CURRICULUM VITAE

Pierre Le Merre, PhD

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CURRENT POSITION

2023 (September) - present, Research Specialist at Karolinska Institutet, lab of Marie Carlén (KI, Stockholm, Sweden).

PREVIOUS POSITION

2017 (September) - 2023 (August), Post-doctoral researcher at Karolinska Institutet, lab of Marie Carlén (KI, Stockholm, Sweden).

2017 (January to June), Post-doctoral researcher at the École Polytechnique Fédérale de Lausanne, lab of Carl Petersen (EPFL, Lausanne, Switzerland).

EDUCATION

2012- 2016, PhD degree in Neurosciences: Thesis title: Cortical dynamics and sensory processing in the awake mouse - impact of the behavioral context.. Thesis co-directed between the University of Lyon by Paul Salin (CRNL, Lyon, France) and the École Polytechnique Fédérale de Lausanne by Carl Petersen (EPFL, Lausanne, Switzerland) and Sylvain Crochet (EPFL, Lausanne, Switzerland). Defended the 16th of December 2016.

2009-2012, Master's degree of Biosciences (MSc) at the École Normale Supérieure of Lyon. Graduated with honors.

2009-2010, Agrégation des Sciences de la Vie, de la Terre et de l'Univers (french national teacher grade in Biology and Geology), ranked 5th.

2007-2008, Bachelor's degree in Fundamental Biology (BSc) at the École Normale Supérieure of Lyon.

2005-2007 Two-year high of selective classes of Biology, Chemistry, Physics and Earth Sciences to prepare for the competitive exams to the Grandes Ecoles at the Lycee Camille Guerin, Poitiers (France).

2004-2005, Scientific Baccalaureat with a very good pass (17,6 / 20) at the Lycee Jean Giraudoux, Bellac (Haute-Vienne), France.

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A. QUANTITATIVE SECTION

PUBLICATIONS

Postdoctoral production:

Research articles:

Esr1+ hypothalamic-habenula neurons shape aversive states.

Calvigioni D*, Fuzik J*, **Le Merre P***, Slashcheva M, Jung F, Ortiz C, Lentini A, Csillag V, Graziano M, Nikolakopoulou I, Weglage M, Lazaridis I, Kim H, Lenzi I, Park H, Reinius B, Carlén M, Meletis K. (2023) **Nature Neuroscience** 2023 26;7 1245-1255.

A latent lineage potential in resident neural stem cells enables spinal cord repair.

Llorens-Bobadilla E, Chell JM, **Le Merre P**, Wu Y, Zamboni M, Bergenstråhle J, Stenudd M, Sopova E, Lundeberg J, Shupliakov O, Carlén M, Frisén J.

(2020) **Science**. Oct 2;370(6512):eabb8795.

Review articles:

The mouse prefrontal cortex: Unity in diversity.

Le Merre P*, Ährlund-Richter S*, Carlén M. (2021) Neuron.109;12 1925-1944.

 $*Equal\ contribution$

Datasets:

Data Set For 'Esr1+ hypothalamic-habenula neurons shape aversive states.'

Calvigioni D*, Fuzik J*, **Le Merre P***, Slashcheva M, Jung F, Ortiz C, Lentini A, Csillag V, Graziano M, Nikolakopoulou I, Weglage M, Lazaridis I, Kim H, Lenzi I, Park H, Reinius B, Carlén M, Meletis K. (2023) DANDI archive. https://doi.org/10.48324/dandi.000473/0.230417.1502.

Ph.D. production:

Research articles:

Reward-Based Learning Drives Rapid Sensory Signals in Medial Prefrontal Cortex and Dorsal Hippocampus Necessary for Goal-Directed Behavior.

Le Merre P, Esmaeili V, Charrière E, Galan K, Salin PA, Petersen CCH, Crochet S. (2018) **Neuron**. 97;1 83-91.e5.

Highly Dynamic Spatiotemporal Organization of Low-Frequency Activities During Behavioral States in the Mouse Cerebral Cortex.

Fernandez LMJ, Comte JC, **Le Merre P**, Lin JS, Salin PA, Crochet S. (2017) **Cerebral cortex**. 27;12 5444-5462.

Sensorimotor function is modulated by the serotonin receptor 1d, a novel marker for gamma motor neurons. Enjin A, Leao KE, Mikulovic S, Le Merre P, Tourtellotte WG, Kullander K. (2012) Molecular and Cellular Neuroscience. 49;3 322-32.

Datasets:

Data Set For 'Reward-Based Learning Drives Rapid Sensory Signals in Medial Prefrontal Cortex and Dorsal Hippocampus Necessary for Goal-Directed Behavior.'

Le Merre P, Esmaeili V, Charrière E, Galan K, Salin PA, Petersen CCH, Crochet S. (2017) Zenodo, doi:10.5281/zenodo.1063897.

^{*}Equal contribution

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TALKS AND POSTERS

 $Major\ conferences:$

- 2023 Talk at 20 years of Barrel Cortex, EPFL, Switzerland
- 2022 Talk at GDR NeuralNet, Lyon (France)
- 2022 Selected Poster at COSYNE, Lisbon (Portugal)
- 2018 Talk at Computational Properties of the Prefrontal Cortex, Nashville (U.S.A)
- 2017 Talk at the Swisskers meeting in Zurich, Switzerland
- 2016 Talk at the Synapses and Circuit meeting, EPFL, Switzerland

Invited talks:

2023 - Seminar at Neurocampus, Lyon; Seminar at NeuroPSI, Paris-Saclay, France; Seminar at ESPCI, Paris, France; Seminar at Neurocentre Magendie, Bordeaux, France.

Posters:

- 2022 Poster at FENS, Paris (France)
- 2020 Virtual poster at FENS, Glasgow (Scotland)
- 2019 Poster at GDR multielectrodes, Bordeaux (France)
- 2017 Poster at SFN, Washington DC (U.S.A)
- 2016 Poster at FENS, Copenhagen (Denmark)
- 2016 Poster at the Barrel Cortex Function meeting, Amsterdam (Nederland)
- 2015 Poster at SFN, Chicago (U.S.A)
- ${\bf 2014}$ Poster at GDR multielectrodes, Gif sur Yvette (France)
- 2013 Poster at GDR multielectrodes, Bordeaux (France)
- 2012 Poster at GDR multielectrodes, Marseille (France)

GRANTS AND AWARDS

2022-2023 Karolinska Institutet fonder, 1 year, coordinator - 110 900 SEK

2020 StratNeuro Postdoc Grant, 1 year, coordinator - 750 000SEK

2019-2021 NARSAD Young Investigator Award (2019) 2 years, coordinator - 35 000 \$ / year (1\$ 9,4 SEK)

2019, NVIDIA GPU Grant program (graphics card worth 5000 €).

2018-2019, Karolinska Institutet fonder, 1 year, coordinator - 93 400 SEK.

2015, Fellowship, International Mobility Fellowship Lyon-St Etienne (PALSE), 6 months, coordinator, (1000€ per month).

REVIEWING ACTIVITIES

2017 — present - Reviewer for the following journals: Nature Communication, Nature Neuroscience, Nature, Current Biology, Cell, Neuron, The Journal of Neuroscience and Neuroimage.

MEMBERSHIP OF SCIENTIFIC SOCIETIES

- 2022 Member of the Swedish Society for Neuroscience
- 2020 Member of the Swedish Society for Neuroscience
- 2017 Member of the Society for Neuroscience
- 2016 Member of the Swiss Society for Neuroscience
- 2015 Member of the Society for Neuroscience
- 2014 Member of the French Neuroscience Society

SUPERVISION AND TEACHING

2017-present Supervision of 7 Master students during the postdoc:

- Eleni Moysiadou, MSc (2022-2023): Established an auditory working memory task for head-fixed mice, and performed Neuropixels recordings and analysis under my supervision. Currently transitioning to start a Ph.D. with Nikolaos Karalis in Paris.
- Sasa Lekic, MSc (2020-2021): Established the computation of timescales from neuronal activity recorded with Neuropixels probes across prefrontal regions. Used deep learning approaches to study the functional properties of the mouse prefrontal cortex. Currently Data Scientist at the H&M group, Stockholm, Sweden.
- Hyunsoo Park, MSc (2019-2020): Performed all the probe tracking in cleared tissue and the histological work for the aversion project. Co-author on our Nature Neuroscience 2023 article. Currently Scientist at AstraZeneca AB R&D, Göteborg, Sweden.
- Ram Yahya, MSc (2019-2020): Performed spike sorting and the training and handling of mice for the functional map of the prefrontal cortex project. The publication is currently in preparation. Currently Laboratory Engineer at Octaparma, Stockholm, Sweden.
- Fredrik Wernstål, MMSc (2019-2020): Performed spike sorting and the training and handling of mice for the functional map of the prefrontal cortex project. The publication is currently in preparation. Currently doing a Ph.D at FyFa in Karolinska Institutet, Stockholm, Sweden.
- Agnieska Limiszewska, MSc (2018-2019): Established our tissue clearing protocol (CUBIC). Trained and recorded mice in a Go/NoGo auditory task.
- Yicheng Wu, MSc (2017-2018): Performed the handling and behavioral test of all the mice used in the collaboration project with Jonas Frisén lab in co-supervision with Enric Llorens-Bobadilla. Co-author of our Science 2020 article. Currently doing a PhD at the University of Zurich (Jessberger lab).

2012-2016 Supervision of 3 Master students during the PhD:

- Nicolas Clairis, MSc (2015): Helped with the handling and training of the mice used in my first Ph.D. publication. Currently doing a postdoc with Carmen Sandi, EPFL, Switzerland
- Agathe Pralus, MSc (2014): Helped with the handling and training of the mice used in my first Ph.D. publication. Currently project leader at Humans Matter, France.
- May Bodrero, MSc (2013): Helped with the handling and training of the mice used in my first Ph.D. publication. Currently team manager at PPD (Thermo Fisher Scientific), France.

2012-2016 - Teaching Assistant, University of Lyon and École Normale Supérieure (64h per year).

COURSES AND MEETINGS

2023 Organizer - Brain Circuit Course, KI, Stockholm. Main confirmed speakers: Tania Barkat, Nicolas Mallet, Jonathan Whitlock, Francesco Battaglia and Kathleen Cho.

2022 Organizer - Brain Circuit Course, KI, Stockholm. Main confirmed speakers: Nelson Totah, Jonathan Whitlock, Gabrielle Girardeau and Anna Beyeler.

2021 Organizer - Brain Circuit Course, KI, Stockholm. Main confirmed speakers: Nick Steinmetz, Laura Busse, Gabrielle Girardeau and Anna Beyeler.

2020 Organizer - NeuroSessions: Large-scale neuronal recordings: advances and challenges in analysis methodology. KI, Stockholm. Speakers: Alon Rubin, Emil Wärnberg, Alex Cayco Gajic, Will Allen and Andrew Peters. **2018** Attendee - Neuropixels course, UCL, London.

ANIMAL EXPERIMENTATION CERTIFICATES

2023 Design of scientific procedures and projects involving animals (FELASA function B; Directive 2010/63/EU) 2017-present Continuous training to carry out animal experimentation on rodents in Sweden by the LAS E & T unit.

2017 Approval to carry out animal experimentation on rodents in Sweden granted by the LAS E & T unit.

2016 Introductory Course in Laboratory Animal Science: Legislation and permit - Ethics - 3R methods. Organized by the Swiss Federation of Cantonal Veterinary Surgeons.

2014 Level 1 Animal Experimentation (FELASA function C) - Ethics and good practices for animal experimentation delivered by the University of Lyon.

INFORMATIC SKILLS

Softwares - Coding languages : Julia - Matlab (Mathworks), Python, Igor Pro (Wavemetrics), LabView (National Instruments), Later (Adobe), HTML5, CSS3.

CAREER BREAKS AND MAJOR LIFE EVENTS

During my postdoc, I took time (5 months) to raise my two daughters resulting in 150 days of Parental leave. COVID-19 had a minor impact on my scientific productivity during the postdoc. The lab was shut down for a couple of months and stress due to the difficulty of supporting family members living in different countries was experienced.

OTHER INFORMATION

Languages: French (native speaker), English (fluent), Spanish (conversational), Swedish (notions).

Driving Licence (B)

Interests: Travelling, DJ and electronic music producer, Short movie director.

Sports: Running, Hiking, Badminton.

B. NARRATIVE SECTION

Cognition is an umbrella term, a black box, encompassing various aspects of mental functions and processes of biological systems. In natural environments, brain circuits are continuously performing neural computations that allow organisms to react to an everchanging external world by following hidden rules. The capacity to extrapolate outcomes from limited observations, decipher rules from complex situations, and maintain focus on specific external inputs exemplifies the range of abstract cognitive operations performed by various species. But what does cognition mean in biological terms? I joined the field of neuroscience in a drive to understand how biological systems implement intricate and abstract mental abilities. After a broad training in biology, which often comes to me as a natural way to answer research questions, I wanted to know more about the available theories and tools used to study brain activity.

I therefore decided, after a couple of master's internships, to perform my Ph.D. between Lyon (Université Claude Bernard Lyon 1) and Lausanne (École Fédérale Polytechnique de Lausanne) under the supervision of Paul Salin, co-directed by Carl Petersen and co-supervised by Sylvain Crochet. During my thesis, I studied cortical network dynamics as mice learn and perform a simple goal-directed tactile detection task. First, I showed that the activity in the prefrontal cortex (PFC) and hippocampus (two associative cortical regions) is significantly elevated as mice make correct decisions compared to incorrect choices. Second, the activation of the PFC and the hippocampus increases throughout learning. Third, I demonstrated that PFC and hippocampal activity were required to perform goal-directed actions using pharmacological and optogenetic inhibition. The results of my Ph.D. confirmed the involvement of associative cortical regions for simple sensorimotor transformations and highlighted the importance of studying brain-wide circuits even for simple behavioral tasks.

Given the main outcome of my thesis, I wanted to better understand how the PFC works using the tools available in mice and to better characterize the role of the different neuronal populations in this region. Looking back, I could not have chosen a better postdoc environment and mentor than Marie Carlén at the Karolinska Institute in Stockholm. Professor Carlén's team is entirely devoted to unraveling the structure and function of the mouse prefrontal cortex as well as the neuronal underpinning of cognition. With her support, I started by performing a research synthesis of the structure and function of the mouse PFC and we shared our views with the scientific community in a well-cited perspective article. We identified conflicting definitions of the PFC in the field and suggested new directions to identify defining features of mouse frontal regions, taking advantage of the extensive genetic and electrophysiological toolboxes available for the mouse. Among all suggested future directions for the field, one clear knowledge gap stands out - the lack of a functional definition of the mouse PFC.

In our pursuit of a functional definition of the mouse PFC, we needed to be able to record neuronal activity from large cortical regions located sometimes deep in the brain. Hence, at the beginning of my postdoc, I took part in the Neuropixels Course at the University College London, granting me early access to a novel high-density recording technique yielding an unprecedented number of simultaneously recorded neurons in multiple brain regions. I abundantly used Neuropixels recordings in vivo (hundreds of recording sessions) to establish a functional signature of prefrontal neurons (unpublished results). Of note, I developed various auditory tasks for head-fixed mice to study the dynamics of prefrontal functional maps.

In parallel, I was involved in a large collaborative project. With the laboratory of Konstantinos Meletis at the Karolinska Institute in Stockholm, we studied how aversive emotional processes are represented in the mouse PFC. We found that the prelimbic region shows the largest modulation in reaction to aversive stimuli, and we identified a representation of the aversive state of the mice in the baseline activity preceding the aversive stimuli. These results sparked my interest in the neuronal representation of emotional states and how the PFC contributes to the appraisal of the emotional content of sensory information.

My postdoctoral journey not only expanded my technical toolkit but also deepened my conceptual insights needed to address my original research question: How are abstract cognitive processes implemented by neuronal circuits? As of now, I have honed in on one single cognitive process within my research scope: my focus centers on the study of the neuronal circuits for natural sound categorization. Categorization, the process of grouping individual instances (individuals, thoughts, experiences) into broader classes sharing similarities, is a core cognitive ability shared across many species. Importantly, studying categorization is at the crossroads of perception and cognition, combining my past scientific expertise into a new line of research.

My work has led to 6 published projects in peer-reviewed journals (3 as first author, 3 as co-author) and 3 articles currently in preparation. Additionally, each first-author publication was accompanied by a data release on public databases.