). DOI: 10.1002/sim.9770. URL: https://inria.hal.science/hal-04095450.

[54] R. Real, A. Martinez-Carrasco, R. H. Reynolds, M. A. Lawton, M. M. Tan, M. Shoai, J. C. Corvol, M. Ryten, C. Bresner, L. M. Hubbard, A. Brice, S. Lesage, J. Faouzi, A. Elbaz, F. Artaud, N. Williams, M. T. Hu, Y. Ben-Shlomo, D. G. Grosset, J. A. Hardy and H. R. Morris. 'Association between the LRP1B and APOE loci and the development of Parkinson's disease dementia'. In: *Brain - A Journal of Neurology* 146.5 (2023), pp. 1873–1887. DOI: 10.1093/brain/awac414. URL: https://hal.science/hal-04106341.

[55] T. Rolland and F. De Vico Fallani. 'Vizaj—A free online interactive software for visualizing spatial networks'. In: *PLoS ONE* 18.3 (23rd Mar. 2023), e0282181. DOI: 10.1371/journal.pone.0282181. URL: https://inria.hal.science/hal-04402600.

[56] B. Sauty and S. Durrleman. 'Impact of sex and APOE-ε4 genotype on patterns of regional brain atrophy in Alzheimer's Disease and healthy ageing'. In: *Frontiers in Neurology*. Frontiers in Neurology, section Dementia and Neurodegenerative Diseases. 14 (2nd June 2023). DOI: 10.3389/fneur.2023.1161527. URL: https://inria.hal.science/hal-03778801.

[57] T. Soulier, O. Colliot, N. Ayache and B. Rohaut. 'How will tomorrow's algorithms fuse multimodal data? The example of the neuroprognosis in Intensive Care'. In: *Anaesthesia Critical Care & Pain Medicine* (Sept. 2023), p. 101301. DOI: 10.1016/j.accpm.2023.101301. URL: https://hal.sorbonne-universite.fr/hal-04227434.

[58] Y. Tamzali, A. Scemla, T. Bonduelle, C. Garandeau, M. Gilbert, S. Randhawa, T. de Nattes, H. Hachad, V. Pourcher, P. Taupin, H. Kaminski, M. Hazzan, V. Moal, M. Matignon, V. Fihman, C. Levi, M. Le Quintrec, J. M. Chemouny, E. Rondeau, D. Bertrand, E. Thervet, S. Tezenas Du Montcel, E. Savoye, B. Barrou, N. Kamar and J. Tourret. 'Specificities of Meningitis and Meningo-Encephalitis After Kidney Transplantation: A French Retrospective Cohort Study'. In: *Transplant International* 36 (18th Jan. 2023), p. 10765. DOI: 10.3389/ti.2023.10765. URL: https://hal.science/hal-03996962.

[59] S. Tezenas Du Montcel, E. Petit, T. Olubajo, J. Faber, P. Lallemant-Dudek, K. Bushara, S. Perlman, S. Subramony, D. Morgan, B. Jackman, H. L. Paulson, G. Öz, T. Klockgether, A. Durr and T. Ashizawa. 'Baseline Clinical and Blood Biomarker in Patients With Preataxic and Early-Stage Disease Spinocerebellar Ataxia 1 and 3'. In: *Neurology* (16th Feb. 2023), 10.1212/WNL.0000000000207088. DOI: 10.1212/WNL.0000000000207088. URL: https://hal.science/hal-03996914.

[60] J. Wen, I. M. Nasrallah, A. Abdulkadir, T. D. Satterthwaite, Z. Yang, G. Erus, T. Robert-Fitzgerald, A. Singh, A. Sotiras, A. Boquet-Pujadas et al. 'Genomic loci influence patterns of structural covariance in the human brain'. In: *Proceedings of the National Academy of Sciences of the United States of America* 120.52 (21st Dec. 2023). DOI: 10.1073/pnas.2300842120. URL: https://hal.science/hal-04362321.

[61] A. Yazdan-Panah, M. Schmidt-Mengin, V. A. Ricigliano, T. Soulier, B. Stankoff and O. Colliot. 'Automatic segmentation of the choroid plexuses: Method and validation in controls and patients with multiple sclerosis'. In: *Neuroimage-Clinical* 38 (Mar. 2023), p. 103368. DOI: 10.1016/j.nicl.2023.103368. URL: https://inria.hal.science/hal-04026889.

[62] R. Zhang, C.-H. Chen, S. Tezenas Du Montcel, J. Lebenberg, Y.-W. Cheng, M. Dichgans, S.-C. Tang and H. Chabriat. 'The CADA-MRIT: An MRI Inventory Tool for Evaluating Cerebral Lesions in CADASIL Across Cohorts'. In: *Neurology* (2023). DOI: 10.1212/WNL.0000000000207713. URL: https://hal.science/hal-04215696.

International peer-reviewed conferences

[63] J. Arslan, M. Ounissi, H. Luo, M. Lacroix, P. Dupré, P. Kumar, A. Hodgkinson, S. Dandou, R. M. Larive, C. Pignodel, L. Le cam, O. Radulescu and D. Racoceanu. 'Efficient 3D Reconstruction of H&E Whole Slide Images in Melanoma'. In: *SPIE Medical Imaging*. SPIE Medical Imaging 2023. San Diego, California, United States, 22nd Feb. 2023. URL: https://hal.science/hal-03834014.

[64] M.-C. Corsi, S. Chevallier, F. de Vico Fallani and F. Yger. 'Ensemble of Riemannian Classifiers for Multimodal Data: FUCONE Approach for M/EEG Data'. In: ISBI 2023 - IEEE International Symposium on Biomedical Imaging. Cartagena de Indias, Colombia, 18th Apr. 2023. URL: https://inria.hal.science/hal-04140126.

[65] N. Fournier and S. Durrleman. 'A Multimodal Disease Progression Model for Genetic Associations with Disease Dynamics'. In: *Medical Image Computing and Computer Assisted Intervention – MICCAI 2023. Lecture Notes in Computer Science*. Medical Image Computing and Computer Assisted Intervention – MICCAI 2023. Vol. 14224. Vancouver, Canada, 1st Oct. 2023, pp. 601–610. DOI: 10.1007/978-3-031-43904-9_58. URL: https://hal.science/hal-04295080.

[66] G. Fu, R. E. Jurdi, L. Chougar, D. Dormont, R. Valabregue, S. Lehéricy and O. Colliot. 'Introducing Soft Topology Constraints in Deep Learning-based Segmentation using Projected Pooling Loss'. In: SPIE Medical Imaging 2023. San Diego, United States, 19th Feb. 2023. URL: https://inria.hal.science/hal-03832309.

[67] F. Galati, D. Falcetta, R. Cortese, B. Casolla, F. Prados, N. Burgos and M. A. Zuluaga. 'A2V: A Semi-Supervised Domain Adaptation Framework for Brain Vessel Segmentation via Two-Phase Training Angiography-to-Venography Translation'. In: BMVC 2023, 34th British Machine Vision Conference. Aberdeen, United Kingdom, 12th Sept. 2023. URL: https://hal.science/hal-04195756.

[68] R. Hassanaly, S. Bottani, B. Sauty, O. Colliot and N. Burgos. 'Simulation-based evaluation framework for deep learning unsupervised anomaly detection on brain FDG PET'. In: SPIE Medical Imaging. San Diego, United States, 19th Feb. 2023. URL: https://hal.science/hal-03835015.

[69] L. J. Hemforth, C. Cury, V. Frouin, S. Desrivières, A. Grigis, H. Garavan, R. Brühl, J.-L. Martinot, M.-L. Paillère Martinot, E. Artiges, L. Poustka, S. Hohmann, S. Millenet, N. Vaidya, H. Walter, R. Whelan, G. Schumann, B. Couvy-Duchesne and O. Colliot. 'Interpretable automatic detection of incomplete hippocampal inversions using anatomical criteria'. In: SPIE Medical Imaging 2023. San Diego (California), United States, 19th Feb. 2023, pp. 1–7. URL: https://hal.science/hal-03994348.

[70] G. Jiménez, P. Mas, A. Kar, L. Ingrassia, S. Boluda, B. Delatour, L. Stimmer and D. Racoceanu. 'A meta-graph approach for analyzing whole slide histopathological images of human brain tissue with Alzheimer's disease biomarkers'. In: SPIE Medical Imaging 2022. San Diego, United States, 19th Feb. 2023. URL: https://hal.science/hal-03936684.

[71] R. E. Jurdi and O. Colliot. 'How precise are performance estimates for typical medical image segmentation tasks?' In: IEEE International Symposium on Biomedical Imaging (ISBI 2023). Cartagena de Indias, Colombia, 18th Apr. 2023. URL: https://hal.science/hal-04104891.

[72] S. Loizillon, S. Bottani, A. Maire, S. Stroer, D. Dormont, O. Colliot and N. Burgos. 'Transfer learning from synthetic to routine clinical data for motion artefact detection in brain T1-weighted MRI'. In: SPIE Medical Imaging 2023: Image Processing. San Diego, United States, 19th Feb. 2023. URL: https://inria.hal.science/hal-03831746.

[73] S. Loizillon, O. Colliot, L. Chougar, S. Stroer, Y. Jacob, A. Maire, D. Dormont and N. Burgos. 'Semi-supervised Domain Adaptation for Automatic Quality Control of FLAIR MRIs in a Clinical Data Warehouse'. In: *LNCS - Lecture Notes in Computer Science Series*. DART 2023 - 5th MICCAI Workshop on Domain Adaptation and Representation Transfer. Vol. 14293. Vancouver (BC), Canada: Springer Nature Switzerland, 14th Oct. 2023, pp. 84–93. DOI: 10.1007/978-3-031-45857-6_9. URL: https://hal.science/hal-04273997.

[74] B. Sauty and S. Durrleman. 'Impact of sex and APOE-ε4 genotype on regional brain metabolism in Alzheimer's Disease'. In: *Proceedings of the 2023 International Symposium on Biomedical Imaging*. ISBI 2023 - IEEE 20th International Symposium on Biomedical Imaging. Cartagena (Colombia), Colombia, 21st Apr. 2023. URL: https://inria.hal.science/hal-03951468.

[75] M. Solal, R. Hassanaly and N. Burgos. 'Leveraging healthy population variability in deep learning unsupervised anomaly detection in brain FDG PET'. In: SPIE Medical Imaging. San Diego (California), United States, 18th Feb. 2024. URL: https://hal.science/hal-04291561.

[76] T. Soulier, M. Hamzaoui, M. Sales Pitombeira, D. De Paula Faria, A. Yazdan-Panah, M. Tonietto, C. Leroy, M. Bottlaender, B. Bodini, N. Burgos, N. Ayache, O. Colliot and B. Stankoff. 'Generating PET-derived maps of myelin content from clinical MRI using curricular discriminator training in generative adversarial networks'. In: SPIE Medical Imaging. San Diego, United States, 20th Feb. 2024. URL: https://hal.sorbonne-universite.fr/hal-04362506.

[77] E. Thibeau-Sutre, J. M. Wolterink, O. Colliot and N. Burgos. 'How can data augmentation improve attribution maps for disease subtype explainability?' In: SPIE Medical Imaging. San Diego, United States: SPIE, 20th Feb. 2023. URL: https://inria.hal.science/hal-03966737.

Conferences without proceedings

[78] J. Arslan, H. Luo, P. Kumar, M. Lacroix, P. Dupré, A. Hodgkinson, C. Pignodel, L. Le Cam, O. Radulescu and D. Racoceanu. 'Reconstruction vasculaire 3D et analyse de lames virtuelles H&E dans l'étude du mélanome'. In: IABM2023 : Colloque Français d'Intelligence Artificielle en Imagerie Biomédicale. Paris, France, 30th Mar. 2023. URL: https://hal.science/hal-03928851.

[79] M.-C. Corsi, P. Sorrentino, D. P. Schwartz, N. George, L. Hugueville, A. E. Kahn, S. Dupont, D. S. Bassett, V. Jirsa and F. de Vico Fallani. 'Using critical dynamics to capture processes underlying Brain-Computer Interface performance'. In: NeuroFrance 2023. Lyon, France, 24th May 2023. URL: https://inria.hal.science/hal-04140131.

[80] N. Fournier and S. Durrleman. 'Longitudinal Modelling for Single Nucleotide Polymorphism Associations with Alzheimer's Disease'. In: AAIC 2023 — Alzheimer's Association International Conference. Amsterdam, Netherlands, 16th July 2023. URL: https://hal.science/hal-04169631.

[81] R. Hassanaly, C. Brianceau, O. Colliot and N. Burgos. 'Unsupervised anomaly detection in 3D brain FDG PET: A benchmark of 17 VAE-based approaches'. In: Deep Generative Models workshop at the 26th International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI 2023). Vancouver, Canada, 8th Oct. 2023. URL: https://hal.science/hal-04185304.

[82] G. Vaillant, N. Gensollen, M. Joulot, O. El-Rifai, M. Diaz, O. Colliot and N. Burgos. 'From Nipype to Pydra: a Clinica story'. In: OHBM 2023 - Annual meeting of the Organization for Human Brain Mapping. Montreal, Canada, 22nd July 2023. URL: https://inria.hal.science/hal-04278898.

Scientific books

[83] O. Colliot. *Machine Learning for Brain Disorders*. Vol. 197. Neuromethods. Springer, 2023. DOI: 10.1007/978-1-0716-3195-9. URL: https://hal.science/hal-04225627.

Scientific book chapters

[84] O. Colliot. 'A non-technical introduction to machine learning'. In: *Machine Learning for Brain Disorders*. Springer, 24th July 2023. URL: https://hal.science/hal-03957125.

[85] O. Colliot, E. Thibeau-Sutre and N. Burgos. 'Reproducibility in machine learning for medical imaging'. In: *Machine Learning for Brain Disorders*. Springer, 2023. URL: https://hal.science/hal-03957240.

[86] B. Couvy-Duchesne, S. Bottani, E. Camenen, F. Fang, M. Fikere, J. Gonzalez-Astudillo, J. Harvey, R. Hassanaly, I. Kassam, P. Lind, Q. Liu, Y. Lu, M. Nabais, T. Rolland, J. Sidorenko, L. Strike and M. Wright. 'Main Existing Datasets for Open Brain Research on Humans'. In: *Machine Learning for Brain Disorders*. Springer US, 23rd July 2023, pp. 753–804. DOI: 10.1007/978-1-0716-3195-9_24. URL: https://hal.science/hal-04254339.

[87] S. Epelbaum and F. Cacciamani. 'Clinical Assessment of Brain Disorders'. In: *Machine Learning for Brain Disorders*. Vol. 197. Springer, 23rd July 2023, pp. 233–252. DOI: 10.1007/978-1-0716-3195-9_7. URL: https://hal.science/hal-04239608.

[88] J. Faouzi and O. Colliot. 'Classic machine learning algorithms'. In: *Machine Learning for Brain Disorders*. Springer, 24th July 2023. URL: https://hal.science/hal-03830094.

[89] J. Faouzi, O. Colliot and J.-C. Corvol. 'Machine learning for Parkinson's disease and related disorders'. In: *Machine Learning for Brain Disorders*. Springer, 23rd July 2023. DOI: 10.1007/978-1-0716-3195-9_26. URL: https://hal.science/hal-03830073.

[90] G. Jimenez and D. Racoceanu. 'Computational Pathology for Brain Disorders'. In: *Machine Learning for Brain Disorders*. Vol. 197. Part of the Neuromethods book series (NM,volume 197). Springer; Humana, New York, NY, 23rd July 2023, pp. 533–572. DOI: 10.1007/978-1-0716-3195-9_18. URL: https://hal.science/hal-03936550.

[91] E. Thibeau-Sutre, S. Collin, N. Burgos and O. Colliot. 'Interpretability of Machine Learning Methods Applied to Neuroimaging'. In: *Machine Learning for Brain Disorders*. Springer, 2023. DOI: 10.1007/978-1-0716-3195-9_22. URL: https://hal.science/hal-03615163.

[92] M. Vakalopoulou, S. Christodoulidis, N. Burgos, O. Colliot and V. Lepetit. 'Deep learning: basics and convolutional neural networks (CNN)'. In: *Machine Learning for Brain Disorders*. Springer, 23rd July 2023. DOI: 10.1007/978-1-0716-3195-9_3. URL: https://hal.science/hal-03957224.

[93] G. Varoquaux and O. Colliot. 'Evaluating machine learning models and their diagnostic value'. In: *Machine Learning for Brain Disorders*. Springer, June 2023. URL: https://hal.science/hal-03682454.

Doctoral dissertations and habilitation theses

[94] P.-E. Poulet. 'Modeling individual disease trajectory: application to the prediction of treatment effect'. EDITE de Paris, 2nd Oct. 2023. URL: https://inria.hal.science/tel-04345196.

[95] B. Sauty. 'Multimodal modelling of Alzheimer's Disease progression'. Sorbonne Université, 13th Sept. 2023. URL: https://theses.hal.science/tel-04338932.

[96] S. Skriabine. 'Mapping of the mouse cerebral vascular network in adults and during development'. Sorbonne Université, 8th June 2023. URL: https://theses.hal.science/tel-04318045.

Reports & preprints

[97] R. Ben Messaoud, V. L. Du, B. C. Kaufmann, B. Couvy-Duchesne, L. Migliaccio, P. Bartolomeo, M. Chavez and F. de Vico Fallani. *Low-dimensional controllability of brain networks*. 2023. DOI: 10.48550/arXiv.2311.11132. URL: https://hal.science/hal-04302540.

[98] R. Hassanaly, C. Brianceau, M. Solal, O. Colliot and N. Burgos. *Evaluation of pseudo-healthy image reconstruction for anomaly detection with deep generative models: Application to brain FDG PET*. 30th Nov. 2023. URL: https://hal.science/hal-04315738.

[99] M. Ounissi, M. Latouche and D. Racoceanu. *Phagocytosis Unveiled: A Scalable and Interpretable Deep learning Framework for Neurodegenerative Disease Analysis*. 26th Apr. 2023. URL: https://hal.science/hal-04067345.

[100] R. A. Poldrack, C. J. Markiewicz, S. Appelhoff, Y. K. Ashar, T. Auer, S. Baillet, S. Bansal, L. Beltrachini, C. G. Benar, G. Bertazzoli et al. *The Past, Present, and Future of the Brain Imaging Data Structure (BIDS)*. 11th Sept. 2023. URL: https://hal.science/hal-04346097.

[101] C. Presigny, M.-C. Corsi and F. de Vico Fallani. *Topological duality of multilayer networks*. 21st June 2023. URL: https://inria.hal.science/hal-04163895.

[102] B. Sauty, E. Maheux and S. Durrleman. *Feature Selection to Forecast Cognitive Decline Using Multimodal Alzheimer's Disease Models*. 9th May 2023. URL: https://hal.science/hal-04195850.

[103] T. Venot, A. Desbois, M.-C. Corsi, L. Hugueville, L. Saint-Bauzel and F. de Vico Fallani. *Intentional binding enhances hybrid BCI control*. 2023. DOI: 10.48550/arXiv.2309.12195. URL: https://inria.hal.science/hal-04244638.

[104] A. Yazdan-Panah, R. El Jurdi, G. Fu, J. Arslan, R. Valabregue, D. Dormont, B. Stankoff and O. Colliot. *Scrolling 2D U-Net for the 3D segmentation of small vessels on 7T magnetic resonance angiography*. 9th May 2023. URL: https://hal.science/hal-04090356.

[105] A. Yazdan-Panah, G. Fu, D. Dormont, B. Stankoff and O. Colliot. *Scrolling 2D U-Net for the 3D segmentation of the internal carotid artery*. 9th May 2023. URL: https://hal.science/hal-04090342.

Other scientific publications

[106] B. Aristimunha, R. Y. D. Camargo, W. H. L. Pinaya, F. Yger, M.-C. Corsi and S. Chevallier. 'CONCERTO: Coherence & Functional Connectivity Graph Network'. In: Journée CORTICO 2023. Paris, France, 9th May 2023. URL: https://hal.science/hal-04121445.

[107] I. Carrara, B. Aristimunha, S. Chevallier, M.-C. Corsi, T. Papadopoulo and M.-C. Corsi. 'Holographic EEG: multi-view deep learning for BCI'. In: Journée CORTICO 2023 - COllectif pour la Recherche Transdisciplinaire sur les Interfaces Cerveau-Ordinateur. Paris, France, 9th May 2023. URL: https://hal.science/hal-04095900.

[108] I. Carrara, B. Aristimunha, M.-C. Corsi, R. Y. D. Camargo, S. Chevallier and T. Papadopoulo. 'Augmented SPDNet: Second-Order Neural Network for Motor Imagery-Based BCI'. In: Soph.IA summit 2023. Sophia Antipolis, France, 22nd Nov. 2023. URL: https://inria.hal.science/hal-04308549.

[109] M.-C. Corsi, S. Chevallier, F. de Vico Fallani and F. Yger. 'Ensemble of Riemannian classifiers for multimodal data: FUCONE approach for M/EEG data'. In: BCI meeting 2023. Bruxelles, Belgium, 6th June 2023. URL: https://inria.hal.science/hal-04140113.

[110] L. Ek-Fliesberg, P. Sorrentino and M.-C. Corsi. 'Neuronal avalanches as alternative features for motor imagery-based brain-computer interface'. In: Journées CORTICO 2023. Paris, France, 9th May 2023. URL: https://inria.hal.science/hal-04140098.

[111] R. Frateur, S. Chevallier, F. Yger and M.-C. Corsi. 'Dimensionality Reduction and Frequency Bin Optimization To Improve a Riemannian-based Classification Pipeline'. In: CORTICO 2023 - Journées COllectif pour la Recherche Transdisciplinaire sur les Interfaces Cerveau-Ordinateur. Paris, France, 9th May 2023. URL: https://inria.hal.science/hal-04140107.

[112] S. Kaisaridi, H. Chabriat and S. Tezenas Du Montcel. 'A multivariate bayesian mixed-effect model (Leaspy) to analyze the trajectory of cognitive decline in CADASIL'. In: 44th Annual Conference of the International Society for Clinical Biostatistics. Milan, Italy, 27th Aug. 2023. URL: https://hal.science/hal-04399800.

[113] J. Ortholand, S. Durrleman and S. Tezenas Du Montcel. 'Longitudinal and survival joint prediction: time reparameterization in amyotrophic lateral sclerosis context'. In: ISCB 2023 - 44th Annual Conference of the International Society for Clinical Biostatistics. Milan, Italy, 27th Aug. 2023. URL: https://hal.science/hal-04216888.

[114] P.-E. Poulet, B. Jedynak, Z. Mari and S. Durrleman. 'Non-parametric modeling for dopaminergic treatment effect in Parkinson's disease'. In: AD/PD 2023 - 17th International Conference on Alzheimer's & Parkinson's Diseases. Goteborg, Sweden, 27th Mar. 2023. URL: https://inria.hal.science/hal-04158200.

[115] P. Sorrentino, M.-C. Corsi, D. P. Schwartz, N. George, A. E. Kahn, S. Dupont, D. S. Bassett, F. de Vico Fallani and V. Jirsa. 'Informing motor imagery-based brain-computer interface via neuronal avalanches'. In: IEEE International Symposium on Biomedical Imaging (ISBI) 2023. Cartagena, Colombia, 18th Apr. 2023. URL: https://inria.hal.science/hal-04140120.