Offre n°2024-07734

PhD Position F/M Exploring the role of gene regulation in learning odors

Le descriptif de l’offre ci-dessous est en Anglais

Type de contrat : CDD
Niveau de diplôme exigé : Bac + 5 ou équivalent
Fonction : Doctorant

A propos du centre ou de la direction fonctionnelle

The Inria research centre in Lyon is the 9th Inria research centre, formally created in January 2022. It brings together approximately 300 people in 17 research teams and research support services. Its staff are distributed in Villeurbanne, Lyon Gerland, and Saint-Etienne.

The Lyon centre is active in the fields of software, distributed and high-performance computing, embedded systems, quantum computing and privacy in the digital world, but also in digital health and computational biology.

Contexte et atouts du poste

Within a long-term collaboration of the BEAGLE team with Dr. A. Fleischmann and Dr. R. Singh at Brown University (USA), you will investigate the gene regulatory processes involved in learning of odor responses in mice. Your goal will be to use both numerical (computational) modeling and bioinformatic data analysis to understand better how gene regulation impacts neuronal and glial behavior during learning in the olfactory system of mice, and vice versa, how learning an odor-response association has consequences for gene expression and gene regulation.

This is a three-year position for a PhD student. You will be advised by Anton Crombach (Centre Inria de Lyon), with expert input from Hugues Berry (Centre Inria de Lyon) and whilst working together with other members of the project. You will be located at Inria’s La Doua site with opportunities to visit the collaborators at Brown University.

You will benefit from the expertise at Inria regarding bioinformatic data analysis and mathematical and computational modeling of biological systems; and you will profit from world-class knowledge at Brown University regarding neuro-biology and machine learning aspects of the project. Overall, the project will foster your career in terms of building up cutting-edge expertise on numerical simulation techniques, high-dimensional data analysis, network analysis, statistical and machine learning, and data visualization techniques – areas that are strongly demanded in academia and industry.

Mission confiée

This PhD project addresses a fundamental question in biology: how do we learn? As an example of learning, we study how mice learn to associate an odor with a positive or negative reward (water with sucrose or quinine, respectively). Specifically, we are interested in the impact of learning on gene expression in the mouse olfactory cortex. To this end, our collaborators at Brown University have generated a rich single-cell RNA sequencing dataset of olfactory cortex (piriform cortex) across a variety of conditions. Complementing the experimental work, our goal is to provide a formal framework to reason about the interplay between neuronal circuitry and the gene regulatory dynamics inside neurons and glial cells. This means we have two main objectives:

1. Create novel computational/mathematical models of olfactory neuronal circuits that interact with their associated gene regulatory networks in neurons and glia.

2. Perform bioinformatic data analysis of single-cell data to explore the role of glial cells, e.g. astrocytes, in learning, and how they interact with neurons in this process.

Regarding Objective 1, the computational modeling, the idea is to propose small “canonical” neuronal circuits present in olfactory cortex and to subject these circuits to different learning tasks, for instance to distinguish odor mixes. Learning is assumed to involve long-term changes of synaptic strength between neurons. The biological, and hence mathematical, details of how this is realized, however, remain an open question. Several phenomenological models have been proposed, but models with an explicit consideration of gene regulatory dynamics are rare (and tied to rather specific case studies). Given that nowadays scRNA-seq and related technologies provide us with the data at this level, our aim
is to connect transcription and regulation of genes to the dynamics at synapses.

We will explore the regulation of synaptic strengths by means of evolutionary simulations. Using evolutionary approaches allows one to discover not only which mechanisms function correctly, but it also gives us an understanding of evolutionary properties, such as evolvability and robustness. Simulation results will then be used to formulate novel hypotheses that we can test given our collaborator's data, public datasets, and dedicated experiments.

Objective 2 will be done in close collaboration with the data analysis efforts by our collaborators at Brown University. They are focused on neurons that changed gene expression patterns due to learning. Complementing these efforts, we will focus on glial cells, exemplified here by astrocytes. Astrocytes are known to be involved in learning and our goal will be to describe, for olfactory cortex, how astrocytes change their expression dynamics. Next, by reaching out to local collaborators, Hugues Berry and Olivier Raineteau, we will investigate how interactions between neurons and astrocytes change due to learning. Insights from our data analysis efforts will allow us to go beyond mathematical models that are neuron-only and propose novel models that take into account the extensive cross-talk between neurons and glial cell types in the brain.

**Principales activités**

Your main tasks are as follows:

- obtain a good overview of the relevant literature ("state of the art") regarding gene regulation, neuronal circuits, interactions between neurons and glial, single-cell data analysis, numerical simulations of evolution. You will be reading literature from both computational and experimental biology communities.

- formulate your approach(es) to address the challenges as described above in "Assignments". For computational modeling tasks, this requires designing and implementing mathematical models, and setting up evolutionary simulations. For bioinformatic data analysis, you will familiarize yourself with standard and advanced analysis software (Scanpy and tools from the scverse and/or Seurat and other R packages).

- conduct computational simulations and single-cell data analysis. Both simulation output and single-cell data are large, high-dimensional datasets. You will be using and adapting tools from statistics and machine learning to detect interesting patterns. It is likely that you will write custom code for specific tasks, for example when working with single-cell data, you will have to detect rare cell types, integrate temporal data, and compare multiple experimental conditions.

- communicate your results at conferences/workshops and via scientific articles. Effectively transmitting the core findings from your work is far from a trivial task, with a career-spanning learning curve.

**Compétences**

The project requires skills in mathematics, computer science, and (neuro) biology. A successful candidate has experience in one or more of the following areas: dynamical systems theory, single-cell data analysis, statistics and machine learning, programming in Python/R and C/C++ (or similar, like Rust, Julia). Moreover, affinity with computational neuroscience is considered a real advantage. Good oral and written communication skills in English are essential.

**Avantages**

- Subsidized meals
- Partial reimbursement of public transport costs
- Leave: 7 weeks of annual leave + 10 extra days off due to RTT (statutory reduction in working hours) + possibility of exceptional leave (sick children, moving home, etc.)
- Possibility of teleworking (90 days / year) and flexible organization of working hours (except for internship)
- Social, cultural and sports events and activities
- Access to vocational training
- Social security coverage under conditions

**Rémunération**

1st and 2nd year: 2100 euros gross salary / month

3rd year: 2190 euros gross salary / month

**Informations générales**

- Thème/Domaine : Biologie numérique
- Ville : Villeurbanne
- Centre Inria : Centre Inria de Lyon
- Date de prise de fonction souhaitée : 2024-11-01
- Durée de contrat : 3 ans
Contacts

- Équipe Inria : BEAGLE
- Directeur de thèse : Crombach Antonius / anton.crombach@inria.fr

A propos d'Inria

Inria est l'institut national de recherche dédié aux sciences et technologies du numérique. Il emploie 2600 personnes. Ses 215 équipes-projets agiles, en général communes avec des partenaires académiques, impliquent plus de 3900 scientifiques pour relever les défis du numérique, souvent à l'interface d'autres disciplines. L'institut fait appel à de nombreux talents dans plus d'une quarantaine de métiers différents. 900 personnels d'appui à la recherche et à l'innovation contribuent à faire émerger et grandir des projets scientifiques ou entrepreneuriaux qui impactent le monde. Inria travaille avec de nombreuses entreprises et a accompagné la création de plus de 200 start-up. L'institut s'efforce ainsi de répondre aux enjeux de la transformation numérique de la science, de la société et de l'économie.

L'essentiel pour réussir

The applicant should have a strong basis in mathematics and biology (Master's degree or equivalent), ideally oriented toward computational biology and/or bioinformatic data analysis. An essential quality for this project is a keen interest to apply one's mathematical and computational skills to help answering biological questions. An interest in the evolution and functioning of gene regulation and neuronal circuits, plus a curiosity for single-cell technologies, is considered a real asset, as is wanting to communicate and collaborate with experimental biologists that study the mouse olfactory sensory system.

Attention: Les candidatures doivent être déposées en ligne sur le site Inria. Le traitement des candidatures adressées par d'autres canaux n'est pas garanti.

Consignes pour postuler

Applications must be submitted online via the Inria website. Processing of applications submitted via other channels is not guaranteed.

Sécurité défense :
Ce poste est susceptible d'être affecté dans une zone à régime restrictif (ZRR), telle que définie dans le décret n°2011-1425 relatif à la protection du potentiel scientifique et technique de la nation (PPST). L'autorisation d'accès à une zone est délivrée par le chef d'établissement, après avis ministériel favorable, tel que défini dans l'arrêté du 03 juillet 2012, relatif à la PPST. Un avis ministériel défavorable pour un poste affecté dans une ZRR aurait pour conséquence l'annulation du recrutement.

Politique de recrutement :
Dans le cadre de sa politique diversité, tous les postes Inria sont accessibles aux personnes en situation de handicap.