PhD and PostDoc positions

Location: EPFL AVP-CP CIBM-AIT, Bâtiment CH F.
Start date: to be agreed
Duration: 4 years each position

Shedding light on the invisible: mapping brain microstructure using diffusion magnetic resonance spectroscopic imaging

Dr Cristina Cudalbu from the MRI EPFL Animal Imaging and Technology Section is looking for two highly motivated PhD and PostDoc candidates working together in the area of **diffusion weighted MR spectroscopy/spectroscopic imaging (dMRS/dMRSI)** at ultra-high magnetic fields and **cross-validation of metabolite diffusion metrics** using both 3D brain cell organoids and in vivo rodent models.
This project is part of an interdisciplinary collaborative SNSF proposal and will take advantage of the: 1) unique bioimaging facilities of the CIBM MRI EPFL, in particular the **ultra-high field 9.4T and 14.1T *in vivo* MR systems, two cryo-probes and the first PET/MR insert for preclinical studies in Switzerland,** and 2) unique **consortium of 4 PIs enrolling 3 PhDs and 5 PostDocs for this project**.

Background

The temporal and regional evolution of the brain during development, disease or injury is characterized by numerous microstructural and metabolic changes, for which new non-invasive methods advancing the quantification of brain microstructure are necessary. Diffusion MRI (dMRI) of water provides information about tissue microstructure non-invasively, but its specificity is limited due to ubiquitous presence of water. Brain metabolites measured by MR spectroscopy (MRS) are predominantly intracellular and some have a reportedly preferential localization in specific brain cell types. Diffusion MRS (dMRS) can thus provide quantification of cell-type specific microstructure, but can be further enhanced by adding spatial information across the brain; in other words, developing diffusion MR spectroscopic imaging (dMRSI).

Project description

Our overall project addresses timely issues of developing a non-invasive microscope into brain microstructure Our goal is therefore to push further a new concept for quantification and validation of brain microstructure through diffusion of brain metabolites and water at cellular and sub-cellular scale, by implementing an in vivo innovative multi-modal approach combining novel dMRSI acquisitions, state-of-the-art postprocessing and metabolite diffusion modeling techniques validated with 2-photon microscopy (2PEF) and mass spectrometry (MS). Our target application is the critical period of brain development and associated potential injury, that we will assess using both 3D brain cell organoids (validation of metabolite diffusion metrics) and in vivo rodent models.

These PhD and PostDoc projects will build on our current work in dMRS and accelerated MRSI techniques at ultra-high field (PUBLICATIONS – MRS4BRAIN - EPFL), with the collaboration and expertise of the 4PIs and with our recognised expertise in multimodal preclinical acquisitions (LIVE Demos – MRS4BRAIN - EPFL).

The aim of the PhD position is to push dMRS methodology to a next level with regards to 1) spatial resolution by developing dMRSI at ultra-high fields; 2) MR acceleration ((sparse k-space sampling, spatial-spectral encoding); 3) combined with denoising techniques and exquisite sensitivity of cryoprobes, thus going beyond the state-of-the-art in preclinical studies.

The aim of the PostDoc position is to: 1) develop a MR compatible bioreactor for alive measurements of 3D brain cell organoids using dMRSI and dMRI. This bioreactor will be also adapted for 2PEF microscopy, cell clamping and measure of cell-specific intracellular metabolites; 2) to measure for the first-time living 3D brain

cell organoids at different stages of development as well as under ischemia and creatine deficiency, using the same dMRSI approaches developed above.

The PhD and PostDoc will work closely together, and will strongly and synergistically interact with the other PhD and PostDocs enrolled on the same project who will: 1) develop advanced modeling approaches, based on the diffusion data acquired by the current PhD and PostDoc, that jointly fit individual spectra and diffusion attenuation of metabolites with underlying diffusion models, while combining additional dMRSI and dMRI mutual information; 2) go beyond traditional microstructural validation for in vivo dMRSI and corresponding diffusion models, using a convergence of new methods based on 2PEF microscopy (validation of exact morphology of living neural cells) and MS (validation of brain metabolite compartmentation in specific neural cells) using for the first time 3D brain cell organoids, a model translating the in vivo structural and metabolic complexity of the brain, to validate our metabolite and water diffusion models and their ability to capture cell structural changes and intracellular metabolites compartmentalization, including in pathological challenges; 3) as a proof of concept we will apply our novel dMRSI methodology to evaluate in vivo the level of biological sensitivity and specificity of underlying microstructural changes through metabolite diffusion models in two pathological conditions.

Supervisors:

- Dr Cristina Cudalbu, CIBM MRI EPFL, https://cibm.ch/community/cristina-cudalbu/, Cristina Cudalbu, PhD – MRS4BRAIN - EPFL, cristina.cudalbu@epfl.ch
- Prof. Dimitri Van De Ville, CIBM MRI EPFL, dimitri.vandeville@epfl.ch -for the PhD only

Consortium/Collaborators:

- Assistant Prof Ileana Jelescu Ileana Jelescu – Microstructure Mapping Lab (unil.ch)
- Prof Olivier Braissant, Olivier Braissant, professeur au Service de chimie clinique du CHUV et à la Faculté de biologie et... | Phototheque UNIGE
- Prof Stéphane Sizonenko https://neurocenter-unige.ch/research-groups/stephane-sizonenko/
- The PhD student and PostDoc will work closely with 2 PhD students and 4 PostDocs recruited on the same project and will also be a part of the Mrs4Brain Group - EPFL where 2 PhD students and 1PostDoc are actually working on ^{1}H, ^{2}H and ^{31}P fast MRSI, DW-MRS, hepatic encephalopathy, epilepsy.

Skills:

Master's degree (for PhD position) and PhD degree (for PostDoc position) in (biomedical) physics, bioengineering, neuroscience or a similar degree. Ideally the two candidates should have complementary skills (i.e. physics/bioengineering *vs* neuroscience). Very good experimental skills for multimodal *in vivo* experiments, natural taste for problem solving, scientific curiosity, motivation to elaborate reproducible quantitative approaches in a cutting-edge research field. Experience in MRS, MRSI and sequence programming is an advantage as well as experience in programming (i.e. Matlab, Python) is a plus. Ready to work in a multidisciplinary research field requiring extension of his/her own expertise and collaboration with researchers from various backgrounds. Open to work on animal and translational biomedical research. Proficient in English, both verbal and in writing.

We offer:

- A dynamic, interdisciplinary, and international team of very motivated people: Mrs4Brain Group - EPFL.
- A stimulating working environment based at CIBM in Lausanne, Switzerland.
- Participation in one of the world's leading transitional brain ultra-high field MRS efforts Mrs4Brain Group - EPFL.
- Access to cutting-edge technology and state-of-the-art resources.
- Salary in compliance with Swiss National Science Foundation guidelines.

How to apply:

Applications will be considered until the position is filled, so interested candidates are encouraged to apply early. Please send your CV and motivation letter to cristina.cudalbu@epfl.ch

About CIBM

The CIBM Center for Biomedical Imaging was founded in 2004 and is the result of a major research and teaching initiative of the partners in the Science-Vie-Société (SVS) project between the Ecole Polytechnique Fédérale de Lausanne (EPFL), the Université de Lausanne (UNIL), Université de Genève (UNIGE), the Hôpitaux Universitaires de Genève (HUG) and the Centre Hospitalier Universitaire Vaudois (CHUV), with the generous support from the Fondation Leenaards and Fondation Louis-Jeantet.
CIBM brings together highly qualified, diverse, complementary and multidisciplinary groups of people with common interest in biomedical imaging.

We welcome you in joining the CIBM Community

cibm.ch