

EVALUATION REPORT OF THE UNIT  
SPPIN – Saint-Pères Paris institute for  
neurosciences

UNDER THE SUPERVISION OF THE  
FOLLOWING ESTABLISHMENTS AND  
ORGANISMS:

Université Paris Cité,  
Centre national de la recherche scientifique,  
CNRS

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**EVALUATION CAMPAIGN 2023-2024**  
GROUP D

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In the name of the expert committee<sup>1</sup> :

Philippe Marin, Chairman of the committee

For the Hcéres<sup>2</sup> :

Stéphane Le Bouler, acting president

Pursuant to Articles R. 114-15 and R. 114-10 of the French Research Code, evaluation reports drawn up by expert committees are signed by the chairmen of these committees and countersigned by the Chairman of Hcéres.

To make the document easier to read, the names used in this report to designate functions, professions or responsibilities (expert, researcher, teacher-researcher, professor, lecturer, engineer, technician, director, doctoral student, etc.) are used in a generic sense and have a neutral value.

This report is the result of the unit's evaluation by the expert committee, the composition of which is specified below. The appreciations it contains are the expression of the independent and collegial deliberation of this committee. The numbers in this report are the certified exact data extracted from the deposited files by the supervising body on behalf of the unit.

## MEMBERS OF THE EXPERT COMMITTEE

### Chairperson:

Mr Philippe Marin, CNRS - Centre national de la recherche scientifique, Montpellier

### Experts:

Mr Maxim Cazorla, Inserm - Institut national de la santé et de la recherche médicale, Marseille

Mr Antony Czarnecki, Université de Bordeaux (representative of CoNRS25), Bordeaux

Ms Valérie Ego-Stengel, CNRS - Centre national de la recherche scientifique, Saclay

Mr Orestis Faklaris, CNRS - Centre national de la recherche scientifique, Montpellier

Ms Sara Morley-Fletcher, Université de Lille (representative of CNU), Lille

Mr Simon Thorpe, Université Toulouse 3 - Paul Sabatier – UPS, Toulouse

## HCÉRES REPRESENTATIVE

Mr Giovanni Stevanin

## REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Ms Nathalie Eisenbaum, Vice-doyenne Recherche, Faculté des Sciences - Université ParisCité

Mr Bernard Poulain, ITMO Neurosciences, CNRS

Ms Kim Charvet, ITMO Neurosciences, CNRS

## CHARACTERISATION OF THE UNIT

- Name: Saints Pères Paris Institute for the Neurosciences
- Acronym: SPPIN
- Label and number: UMR8003 CNRS, UPC
- Composition of the executive team: Mathieu Oheim

## SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement  
 SVE5 Neurosciences et troubles du système nerveux

## THEMES OF THE UNIT

The 'Saints-Pères Paris Institute for the Neurosciences' (SPPIN, UMR 8003) is a neuroscience research institute that aims at characterising mechanisms underlying higher brain functions, from synaptic transmission to the activity of neuronal networks and how they translate into specific behaviours. To achieve these goals, the SPPIN uses a multidisciplinary strategy combining optical physics, biophysics, biochemistry, molecular biology, electrophysiology, imaging, neurophysiology and behavioural experiments and performs multiscale studies from single molecule to small networks of cells. A hallmark of the SPPIN is its strong commitment in instrumental and technological developments, especially in super-resolution and two-photon microscopy, which position the unit at the forefront of neuroscience methods at the international level. Over the previous contract period, this project has been conducted by seven independent teams. These include four teams (Teams 1–4) that joined the SPPIN when it was created in 2019, one team (Team 5) that emerged from an existing SPPIN team and two novel teams (Teams 6 and 7) created in 2022. Another team (Team 8) will join the unit at the beginning of the next contract. Team 1 combines biophysics and imaging to explore the contribution of different astrocyte populations to the cerebellum function and signalling. Team 2 investigates how sensorimotor information is encoded, integrated and translated by the cerebellar cortex and explores the recruitment and the role of the local inhibitory network during motor and navigation tasks. Team 3 investigates all aspects of the motor units, from motoneurons and their regulatory circuits in the spinal cord to the development and pathologies of the neuromuscular junctions, and develops new strategies based on repetitive magnetic stimulation applied at the spinal level to repair spinal cord injury. Team 4 investigates lysosomal functions with a focus on the lysosomal membrane, and especially their role in lysosomal storage disorders and neurodegeneration. Team 5 develops advanced optical techniques for biological imaging, with the aim to characterise and control the optical properties of wavefields through random and complex media. Team 6 investigates how molecular mechanisms contributing to the processing of inhibitory and excitatory inputs in neurons are integrated into neural circuits and translated into affective and emotional behaviours. Team 7 investigates the molecular mechanisms underlying neuronal functions and behaviour, with a focus on the role of importin nuclear transport factors in physiological and pathological conditions. During the future contract, Team 8 will investigate spatial orientation and motor control and especially how the brain codes and combines information arising from internal and external sources to perceive the environment, to produce a sense of orientation, and to execute appropriate behaviours. The SPPIN also includes a shared infrastructure that provides SPPIN scientists with administrative and technological supports and is in charge of the development of shared technologies and methods such as:

- i) a light-sheet microscope designed for micro-, meso- and macroscopic observations,
- ii) a universal, rapid and non-noxious, tissue clearing technique
- iii) and the preparation and characterisation of hiPSCs and organoids.

## HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The SPPIN was created in January 2019 as the result of a restructuration of the neurosciences at the Saints-Pères Biomedical Sciences Site (today designated as 'Campus Saint Germain'), which led to the merge of three former CNRS units working in the field of Neuroscience:

- i) the CNRS UMR8118 'Laboratoire Physiologie du Cerveau', from which Teams 1 and 2 was created,
- ii) the CNRS UMR 8242 'Centre de neurophysique, physiologie, pathologie' from which Team 3 emerged
- iii) and the CNRS UMR 8250 'Laboratoire de Neurophotonique' from which Team 4 was created, and one researcher also joined Team 1.

The SPPIN occupies dedicated lab and office spaces with a total surface of around 1,500 m<sup>2</sup> on the 3<sup>rd</sup>, 4<sup>th</sup>, and 6<sup>th</sup> floors of the Saints-Pères Faculty building (Campus Saint Germain) located in the center of Paris, where the newly created teams have received rehabilitated or renovated space with air-conditioned labs.

## RESEARCH ENVIRONMENT OF THE UNIT

The SPPIN benefits from an excellent environment at the Campus Saint Germain which regroups several disciplines (physics, chemistry, pharmacology...) applied to the life sciences. It is also one major French training site for medical students, and houses several Master programs (Biomedical Engineering, Neuroscience, ...). Finally, the

core facilities of the *Unité Mixte de Service BioMedTech Facilities*, CNRS UMS 2009, Inserm US 36, runs and develops the on-campus common services, platforms and shared research infrastructure (animal housing, mechanical workshop, imaging core facility, etc.). The SPPIN personnel is highly involved in the UMS at many levels, such as the level of the deputy director, the scientific heads or co-heads of individual platforms, or as members of the various user committees. Within the campus, the SPPIN collaborates with other units, including the Laboratory of Chemistry and Pharmacological and Toxicological Biochemistry (LCBPT, CNRS UMR8601), the Integrated Neuroscience and Cognition Center (CNRS UMR 8002), and the MSC-biomed laboratory (an on-site antenna of the *Matières et Systèmes Complexes* laboratory, CNRS UMR 7057). The SPPIN is one of the founding members of the UPC-wide, multisite INC Neuroscience and Cognition Institute as well as a major actor in the Greater Paris Region Excellence Cluster 'DIM C-BRAINS', of which the SPPIN's director is one of the members of the executive board. The SPPIN has also been for many years a co-organiser and hosting institute for the Paris Neuroscience Spring School, and currently for its 13th edition. The two teams of SPPIN that focus on instrumentation (Teams 1 and 5) are active members of the CNRS C'Nano Excellence network (CNRS UAR 2205, <https://cnano.fr/en>), as illustrated, e.g. by the NANOSCALE2022 international conference organised on-site. The same teams run valorisation projects, either with the Greater-Paris Valorisation agency (SATT/ERGANE0), or directly with companies.

### UNIT WORKFORCE: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	6
Directeurs de recherche et assimilés	8
Chargés de recherche et assimilés	6
Personnels d'appui à la recherche	13
<b>Sous-total personnels permanents en activité</b>	<b>32</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	5
Personnels d'appui non permanents	15
Post-doctorants	0
Doctorants	17
<b>Sous-total personnels non permanents en activité</b>	<b>37</b>
<b>Total personnels</b>	<b>69</b>

### DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons at 31/12/2022. Non-tutorship employers are grouped under the heading 'autres'.

Nom de l'employeur	EC	C	PAR
CNRS	0	11	9
UNIVERSITÉ PARIS-CITÉ	7	0	4
AUTRES	1	3	0
<b>Total personnels</b>	<b>8</b>	<b>14</b>	<b>13</b>

## GLOBAL ASSESSMENT

The SPPIN is a young institute created in 2019 as a result of a bottom-up initiative carried by a group of scientists with expertise in Optics, Biophysics, Molecular and Cellular Neurosciences and Neurophysiology and sharing a common set of values and ways of functioning. Thanks to the remarkable work carried out by the unit director and all the unit's staff whom he has succeeded to federate, the SPPIN has become within a few years a thematically and methodologically coherent, respected institute. A hallmark of the SPPIN is its original positioning at the interface of optics and biophysics and fundamental neuroscience with a strong and well-recognised technological component, which collectively provided the unit identity and visibility at the national and international levels, as shown by its capacity to federate existing teams, create new ones (Team 5) and attract talented young scientists and/or team leaders (Teams 6 and 7) over the reporting period. Although the SPPIN is made of seven research teams that develop their own research projects in an independent manner, the unit has implemented a mutualised support service (called the Core Unit) with a critical mass of highly skilled engineers/technicians, that not only provides all research teams with administrative, IT and technological support, but also orchestrates the development of new technologies or methods in the fields of microscopy, organoids and tissue clearing. The Core Unit has been tremendously successful over the past years, as shown by:

- i) the conceptualisation, prototyping and construction of a modular light-sheet microscope designed for micro-meso- and macroscopic observations (M-Cube) that is currently being used by 6 teams of the SPPIN,
- ii) the development of a universal, extremely rapid and non-noxious, tissue clearing technique that was patented and has been largely diffused to the community;
- iii) and the implementation of several human iPSC-derived brain organoids.

The SPPIN also stands out by its technological developments in photonics and microscopy, including the conceptualisation and development of a fast, large-field, high-resolution two-photon spinning microscope and the development of compressive three-dimensional super-resolution microscopy with speckle-saturated fluorescence excitation that allows considerable reduction of acquisition time and photobleaching. However, some of the developments still remain to be applied to the biological questions addressed by the unit. Regarding the scientific production, the SPPIN published 96 articles over the reporting period, with roughly 30 of them in the excellent journals, such as Cell, eLife (n=3), PLoS Biol, Curr Biol, Nat Chem, Nat Commun, Brain and Cereb Cortex. However, only a handful of publications involved more than one team, suggesting that most of the joint efforts of the teams to develop collaborations have yet to materialise in terms of publications. Among the major scientific achievements of the SPPIN, one can quote:

- i) the fine characterisation of the 3D architecture of the enteric nervous system by using the new tissue clearing method combined with a label-free approach based on tissue autofluorescence and the use of the fast 2-P microscope;
- ii) the description of a new form of associative plasticity of granule cell inputs to cerebellar Purkinje cells;
- iii) the demonstration that Purkinje cells in the cerebellum facilitate movement refinement by converting movement error signals into graded signals that encode the error's direction and magnitude;
- iv) the discovery that the most vulnerable motoneurons in a preclinical model of amyotrophic lateral sclerosis are hypoexcitable;
- v) and the characterisation of the physiological roles or effects of new lysosomal transport mechanisms in cancer and neurodegenerative disorders.

The SPPIN has implemented a well-structured management organisation made of the Direction Committee, the Team Leader Committee, the General Assembly and the Unit Council that collectively ensure collegiality and fluidity of the decision-making process as well as a good spirit and strong cohesion within the institute. A particular attention is paid to early career scientists (trainees, PhD students and postdocs) who have many opportunities to interact in a convivial atmosphere and to present their data during the regularly organised progress meetings gathering all SPPIN staff, as well as young team leaders who benefit from a mentoring program that is an important asset for their successful integration within the institute. The SPPIN scientists occasionally give lectures to the lay public in France and abroad, but their scientific outreach activities remain sparse and could be enhanced. However, the SPPIN links with the economic world are remarkable, with seven patents filed over the reporting period, three pre-maturation projects funded by the SATT, numerous partnerships established with various companies (Olympus, Nikon, Zeiss, Interherence, TILL. i.d, Dassault and Rapp photonics, Photon Lines, Essilor Instruments) and the large diffusion of the innovative tissue clearing method developed by the institute through the Idylle company.

All in all, the SPPIN is an excellent multidisciplinary institute which has reached maturity within a few years and should rapidly capitalise on its recent technological developments and scientific successes to further enhance its visibility in France and abroad.

## DETAILED EVALUATION OF THE UNIT

### A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous committee recommended that the SPPIN keep up its high productivity and grant application success through the submission of publications combining technical innovations with novel discoveries, and to submit joint publications involving several teams and/or emphasising biomedical implications of their work. During the reporting period, the SPPIN kept a similar productivity, compared to the corresponding teams in the previous contract period. Overall, the SPPIN scientists published around 100 articles. Around 50% of them were published excellent journals, five of which were in outstanding journals. Some of them combined technical innovations with novel observations (see, for instance, Rakotoson et al. *Front Neuroanat*, 2019; Pascucci et al. *Nat Commun*, 2019). However, the number of publications involving several SPPIN teams remains quite low (4 over the reporting period).

The committee recommended that the SPPIN set up a program for transnational PhD student and postdoc exchanges. To respond to this recommendation, the SPPIN director has initiated negotiations about a transnational (Franco-German) PhD program, but this project failed due to the Covid-19 pandemics.

The committee recommended that the SPPIN integrate all teams into a collaborative network. Since its creation, the SPPIN has set up the so-called Core Unit, an original structure funded by the unit and in charge of developing collaborative research projects involving at least three SPPIN teams to provide a shared research infrastructure that could not easily be accessed by a single team. Over the reporting period, the Core Unit has been very successful, as it conceptualised, prototyped and built a compact, modular light-sheet microscope designed for correlative micro-meso- and macroscopic observations (M-Cube) that is currently being used by 6 SPPIN teams. The Core Unit also implemented and patented a universal, rapid and non-noxious tissue clearing technique.

The committee recommended that the SPPIN implement computer modelling through the recruitment of additional teams or through collaboration. This remains to be done but the SPPIN hosted a German researcher for a short period to work on computational models of spinal locomotor circuitry.

The committee recommended that the SPPIN improve gender balance in leading positions. There will still be only one team (out of eight) co-headed by a woman in the next contract period. So, there will be still a strong gender imbalance in leading positions.

The committee recommended that the SPPIN create opportunities for informal interactions between members of different teams. To respond to this recommendation, the SPPIN has created a new, large common room equipped with a white board, large screen, and audio/video equipment for hybrid meetings and seminars to foster informal discussions between the SPPIN's teams and staff and cohesion within the unit. Furthermore, the teams have implemented frequent meetings and committees to encourage internal collaborations.

The committee recommended that the SPPIN continue on its course to develop and apply novel imaging methods to brain research towards as a scientifically outstanding and internationally highly visible center for imaging-based neuroscience research. Over the reporting period, the SPPIN has been very active in developing and applying novel imaging methods (development of the M-Cube light-sheet microscope, conceptualisation and development of a fast, large-field and high-resolution two-photon spinning microscope in collaboration with TILL Photonics in Gräfelfing/Munich, use of a compressive sensing approach to achieve efficient three-dimensional super-resolution microscopy, etc.).

Overall, the SPPIN followed the majority of the recommendations of the previous committee.

## B – EVALUATION AREAS

### EVALUATION AREA 1: PROFILE, RESOURCES AND ORGANISATION OF THE UNIT

#### Assessment on the scientific objectives of the unit

Overall, the scientific objectives of the SPPIN were considered as excellent to outstanding by the committee. The scientific objectives of the unit are ambitious and well aligned with advancing knowledge and innovation in the field. The emphasis on developing a multiscale integrated analysis indicates a holistic approach to research, which is essential for addressing complex biological systems. Moreover, the incorporation of high-cut technological innovations indicates a commitment to leveraging cutting-edge tools and methodologies to push the boundaries of scientific inquiry, even though they often remain to be applied to the biological questions addressed by the unit. The initiative to implement transverse research programs underscores a collaborative and interdisciplinary approach to problem-solving, and accelerates innovation. By prioritising strategic filing of patents for commercialisation, the SPPIN demonstrates a proactive approach to maximise the impact of its research outcomes.

#### Assessment on the unit's resources

Overall, the committee considered that the SPPIN resources are excellent to outstanding. The SPPIN benefits from strong financial support, competitive fundings, and extensive, well-equipped space. The unit has a recurrent funding of 0.224 M€, with 149 k€ from CNRS (2/3) and €75k from UPCité (1/3). In the 2017–2022 period, the unit secured twenty research contracts totalising 7 M€, most from competitive calls (18 ANR including 11 as coordinator, 1 JPND as partner), thus emphasising the significance of competitive funding. The unit boasts a significant park of recent and top-of-the-line instrumentation, including custom-built and unique equipment. These include 6 two-photon microscopes (4 for *in-vivo* recordings, 2 for slice work), a setup for holographic light stimulation of optogenetic actuators, various super-resolution techniques, and a light-sheet microscope. Efforts are undertaken to adapt the space and provide shared facilities, thereby contributing to a collaborative and dynamic research environment. In terms of human resources, the unit is composed of 22 permanent researchers (including associate professors/professors with heavy teaching duties), 28 technical staff (40% permanent) and seventeen PhD students, but no postdoctoral fellow at the end of 2022.

#### Assessment on the functioning of the unit

Overall, the committee considered that the functioning of the unit is excellent to outstanding. The SPPIN has implemented an efficient, multi-level management structure that ensures cohesion, collegiality, as well as transparency and reactivity of decision-making, and seems to be well accepted by the unit's staff. If the SPPIN is made up of 7 scientifically autonomous research teams that define their own scientific strategies, it has created an original structure (the Core Unit) in charge of transverse axes and of developing mutualised technologies that have proved its effectiveness over the past years.

*1/ The unit has set itself relevant scientific objectives.*

#### Strengths and possibilities linked to the context

The SPPIN's research policy lies in its promotion of scientific independence, collaborative initiatives, strategic planning for career development, commitment to innovation and patents, and adaptability to challenges. The scientific production is devoted to the targeted publication in high-impact journals, a diverse publication portfolio (1/3 of the articles are in journals with a large readership such as Cell, eLife, PLoS Biology), and an appropriate volume of production (~ 100) is provided relative to the unit's size (mean of >5 articles per PI during the reporting period). The unit also displays adaptability during the reorganisation, commitment to research integrity and ethics, and a proactive stance towards open science. These strengths contribute to the unit's



reputation, impact, and its ability to navigate changes effectively providing a vibrant and impactful research environment.

### Weaknesses and risks linked to the context

Although the SPPIN is strongly committed in the development of tools, methods and technologies that are especially relevant to the neuroscience field, their application to the biological questions addressed by the Unit remains sparse.

## *2/ The unit has resources that are suited to its activity profile and research environment and mobilises them*

### Strengths and possibilities linked to the context

The SPPIN exhibits strengths in diversified funds and competitive funding success. In particular, the SPPIN benefits from a mix of recurrent funding and competitive funding, demonstrating financial stability and the ability to secure additional resources through successful grant applications, at the national (18 ANR, 11 as coordinator) and international (1 JPND, 1 NIH, 2 Eureka-Eurostar as partners) levels. The presence of a large park of recent and top-of-the-line instrumentation, including custom-built and unique equipment, enhances the unit's research capabilities and positions it at the forefront of technological advancements in its field. Another strength is the ongoing effort to renovate and adapt the lab and office spaces to accommodate new teams and changing research needs, thus indicating a commitment to providing a conducive and up-to-date research environment. Its collaborative infrastructure with commitment to team interaction (i.e. the core unit and seeding funds are used to promote collaborative studies), in-house workshops, strategic location in a dynamic campus with research in physics, chemistry and biology nearby, and efficient budget utilisation, position it as a robust and dynamic research entity. The unit has also experienced and well-equipped research teams, as demonstrated by the existence of six home-made two-photon microscopes, specialised setups (phase imaging, super-resolution speckle imaging), and a light-sheet microscope, showcasing the unit's commitment to cutting-edge research.

### Weaknesses and risks linked to the context

While the SPPIN has been successful in securing competitive funding, there is a potential risk associated with dependence on external grants. Fluctuations in funding availability or unsuccessful grant applications could impact the unit's financial stability. Further weaknesses are the risk of equipment breakdown, budgetary constraints, limited recurrent funding, potential space constraints, ageing equipment challenges, limited autonomy in budget planning, potential recruitment challenges, and uncertainties in the external funding environment.

The implementation of a multi-year strategy for presenting a single SPPIN candidate for CNRS positions may face challenges. External factors, evolving research priorities, or unexpected events could impact the effectiveness of this strategy. The reliance on CNRS permanent positions as a significant aspect of the SPPIN strategy may limit flexibility in workforce planning, considering the scarcity of such positions. While the mentoring program for young faculty is a strength, the diverse responsibilities mentioned (research funding, recruiting, defining research lines) could be overwhelming. Ensuring effective mentorship and support for the mentees may require additional resources and structured programs.

## *3/ The unit's practices comply with the rules and directives laid down by its supervisory bodies in terms of human resources management, safety, environment, ethical protocols and protection of data and scientific heritage.*

### Strengths and possibilities linked to the context

The SPPIN has implemented a well-structured multilayer governance that ensures collegiality and transparency of decision-making. It includes the Direction Committee, which meets every week to deal with day-to-day administrative and scientific issues, the Team Leader Committee, which meets every other week and is the central place for decision-making regarding the SPPIN scientific policy and any strategic issues, and two consulting bodies, the General Assembly, which meets once a year, and the regulatory unit council, which meets three times per year. The SPPIN's scientific strategy also relies on an international SAB that gathers renown scientists from France and abroad and is consulted for recruiting new teams and team restructuration, as well as for validating interviewed candidates but, surprisingly, not for the teams' scientific strategies. A deputy director will be appointed for the next term, which is a wise decision given the increase in the unit size and the

constant increase of the daily administrative duties falling to unit directors. The SPPIN complies with the rules of its institutions regarding recruitment and human resource management: open positions are published on the dedicated institutional sites and the different stages of recruitment follow the CNRS and University Paris-Cité procedures. Annual interviews of technical staffs (permanent and non-permanent) are often conducted successively by the unit director and the line managers, which ensures a close follow-up of careers. A large proportion of the technical staff (especially the newly recruited ones) are affected to the Core Unit in order to mutualise resources and workforces and to offer engineers better career opportunities. The promotion rate for technicians/engineers is satisfactory (4 out of 13 permanent staff over the reporting period). The SPPIN has implemented a mentoring program dedicated to young faculties, which is an important asset for the success of newly integrated scientific staffs and/or team leaders. The SPPIN is strongly committed in safety/security issues. It appointed three prevention assistants (one for each floor where the unit is located) who are responsible for ensuring the application of health & safety rules and for establishing internal procedures. Newly arrived staff undergo a mandatory safety training as part of the newcomer welcome process. The SPPIN strictly follows the procedures and recommendations related to the prevention of environmental risks in terms of chemicals, radioactivity and biological products. As part of University Paris-Cité, it also applies the business continuity plan of the university that deals with emergency situations. With regard to the protection of scientific data, the unit applies the French and EU data safety regulations. It has appointed specialised IT engineers who manage the SPPIN information system in close collaboration with the IT department of the University, giving access to a powerful computing infrastructure. The unit has implemented a data preservation strategy that relies on *i)* a 1-TB personal data backup space for each user with data history preservation and *ii)* a scientific data archiving system, which guarantees the protection of experimental data and offers a large space for the joint work of the teams. Remote backups on servers are present in a different room and in another site of the University, minimising the risk of data loss.

### Weaknesses and risks linked to the context

The dispersion of the teams between different floors of a huge building is detrimental to scientific interactions between the teams and the cohesion within the unit, even though big efforts have been made since the creation of the SPPIN to create common spaces allowing for scientific interactions and informal discussions between the teams. While women are quite well represented in the governance bodies of the SPPIN, they are underrepresented among the team leaders (2 out of 10 at the beginning of the future contract and in the SAB (1 out of 6 members)). The newly created teams (in general of small size) suffer from a lack of technical support. There is no human resource contact person to provide information to the staff employed by the University. It seems that the SPPIN has not yet implemented an electronic laboratory notebook, which would strongly guarantee data traceability, durable follow-up of experiments, rapid access to data and aid to decision-making.

## EVALUATION AREA 2: ATTRACTIVENESS

### Assessment on the attractiveness of the unit

The SPPIN's attractiveness is excellent, as shown by *i)* the recruitment of two new team leaders during the previous contract, *ii)* the fundraising capacity of SPPIN scientists (~7 M€ collected over the reporting period from various national and international agencies), *iii)* their participation in international programs (CNRS-Univ of Toronto 'Twin Scholar' program, cooperation between the University Paris Cité and Bar-Ilan University (Israel)), *iv)* the organisation of international meetings or sessions at meetings (GRC, Neurochem. Soc. Meeting, Nanoscale meeting etc.) and *v)* their participation in editorial boards. SPPIN researchers also received around twenty awards, including prestigious prizes from academic and private institutions (Sackler, Tenne and Krill prizes, CNRS medal).

- 1/ *The unit has an attractive scientific reputation and is part of the European research area.*
- 2/ *The unit is attractive because for the quality of its staff support policy.*
- 3/ *The unit is attractive through its success in competitive calls for projects.*

#### 4/ The unit is attractive for the quality of its major equipment and technical skills.

##### Strengths and possibilities linked to the context for the four references above

The SPPIN has been very successful in attracting new team leaders (2 joined the SPPIN over the evaluation period and one will join it at the beginning of the next contract to manage Team 8 with another SPPIN scientist). The SPPIN also recruited three assistant professors and a full professor in Neuroscience. The SPPIN's attractiveness benefits from the implementation of a mentoring program directed towards young faculty members to help them find funding, recruiting co-workers, defining and pursuing an original research line, supervising post-docs and PhD students, collaborating with other teams, doing on-site politics, teaching and maintaining an international scientific visibility on conferences and symposia, etc. The SPPIN received ten visiting professors from prestigious foreign universities (University of Kyoto, Max-Planck Institute in Göttingen, Bar-Ilan University, Yale University, Max-Delbrück Zentrum in Berlin etc.).

Reciprocally, the SPPIN director was invited as a Joseph Meyerhof distinguished professor at the Weizmann Institute. The SPPIN scientists obtained a large number of competitive grants, which reflect the relevance of the research topics covered and their contribution to global research strategy at the national and international levels. These include international grants (two Eurostars grants, Neurodegenerative Disease Research (JPND), ERA-NET Neuron, NIH, all as partners), ANR grants (18 over the evaluation period totalising ~ 4 M€, 11 of which is being coordinated by SPPIN members) and from other French public agencies (IDEX, SATT, France BioImaging, DIM C-Brains, Cancéropôle, SESAME...), and grants from national (Fondation de France, Association pour la recherche sur la SLA, AFM, la Ligue contre le Cancer, Vaincre les Maladies Lysosomales, Fondation Alzheimer) and international (Thierry Latran Foundation, Radala Foundation for ALS Research, Cystinosis Research Foundation) foundations, totalising ~1.5 M€.

The SPPIN's attractiveness relies on its large park of recent, state-of-the art instrumentation, many of which are being custom-built, which is quite unique. These include six two-photon microscopes equipped for electrophysiology (four of them allowing *in vivo* recordings, and two being used for recordings on slices), one setup allowing holographic (spatially targeted) light stimulation of optogenetic actuators, several setups offering different super-resolution techniques, and a light-sheet microscope. The attractiveness of the SPPIN also benefits from the technological developments orchestrated by its core unit which resulted in an entire pipeline for multi-scale tissue imaging from the  $\mu\text{m}$  to cm, including tissue clearing, labelling and sample preparation. The quality of technological developments made at the SPPIN is shown by the recognition of one of its teams 'R&D platform' of the France-BioImaging (FBI) infrastructure, the French Node of the European research infrastructure euro BioImaging. Scientists of the SPPIN (including the youngest ones) were recognised for excellence through a number of prizes (Sackler Prize, Tenne Prize, Krill Prize for excellent young scientists, CNRS medal of honour - 2) and several awards at international meetings (best talk at the 9<sup>th</sup> Young Medicinal Chemists' Symposium from the European Federation for Medicinal Chemistry, Young Investigator Award at the 21<sup>st</sup> Workshop of the European Study Group on Lysosomal Disorders, etc.).

The SPPIN scientists are regularly invited to give talks at international conferences and symposia (Biophys Soc Annual meeting, European Microscopy Congress, ENCALS meeting, European Calcium Society meeting, Israeli Molecular Neuroscience Society Meeting, Polish Neuroscience Society meeting, etc.), or seminars at several universities or research institutes. They organised several meetings or meeting sessions (3rd Gordon Research Conference (GRC) on Organellar Channels and Transporters, Neurochem. Soc. Meeting, the Nanoscale2002 international conference on axial super-resolution microscopies, the 'Let's meet at the NMJ' European colloquium, etc.). Several researchers of the SPPIN are editors or members of the editorial board of scientific journals (Frontiers in Cellular Neuroscience, Frontiers in Neuroanatomy Microscopy Technique & Research), and members of research governing bodies or evaluation committees (C-DIMS, ED3C doctoral school, the French Observatory of Micro- and Nanotechnologies, INSERM CSS7, the Scientific Advisory Board of the DFG research center SFB in Homburg).

##### Weaknesses and risks linked to the context for the four references above

The constant change in the organisation of the University and its successive re-naming from Paris 5 University to Paris Descartes University, then to University of Paris to finally University Paris-Cité over the past decade has been detrimental to the legibility of the University's policy and the visibility and attractiveness of its affiliated units, such as the SPPIN. For instance, the turmoil created by the fusion of Paris Descartes and Paris Diderot universities resulted in a loss of an Excellence chair package and the recruitment of the SPPIN's candidate at Pasteur institute. There are limited collaborations between the SPPIN and other local neuroscience institutes, and the emerging initiative federating the neuroscience community within the University Paris-Cité needs to be consolidated by concrete actions. The low number of permanent researcher/faculty positions at CNRS and University Paris-Cité makes it difficult for the SPPIN to attract talented young scientists. Likewise, the increasing gap between the living cost in Paris area and the relatively low salaries offered to young scientists makes difficult to attract students, post-docs and young researchers even though the SPPIN should consider opportunities offered by the Atip/Avenir and Chaire de Professeur Junior (CPJ) programs. In the same line of thinking, the difficulty of recruiting tenured technicians and engineers following retirements and mobilities has led to a drop

in the technician engineer/researcher ratio in the unit which seriously compromises the pursuit of technological developments and the sustainability of the technological know-how that are the hallmark of the SPPIN.

### EVALUATION AREA 3: SCIENTIFIC PRODUCTION

#### Assessment on the scientific production of the unit

The scientific production of the five main teams is globally excellent. The teams have all produced a reasonable number of publications, ranging from 11 to 23 articles, with a combined total of 96 publications. There are only a handful of publications that involve more than one team, indicating that the impact of collaborations within the unit in terms of publications remains to be seen. Roughly 30% of the publications are in excellent journals, suggesting that the unit's researchers are able to publish in high quality journals including Cell, eLife, PLoS Biology, Current Biology and Nature Chemistry. The citation rates for the unit's production are around what would be expected. However, the number of excellent papers is less than ten, which implies that the unit's citation rates could be improved. It is notable that the percentage of publications in journals that are not open access is commendably low (around 8%), although this could be further improved. It is important to note that the report provides no information about the publications of the two new teams, and it is clearly too soon to evaluate the production of these teams.

- 1/ *The scientific production of the unit meets quality criteria.*
- 2/ *The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.*
- 3/ *The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.*

#### Strengths and possibilities linked to the context for the three references above

The fact that the roughly 30 of the publications are in excellent journals indicates that the unit's researchers have been able to target high-quality journals that include Cell, eLife (3 publications), PLoS Biology, Current Biology, Nature Chemistry, Nature Communications, Brain and Cerebral Cortex. The SPPIN's scientists have also published high-quality review articles in journals that include Trends in Neuroscience. The volume of the SPPIN's scientific production is roughly what would be expected for a unit of its size. Given that there are 22 full-time researchers, and eight with teaching responsibilities, this means that there are roughly 25 equivalent full-time researchers. And given the lab produced 96 publications during the six-year period under evaluation, this amounts to around a little under one publication per full-time researcher per year. Given that the period has been marked by a considerable degree of reorganisation, this is a perfectly acceptable level of activity. There is no reason to doubt that the unit's research complies with the principles of research integrity and ethics. In terms of open science, it is notable that only a small fraction of the unit's output is not already in open access journals. This could undoubtedly be fully resolved for the next reporting period.

#### Weaknesses and risks linked to the context for the three references above

The two new teams (Teams 6 and 7) reported no publications for the period under evaluation. Since they only arrived recently, it is normal that SPPIN would not have been on the list of affiliations for research that was produced elsewhere. The self-evaluation document notes that moving and setting up in a new environment will not have made it easy to produce new research.

### EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

#### Assessment on the inclusion of the unit's research in society

The inclusion of the SPPIN research in society is excellent to outstanding. The SPPIN is strongly supported by

numerous charities (> 1.2 M€ collected during the reporting period) and has developed interactions with patient associations such as Fondation Vaincre les maladies lysosomales. The SPPIN's scientists are strongly committed in teaching and student training as well as in scientific integrity, but their participation in outreach events is sparse and the diffusion of scientific knowledge to the lay public could be increased. The interactions of the unit with the economic world are outstanding, with 7 patents filled over the reporting period, three pre-maturation projects funded by the SATT, partnerships with several private companies (Nikon, Zeiss, etc.) and the ongoing creation of two start-ups.

- 1/ The unit stands out for the quality and the amount of its interactions with the non-academic world.*
- 2/ The unit develops products for the cultural, economic and social world.*
- 3/ The unit shares its knowledge with the general public and takes part in debates in society.*

#### Strengths and possibilities linked to the context for the three references above

The SPPIN is committed to inclusion and two of its members participated in the national DuoDay operation with students suffering from disabilities. Several SPPIN's scientists also participate in the activities of foundations, study groups and patient organisations (STAR Foundation [USA], Fondation Vaincre les maladies lysosomales, European Study Group on Lysosomal Diseases, NCL Foundation, Association Réseau Mer). The SPPIN's scientists occasionally participate in outreach scientific events and give lectures to the lay public in France and abroad (e.g. public lecture on advanced imaging techniques organised by the Association Mer, conference on the contribution of new microscopies for young children in a German Private School, animation of the evening 'Science at the Bar', an open-to-the public satellite event of the NANOSCALE2022 conference, conference on 'the contribution of viruses for understanding the brain' organised by the local Rotary Club, conference in support of open peer review given to the United States House of Representatives). One SPPIN's researcher participated in a program called 'mille chercheurs' in frame of the Telethon. Another one co-organised the 'Brain Day' of the INC Neuroscience Institute, open to the public. The SPPIN is strongly committed in teaching. All researchers and University teachers regularly train visiting and ERASMUS students, L3 and Master students, PhD candidates and young post-docs.

The SPPIN also hosted several secondary school pupils for short internships and interns from schools that train future technicians. It has established contacts with other institutions that regularly send students, like the Institut d'Optique and the Université Technologique in Troyes. The SPPIN is also strongly committed in scientific integrity and ethics in science. One SPPIN's researcher is a co-founder and is still co-head of the Pubpeer foundation. The SPPIN supported Paris Hospitals during the Covid-19 pandemics. Together with other units of the Saint-Pères Biomedical Sciences Site (Campus Saint Germain), the unit provided hospitals consumables (masks, gloves, lab coats, hair restraints, hydro-alcoholic gel, PCR kits) and lab materials (lent syringe pushers, PCR devices, water baths, stirrers etc.). Regarding the development of products for the socio-economic world, the SPPIN has filed seven patents over the reporting period and is currently running three pre-maturation projects funded by the SATT (local greater Paris region valorisation agency), which is remarkable with respect of the size of the unit. The creation of two start-up companies dedicated to phase imaging and tissue clearing, respectively, is ongoing. The SPPIN's teams have developed long-stranding interactions with industry. Partnerships have been established with various companies, including Olympus, Nikon, Zeiss, Interherence, TILL. i.d, Dassault and Rapp photonics, Photon Lines, Imagine Optic and Hales, and Essilor Instruments. The Nanoscale2022 meeting organised by the SPPIN benefited from a large funding component from industrial partners that allowed an inscription fee waiver for students and young post-docs and the funding of poster and presentation awards.

#### Weaknesses and risks linked to the context for the three references above

The interactions of the SPPIN scientists with the general public and their participation in debates in society are sparse. The SPPIN does not participate in yearly organised scientific outreach events like 'la Fête de la Science' and 'la Semaine du Cerveau'. The interactions of the SPPIN with clinicians of Paris University hospitals are somewhat limited, in spite of the potential translational outcomes of some research projects conducted in the unit.

## ANALYSIS OF THE UNIT'S TRAJECTORY

The SPPIN is a young institute which was created with the goal to build an interface of biophysics, neuroscience and neurophysiology, and which within a few years has become a respected institute working in the field of neuroscience at the University Paris-Cité, in the area of Paris and more largely in France and abroad. This success relies on the capacity of the SPPIN to gather a critical mass of motivated and top-notch scientists who master a multitude of state-of-the-art technologies requiring high technicity, and an exceptional R&D potential, as shown by the publication and patent record. The SPPIN's director and PIs must be congratulated for this past success. Capitalising on its technological developments in optics, photonics and microscopy techniques and its exceptional attractiveness, the SPPIN has considerably strengthened its resources and workforce by the recent recruitment of several talented scientists and the creation of two new teams, and will continue to strengthen them with the creation of an 8th team at the beginning of the next term. These recruitments perfectly fit with the SPPIN's project and scientific policy and represent a unique opportunity to broaden the institute's fields of investigation to new research themes, while at the same time continuing to develop the research axes that have made its reputation and strengthening its multi-scale strategy, that combines investigations at the cellular level (neuronal signalling and trafficking) with studies of neural networks and circuits. Overall, the committee acknowledges that the SPPIN has now reached an optimal size, sufficiently large to have a critical mass and small enough to allow for true interactions, even though opportunities to recruit a few additional teams may be considered given the possibility of increasing the space allocated to the unit in the Saints Pères building.

The main challenge will now be to consolidate the newly implemented teams by favouring their interactions with the historical SPPIN's teams and the transfer of the unique technological know-how of the SPPIN to the new teams, by providing them technological support whenever possible and helping them to attract students and tenured scientists to achieve a critical mass. The SPPIN has a number of assets to make the integration of new teams and recruitment of new permanent scientists a success. These include its mentoring program dedicated to young PIs and its Core Unit. In this respect, given the limited number of technical staff permanent positions available at the CNRS and the University and the forthcoming retirement of several technical staff, the committee encourages the SPPIN to pursue its efforts to mutualise technical support in frame of the Core Unit by extending its expertise to additional techniques.

The committee acknowledges and endorses the SPPIN's positioning as a fundamental neuroscience institute, but it recommends that the institute better exploits the translational potential of some of its research by fostering interactions with the Groupement Hospitalo-Universitaire (GHU) Paris Psychiatry and Neuroscience, and clinicians. This would certainly offer new opportunities for applying to dedicated calls and attract medical students or clinicians interested in the research topics and technologies developed at the SPPIN.

Over the past years, the SPPIN has demonstrated excellent capacities to raise funds in response to competitive calls, which demonstrates its ability to become a leading neuroscience institute in France and Europe on the medium to long term and guarantees the feasibility of the projects of its teams. One important threat is, however, the ageing of key equipment and their replacement cost with limited funding opportunities. One of SPPIN's key assets is its strong partnerships with private companies for technological developments, and these should be encouraged. At the same line, the committee recommends that the SPPIN strengthens its interactions with other institutes working in the field of neuroscience in order to allow them to benefit from its unique technological know-how and to open up new possibilities for pooling resources and funding the replacement of the most expensive equipment. Another issue is the ageing of permanent staff in a low-recruitment national landscape and it is essential that the SPPIN remains proactive in attracting young scientists and technical staff by applying to European calls such as doctoral networks or Marie Skłodowska-Curie fellowships and considering all opportunities for the funding of young PIs who wish to set-up their teams.

## RECOMMENDATIONS TO THE UNIT

### Recommendations regarding the Evaluation Area 1: Profile, Resources and Organisation of the Unit

Given the translational potential of the research made in several SPPIN's teams (for instance for lysosomal disorders, neuro-muscular junction disorders and amyotrophic lateral sclerosis), the unit should increase interactions with Paris Hospitals and clinicians. This would offer new opportunities for funding and attracting medical students in the unit. In the same line of thinking, the SPPIN should also increase its interactions with other local Neuroscience institutes, both within Paris-Cité Université and beyond. Even though the SPPIN is already engaged in scientific exchanges with clinicians of the GHU and researchers of the Institute for Neurosciences and Cognition (INC) in frame of the '12 h 30 de la recherche' meetings dedicated to the fostering of translational research, there is certainly room for improvement in those fields.

The SPPIN should make an effort to transfer its innovative microscopy technologies to a dedicated facility. This can be through the Core Unit or/and the facility of the UAR Biomedtech. In that way the whole community could benefit from the technologies, the ageing equipment could be renewed and new funding and human resources opportunities could be created (through infrastructure projects like FranceBioImaging).

Most of the group leaders and the personnel who fill in the annual reports of the technical staffs seem not to fully understand the promotion and career advancement system. They need to follow a training or information seminar by the unit director or the institutions on how to fill in the annual reports and how the annual bonus are distributed among the technical staff.

### Recommendations regarding the Evaluation Area 2: Attractiveness

The committee recommends that the SPPIN's scientists take advantage of the originality of their research and technological developments, and of their strong international positioning to increase their participation in Doctoral networks and their application to Marie Skłodowska-Curie postdoctoral fellowships, in order to attract high-potential research fellows from abroad who will be potential candidates to CNRS/University tenure positions at the SPPIN. It also recommends that the SPPIN considers opportunities of funding such as the Atip/Avenir program, the 'Chaire de Professor Junior' (CNRS or University) packages and FRM funding for emerging teams, to attract young talented scientists and secure their position within the SPPIN.

### Recommendations regarding Evaluation Area 3: Scientific Production

The committee recommends that the SPPIN's scientists continue to exploit their technological developments and apply them to their biological questions. It also recommends that they pursue their efforts to increase the number of publications in top-notch journals. The committee recommends that the SPPIN increases the proportion of publications involving several teams of the unit, for instance by encouraging collaborations between the teams through the internal funding of common projects, in line with what was previously done at the level of the Core Unit.

### Recommendations regarding Evaluation Area 4: Contribution of Research Activities to Society

The committee recommends that the SPPIN's scientists, including PhD students and post-docs, participate more actively in yearly science outreach events, such as 'la fête de la Science', 'la semaine du cerveau' etc.

The SPPIN should also increase its interactions with the young public through, for instance, the participation in dedicated programs such as 'apprentis chercheur', in order to raise young people's awareness of research careers and encourage them to take up a career in research.

## TEAM-BY-TEAM OR THEME ASSESSMENT

**Team 1:** Biophysics of the Brain  
 Name of the supervisor: Martin Oheim

### THEMES OF THE TEAM

The overall research theme of the team is the study of neuron-glia interactions in the central nervous system (CNS) and enteric nervous system (ENS) through the development of unique, home-built optical tools for super-resolution and 3D tissue imaging. The group addresses scientific questions using *in-vivo* electrophysiology and optical recordings of glia and neurons in cell cultures, brain slices, hiPSC-derived 3D organoids, or mice. In particular, the team investigates the role of Fañanas cells of the cerebellum, the role of calcium microdomains in mouse and human astrocytes, ER/Plasma membrane interactions, as well as the role of glial pathways in the enteric nervous system. The group has made important contributions to the development of cutting-edge microscopes and imaging techniques. Team 1 is a founding member of the SPPIN since 2019.

### CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Following the recommendations of the previous report, the team has continued to apply cutting-edge imaging techniques to its biological questions, such as the large-scale neuro-anatomical imaging of brain organoids (e.g. Rakotoson et al., 2019), the organisation of glial and neuronal cells in the ENS (e.g. Hazart et al, 2022) or calcium microdomains in astrocytes (e.g. Schmidt and Oheim, 2020). The work on Fananas cells is highly innovative but still not published (two publications are in preparation). This line of research is highly relevant and proposes exciting research topics, in line with previous recommendations.

It was also recommended that specific efforts are made to increase the number of PhD students, particularly through international programs. However, during the reporting period, the group has trained only four new PhD students (vs. five previously), all recruited in 2021 and 2022. Only three Master students performed an internship in the lab (vs. more than 10 previously). Nevertheless, one student has been recruited and co-supervised in frame of an international program with the University of Toronto, in line with previous recommendations to the team. The quality of training is excellent as two Master students published articles in *Frontiers in Neuroanatomy* during their internship (Hazart et al., 2022; Rokotoson et al., 2019).

### WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
<b>Sous-total personnels permanents en activité</b>	<b>6</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	4
Post-doctorants	0
Doctorants	4
<b>Sous-total personnels non permanents en activité</b>	<b>9</b>
<b>Total personnels</b>	<b>15</b>



## EVALUATION

### Overall assessment of the team

This is an excellent to outstanding team that is internationally recognised for its work on designing and building novel microscopes and applying them to fundamental biological questions. The team leader is internationally highly regarded and the group is tremendously innovative. The team has been very active in protecting intellectual property and has shown outstanding activity in technology transfer through maturation projects financed by national and European initiatives. The team also shows strong collaborative links with industrial partners, including both small and large companies. The team has an excellent profile of external collaborations (Israel, Canada, Germany) and has a high international visibility. This high level of active technological valorisation seems to impact the team's academic production as well as the training of students. Accordingly, the team secured funding mainly from industrial contracts and technological valorisation, with more limited revenue from international or European funding agencies. The team would greatly benefit from strategic consideration to transform its excellent collaboration profile into attracting a significant cohort of international students.

### Strengths and possibilities linked to the context

The team has an outstanding activity in technology transfer through maturation projects financed by national and European initiatives (SATT Erganeo and UPC, EU-Eurostars). The team has also outstanding and highly productive relations with industry, as documented by its links with small and large companies (e.g. Interference; Olympus). Together with other SPPIN's teams (Teams 3, 4 and 5), the team has been a driving force in the development of a new, non-toxic, clearing technique that is now being transferred to Idylle for commercialisation. The team has been particularly active in protecting intellectual property through several patents (two patents filed in 2020 and 2022). One patent filed during the evaluation period by a member of the team (Armand et al., 2017) does not seem to reflect work from the current team. The team had a very good to excellent scientific production during the evaluation period, publishing eleven peer-reviewed articles with group members as first and/or last authors. The team secured funding mainly from industrial contracts and technological valorisation (288 k€), with limited revenue from international or European funding agencies (108 k€). The team leader has an outstanding reputation both nationally and internationally. In particular, the team is internationally recognised as a leader in microscopy. Members of the team have been invited to give conferences about biophotonics and biological imaging at twelve international meetings. The team is also well integrated in international networks (Uruguay, Israel, Toronto), and has organised the Nanoscale 2022 meeting, to disseminate results obtained in the context of the EU-funded NANOSCALE project together with Bar-Ilan University. This meeting incited follow-up grant applications with private companies (Interference from Germany) and to European funding bodies (ERC Synergy between the Oheim, Salomon and Enderlein groups). Group members have also received numerous scientific awards, including the prestigious Sackler Prize as well as professor chairs, such as distinguished Joseph Meyerhoff Professorship. The highly interdisciplinary research program of the group brings together scientists from different backgrounds (mainly Physics, Biology, and Physiology). The team has also successfully attracted visiting researchers from abroad at both senior and junior levels (Israel, Canada), making for a multicultural environment. The team hosted one visiting professor from Bar-Ilan University and appears to be a very attractive place for visits of international experts who significantly contributed to its high visibility. The team encourages the independence of young researchers by allowing them to lead their own project, to sign articles as last author and to evolve towards setting up an independent team.

### Weaknesses and risks linked to the context

The strong focus on new imaging technique development has resulted in a relatively large proportion of publications in specialised technological (13 out of 19 articles report technical innovation) rather than more Neuroscience- or Biomedical-oriented journals. During the evaluated period, only one out of four PhD students trained by the group published as first author (Hazard et al., Front Neuroanat 2022). Several articles by other PhD students are now in preparation, some of them covering biological questions such as the role of Fananas cells. The team possesses and maintains ageing equipment requiring high and costly maintenance and replacement (e.g. some femtosec-pulsed lasers are outdated in terms of spare items and repairing if needed as they are more than 10 years old). This potentially represents a considerable risk for the team and its projects. The team is strong in terms of international collaboration, but this is not yet translated in the acquisition of funding at the international level. However, the team has successfully secured funding through industrial contracts and technological valorisation (288 k€), with more limited revenue from international or European funding agencies (108 k€). The gender balance within the team is excellent (10 H/11 F), but the ageing of permanent staff and the low-recruitment rate of young profiles (particularly postdocs and students) put the team at risk for the

renewal of taskforce. In addition, the departure of engineers will compromise the know-how and hands-on knowledge of the team on critical techniques for most projects (e.g. anatomical and histochemical techniques). Engagement of the team with the public appears to be relatively low. Although the team has contributed to outreach events, the majority of engagement forums listed involved pre-existing collaborations. This strategy comes at a risk of a missed opportunity to engage the public, particularly with new students, postdocs and young researchers. One productive researcher of Team 1 is now heading the new Team 5 since 2019.

## Analysis of the team's trajectory

The team's success over the evaluation period in terms of scientific output, technological transfer, impact within the scientific community, and acquisition of funding clearly indicates that they will continue to excel in these areas in the coming years. The team's proposed trajectory, which is described in relatively general terms, is compelling and clearly builds on the scientific and technical achievements from the previous years. Particular focus will be placed on fundamental research using the techniques and instruments previously developed by the team. This includes *i)* studies on calcium signalling and membrane dynamics in cortical astrocytes using TIRF microscopy, *ii)* investigations on the physiological role of Fananas cells using electrophysiology and 2-photon holographic microscopy in cerebellar slices, and *iii)* exploration of the enteric system using 3D imaging techniques. However, these lines of research are relatively disparate, presenting two challenges that the team will need to address. The first challenge concerns the progressive departure of several members of the team during the next period, in a context of a low recruitment rate of students and young researchers. The second challenge will be to replace and maintain ageing equipment by securing important funding through competitive international grants and/or collaborative initiatives.

Given the team's previous experience, it is likely that it will be able to overcome these obstacles and generate interesting scientific findings.

Overall, the team's trajectory appears realistic in terms of expertise and already obtained results. The project based on newly developed optical techniques and innovative models (incl. iPS cells and minibrains) to investigate critical questions in neurobiology and physiology is excellent.

The team has several grants to start the next period and its excellent track record in securing funding with private partners during the evaluation period gives hope that it will be successful in acquiring additional funds during the next period.

## RECOMMENDATIONS TO THE TEAM

The team should pursue and accelerate its shift from technical development to investigating fundamental biological questions. Although the ongoing push to engage in maturation programs and technological transfer with private companies should be pursued, it should not come at the detriment of fundamental research on biological questions. The research program proposes exciting research projects, particularly studies on Fananas cells. This topic seems to be a promising avenue to achieve this objective and should probably be prioritised compared to other research lines.

The number of Master and PhD students should be increased. Active effort will be necessary to create strong links with the University, including the Faculty of Medicine, and attract candidates in a very competitive environment.

The team might suffer from a dramatic loss of human resources within the next period, after the departure of one of its senior scientists to create and lead Team 5, the retirement of most permanent scientists and technical staff, and the planned departure of another researcher to lead his own group. A clear strategy is needed to replace this loss and consolidate the team on the long term.

The team needs a clear strategy to:

- i)* restrict the number of projects and focus on a common line of research,
- ii)* and attract new, young members.

**Team 2:** Cerebellar Neurophysiology

Name of the supervisor: Thibault Colin/Brandon Stell

## THEMES OF THE TEAM

This team has brought together several senior researchers, who all share a longstanding interest in cerebellar neurophysiology. The team aims to understand cerebellar function by studying it at all levels, from molecules and synapses up to behaviour. The team develops three main axes:

- i) biophysics of synaptic transmission in the cerebellar microcircuits,
- ii) plasticity underlying sensorimotor adaptation
- iii) and neuronal activity during motor adaptation of awake behaving mice.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Several recommendations were made in the previous report, with mitigated success in implementing them. Maintaining scientific excellence through publication, funding, and international reputation has been mostly achieved. Twenty-three articles were published, 1.5 million euros were obtained, and one team co-leader was invited for 2–3 conferences abroad in the period.

The development of models linked to human diseases and collaborations with the industrial and non-academic world are not mentioned in the auto-evaluation document.

The outstanding level of training activity has been maintained, except for the fact that one of the senior scientists is still lacking the HDR diploma.

Concerning the team size, it has rather shrunk, but the gender balance is satisfactory.

Lastly, *in vivo* studies have been pursued and continue to be a large component of the scientific strategy.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	1
<b>Sous-total personnels permanents en activité</b>	<b>5</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	3
Post-doctorants	0
Doctorants	3
<b>Sous-total personnels non permanents en activité</b>	<b>8</b>
<b>Total personnels</b>	<b>13</b>

## EVALUATION

### Overall assessment of the team

This is an excellent team that investigates the organisation and function of the cerebellar networks, focusing on fundamental mechanisms underlying synaptic function and plasticity up to motor coordination. Highly ambitious *in vivo* studies during awake behaviour have been developed during the period, complementing a more established line of research on cerebellar synaptic plasticity and physiology. The team has continued to organise yearly an internationally recognised course in Neuroscience Recording, and to be active for open peer review through the management of the Pubpeer Foundation. The team has achieved a very good scientific output, with twenty articles over the 2017–2022 evaluated period. Grant resources have been excellent to outstanding during the period (1.5 M€ collected) but at a lower level at the end of the period.

## Strengths and possibilities linked to the context

The team works on the mechanisms underlying motor coordination, particularly those involving cerebellar circuits. All levels of investigation are pursued, from molecules and synapses up to network interactions, through *in vitro* and *in vivo* approaches. *In vitro* projects have focused on synaptic mechanisms, including synaptic plasticity, at specific glutamatergic and GABAergic synapses of the cerebellar networks. They have led to several outstanding publications, such as three articles in PNAS and two in eLife over the 2017–2022 period. *In vivo* projects combining behaviour and neuronal calcium imaging have been started over the evaluation period, and thus only reach now the level of efficiency required for full-size data collection. In the behavioural task, forelimb movements are required in order to move a water reward port, while perturbations may be applied to interfere with the consequences of the forelimb movement on the water port. This study, involving one PhD student, has led to two posters at SfN (2021, 2022). One of the team leaders has been invited for national and international presentations (Portugal 2018, USA 2018), which include a testimony to the US House of Representatives in support of open peer review. One DR emeritus has received the CNRS medal of honour (2019). During the evaluation period, the team has published twenty articles in peer-reviewed journals (including one review in TINS), of which fourteen were published with members of the team as first and/or last author. Some publications have appeared in renowned journals (Elife (2), Nat Commun (3), PNAS (3), Cerebral Cortex (1), J Neurosci (1)). One book chapter has also been published. The team has raised about 1.5 M€ from five ANR grants obtained by five different scientists of the team, and ending in 2020, 2021, 2022, 2023 and 2024. The team's ability to raise funding has thus been excellent to outstanding. Three PhDs are listed as currently being in the team (starting in 2019, 2019, 2022, but none before). Importantly, since its beginning fourteen years ago, members of the team have been major organisers of the internationally renowned annual course 'Optical Imaging and Electrophysiological Recording in Neuroscience' (2 weeks, 10 setups for hands-on sessions). This remarkable involvement of the team in training, as well as in supporting open science, could help attract young researchers.

The team benefits from the presence of two highly active and internationally renowned DR emeritus, who have a critical role in the team's research activity by leading most *in vitro* projects.

## Weaknesses and risks linked to the context

The team has suffered from an important decrease in size over the period, notably in permanent researchers. Sadly, two DR emeritus who were still very active passed away in 2021 and 2022, leaving some of the scientific projects not completed. One MCU left the team in 2020, and one DR became emeritus in 2018. The team currently hosts no postdoc and three PhDs at the end of their contract, so that there is a risk of workforce shortage to carry out the projects, notably the highly demanding *in vivo* studies. Many grant resources have ended or will end in 2024, which could put some scientific projects at risk. Concerning the scientific production, there has been an imbalance in productivity across the different projects. The team co-leaders have either not published or published only one article as co-author over the period (Front Cell Neurosci 2018). More than half of the articles have been contributed by DRs emeritus, and among the three PhD students who defended in 2023, only one has published a peer-reviewed article at this time.

## Analysis of the team's trajectory

Over the evaluation period, the team has embarked in state-of-the-art *in vivo* studies focused on the involvement of cerebellar networks in motor coordination, through imaging and electrophysiological recordings of populations of neurons. These projects have taken many years to develop, but represent highly innovative and exciting studies that are bound to reveal important mechanisms of cerebellar function. They will also offer a link between the *in vitro* mechanistic studies and their consequences at the behavioural level. Both *in vitro* and *in vivo* projects will be pursued. One *in vitro* project will involve a collaboration with a laboratory in Austria, with the support of a binational ANR/FWF grant for 2023–2025. The committee found the project promising for the five years to come, and suggest publishing more now that they have the technics on hands. The strong expertise of the team in synaptic physiology will surely help understand better how synaptic properties influence animal behaviour.

One researcher will leave the team in January 2025 to co-lead a new team (Team 8).

## RECOMMENDATIONS TO THE TEAM

The team should be more proactive to publish ongoing work, especially involving PhD students and/or postdocs. The permanent researchers of the team need to attract new PhD students and/or postdocs. The team should also pursue its efforts to apply for new grants. Only one collaboration concerning the 2023–2025 period is mentioned in the document, and efforts should be made to solve this issue.

**Team 3:** Motor-Neurons & Neuromuscular Junctions  
 Name of the supervisor: Boris Lamotte-d'Incamps and Daniel Zytnicki

## THEMES OF THE TEAM

The team studies the biology and pathophysiology of the motor system in the context of congenital myasthenic syndromes and Amyotrophic Lateral Sclerosis (ALS). Using *in vitro* and *in vivo* models, the team investigates new regulation pathways at the neuromuscular junction (NMJ) and the premotor network controlling motoneurons and its evolution during ALS. The team recently initiated a new axis of research on Spinal Cord Injury (SCI) and the development of new strategies to repair the spinal cord.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No recommendations were made on the scientific production and activities except a comment concerning the potential for interactions with the clinical world. The team is currently developing interactions with clinicians and collaborations for translational research. The team has submitted a patent at the SATT-LUTECH for the development of bio-implants for nerve reparation and developed a collaboration with the Cochin Institute to evaluate a new drug on inflammation in ALS. The team has close links with the hospital environment and the ARSLA patient association as well as the IRME association.

The previous committee considered that the interactions between the members of the team were not optimal due to a physical separation on two different floors. The team is still split between the 3<sup>rd</sup> and the 4<sup>th</sup> floor but its members remain in close proximity on the same side of the building.

Encouragement to take advantage of the creation of the SPPIN to integrate innovative technologies into the team's projects was also expressed. This objective has been partially achieved since two new projects are now developed in collaboration with Team 4 and the future Team 8.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
<b>Sous-total personnels permanents en activité</b>	<b>6</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	3
<b>Sous-total personnels non permanents en activité</b>	<b>4</b>
<b>Total personnels</b>	<b>12</b>

## EVALUATION

### Overall assessment of the team

This is an excellent to outstanding team that studies the physiopathology of the spinal cord in the context of the amyotrophic lateral sclerosis (ALS) and also now spinal cord injury (SCI). The team investigates both fundamental mechanisms and rehabilitation strategies after spinal cord injuries, axonal injuries and neurodegenerative diseases. The team has an excellent scientific production, both quantitatively and qualitatively with nearly 30 articles and reviews over the evaluated period. The team is excellent to outstanding in terms of industrial and clinical interactions with the submission of a patent on bio-implants for nerve reparation and the test of a new drug on neuroinflammation in ALS. The reputation of the team and its attractiveness are excellent with the recruitment of a professor in 2022.

## Strengths and possibilities linked to the context

The productivity of the team over the evaluation period has been excellent with fourteen research articles published as first or last and corresponding author for a total of 30 articles and reviews. One book chapter 'De la molécule au neurone' has also been published in 2018. The research is very well funded through the acquisition of highly competitive grants from ANR (2 as coordinator and 3 as partner) and charities (Thierry Latran Foundation, Radala Foundation for ALS, AFM) and from the Polish National Science Agency on international collaborations. The future team '(Patho-) Physiology of the Spinal Cord' benefits from the excellent reputation of the previous leaders and the excellent visibility and attractiveness of the team, which led to recruit an additional professor (UPC) in 2022 who will be the new team leader. The team will be further reinforced by the recruitment of an associate professor (UPC) in physics. These recruitments enable the team to perpetuate important know-how (particularly *in vivo* spinal cord recordings) and give the opportunity to develop new techniques and a new research axis on SCI with fundamental and preclinical approaches. The multiple interactions between the team's members on the different projects are also an important strength. The team develops a transverse axis to set up a method aimed at monitoring the rehabilitation of motor activity of the mice after SCI or after different treatments in the context of ALS. This method will benefit all projects of the team. Three PhD students were recruited during the previous contract. The team has been involved in training and interaction with society, by carrying the presidency of the ED3C doctoral school up to 2023, co-organising the 'Brain Day' of the INC institute (Saint-Pères location) and being member of the International Motoneuron Society.

## Weaknesses and risks linked to the context

The committee did not identify real weaknesses, but one point merits attention. The team has been facing an important change of its members with the departure in 2021 of a CNRS CR and a CNRS engineer, the retirement of a Professor in 2022 (now emeritus) and the upcoming retirement of the co-leader of the team (CNRS DR who should become emeritus). Even though a Professor has been recently recruited, and while some members, including the previous team leader, will remain in the team as emeritus, these marked changes in the team's human resources represents a major challenge for the future of the team and the execution of the different projects.

## Analysis of the team's trajectory

The team's trajectory is very coherent, consisting of the continuation of recently published work and new well-structured and well-funded projects but ending in 2024. The new PI (professor at UPC) has a strong experience in preclinical neuroscience matters and will develop new strategies based on spinal repetitive magnetic stimulation in SCI. The team will focus its research on two main spinal cord pathologies: amyotrophic lateral sclerosis (ALS) and traumatic spinal cord injuries (SCI). The research project is organised around four main axes. The two first axes, namely *i*) spinal motoneuron excitability and the regulation of inflammation in ALS, and *ii*) the contribution of the early defects of the neuromuscular junctions to the degeneration of motoneurons in ALS, are in logical continuation of the previous work on ALS. The recent recruitment of a professor and the arrival of an associate professor in physics bring new skills and offer the opportunity to open two new axes of research dedicated to *i*) the development of peripheral implants for repairing peripheral nerve injury and *ii*) the effects of repetitive trans-spinal magnetic stimulations after SCI on the regrowth of reticulospinal tracts, endogenous stem cell recruitment and cerebral inflammation. These lines of research are in perfect concordance with their previous work and are highly relevant and innovative.

## RECOMMENDATIONS TO THE TEAM

The permanent researchers of the team need to attract new PhD students and also post-docs from abroad. The team must be vigilant in the gender ratio among scientists.

**Team 4:** Membrane dynamics

Name of the supervisor: Bruno Gasnier

## THEMES OF THE TEAM

The main research topic of the 'Membrane dynamics' Team is the investigation of lysosomal functions with a focus on the lysosomal membrane, which remains poorly characterised, and especially its role in lysosomal storage disorders and neurodegeneration. The team uses a large set of techniques (biochemistry, molecular and cell biology, molecular electrophysiology and molecular modelling) applied at diverse scales from the molecular and cellular levels in cultured cells and *Xenopus* oocytes to the organismal level in mouse models.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Globally, following the recommendations of the previous committee, the team has upheld its productivity and leadership in the lysosomal biology field with eleven versus eight published articles. However, some recommendations from the previous report still need to be addressed to ensure continued success and growth, such as broadening grant support beyond foundation grants, and establishing formalised international PhD training opportunities which can enhance the team's reach and impact. Lastly, strengthening recruitment efforts from medical schools can enrich the team with interdisciplinary expertise and perspectives. Actively engaging with medical schools through seminars, workshops, and recruitment events can attract top talents and foster fruitful collaborations. Incorporating these recommendations more actively into consideration will not only bolster the team's capabilities but also position it for continued success and impact in the field of lysosomal biology.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	4
<b>Sous-total personnels permanents en activité</b>	<b>7</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	5
<b>Sous-total personnels non permanents en activité</b>	<b>7</b>
<b>Total personnels</b>	<b>14</b>

## EVALUATION

### Overall assessment of the team

The team is globally excellent. This is shown by its very good to excellent list of publications in the quantitative (n=11, 45% signed in position of responsibility) and qualitative (3 in highly recognised journals with large readership such as PNAS, FASEB or J Med Chem) points of view. The funding of the team is excellent to outstanding, with a total of 2 M€ obtained over the past six years through successful applications to national and international calls, including 6 contracts from ANR (2 as coordinator) and two from patient associations (VML...). Attractiveness is excellent as shown by twenty talks in international conferences and the presence of the team in national networks, and the attraction of foreign students. The contribution to society is somewhat limited and should be improved.

## Strengths and possibilities linked to the context

The team's strengths lie in its profound understanding of lysosomes and neurodegeneration as shown by its involvement in the organisation of a Gordon conference on lysosomes, but also collaborative endeavours within the SPPIN. Indeed, the team benefits from a collaborative synergy with Teams 1 and 3, which extends to areas such as ALS, brain organoids, cutting-edge microscopy, and tissue clearing. This interconnectedness fosters a rich environment for interdisciplinary research and potential collaborative projects, maximising the team's collective capabilities. Also, the team leverages complementary expertise through international networks, such as the mouse model of Salla disease and neural stem cells. These collaborative efforts enhance the team's capacity to tackle complex challenges and broaden its perspective, enriching research initiatives and potentially leading to innovative solutions.

The team published eleven original papers, 45% of them as leader and sometimes in highly cited – journals such as PNAS or FASEB.

They obtained a significant amount of funding (2M€) at the national (2 ANR as coordinator and 4 as partner) and international (5 contracts from the Cystonosis research Foundation USA as leader) level but also from national patient associations (VML, etc.).

## Weaknesses and risks linked to the context

The team operates within a highly dynamic international environment marked by escalating competition. Despite its dynamic activities, the team faces challenges in attracting well-trained postdocs. Additionally, the recent departure of two CNRS engineers has led to a reduction in size, impacting the team's overall manpower and its ability to meet extensive demands. The ageing of permanent staff members further poses a current threat, potentially affecting the team's agility and adaptability to emerging trends and technologies. These factors collectively contribute to the team's vulnerability in the competitive landscape, requiring strategic measures to address recruitment challenges and rejuvenate the workforce.

## Analysis of the team's trajectory

The team's trajectory is highly coherent, focusing on the analysis of lysosomal amino acid transport at both the organismal level in a mouse model and the investigation of the interaction between PQLC2 and the C9 complex. Additionally, a significant research line will involve the continued development of drug therapy for lysosomal-associated disorders, particularly Salla disease, and the exploration of extracellular vesicles.

Of note, an amount of 600 k€ from recently acquired funds have been secured for the future contract.

The team will be composed of eleven people including 4 full-time researchers, one lecturer from University Paris Cité, three invited researchers from abroad (Yale University) and two technical staff. This should put them in good conditions to perform the project planned but more links with clinicians may be helpful.

## RECOMMENDATIONS TO THE TEAM

The committee recommends that the team capitalises on the expertise of its full-time researchers and its relatively low involvement in teaching activities to enhance its publication rate. It is advised to be more proactive in publishing ongoing work, particularly involving PhD students and/or postdocs. The committee recommends that the team develops interactions with the medical community at the national and, if possible, also at the international level.



**Team 5:** Singular Imaging  
 Name of the supervisor: Marc Guillon

## THEMES OF THE TEAM

The team focuses on fundamental optics and optical instrumentation to biological imaging. They use scattering media and random light patterns for fluorescence microscopy and phase imaging. They developed novel microscopes, like the speckle-based 3D super-resolution microscope, as an alternative to the STED technique. They have conceptualised and mounted various (4) setups on wavefront sensing techniques, for biological imaging but also for laser metrology (collaboration with LULI laboratory and private company Imagine optics).

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team is new (the PI was in Team 1 and started the team in 2019). There were then no recommendations from the previous HCÉRES report.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	0
<b>Sous-total personnels permanents en activité</b>	<b>1</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	3
Post-doctorants	0
Doctorants	2
<b>Sous-total personnels non permanents en activité</b>	<b>5</b>
<b>Total personnels</b>	<b>6</b>

## EVALUATION

### Overall assessment of the team

This new team focuses on optical instrumentation and its applications in biological imaging. The team is globally excellent. The scientific production is excellent to outstanding, considering the small size of the team. However, the team lacks permanent positions. The instrumental development is well valorised, with four patents during the evaluated period. The team trained seven master students and two PhD defended their thesis since 2019. The links with society are thus excellent to outstanding. The team obtained two projects supported by ANR and pre-maturation grants with the industry that finance the team. The resources and fundings are then very good to excellent. The attractiveness is excellent as the team actively participates in international conferences, is present in national networks and attracts international students.

### Strengths and possibilities linked to the context

The team has an excellent activity in technological transfer through maturation projects and tight partnerships with industry (collaborative ANR with Imaging Optic, Photon-Lines, Thalès, etc.). The team is involved in 4 patents and protects the intellectual property. They develop innovative microscope setups and try to make them available to the community (example of the diffuser-based wavefront imager that was developed with the support of SATT ERGANEO technology transfer company and a prototype was transferred to the imaging facility

of Pasteur Institute). The team is scientifically very productive, considering its small Human resources size. They published fourteen peer-reviewed papers with members of the team involved in the work and ten papers with group members as first/last authors during the 2017–2022 period. All PhD students from the team have at least a paper with first name authorship. The team gathered ~389 k€ of grant funding from national sources (ANR) and 223 k€ from industry contracts and technological valorisation over the 2019–2022 period. The team trained two PhD students, hired three technicians/engineers on fixed-term contracts and trained 7 master students (internships). The PI and unique permanent member is highly involved in teaching which offers him opportunities to attract local students.

### Weaknesses and risks linked to the context

The team shows excellent results in terms of publications and collaborations with the industry. The technological development is innovative and the team is doing the necessary for its valorisation (patents, links with industry). What is missing, in the SPPIN unit environment, is the dissemination of these technologies to the other teams of the unit. The biological teams could test the technologies on their own applications and Team 5 could adapt these technologies to the applications. One needs to consider that the dissemination is part of the team's missions. Either that part should take place on the Core Unit of SPPIN or the institutions and the unit should give more HR to the team to realise it by itself. The team lacks permanent staff. The PI is highly involved in various R&D projects, but due to his teaching duties, time for R&D is limited, especially if the R&D conception is based on one person.

### Analysis of the team's trajectory

The team's trajectory is coherent, as they continue the technological development on phase imaging. They want to couple their recently published speckle saturated excitation technique with STED microscopy for super-resolution imaging. In 2024, a new research engineer will join the Core Unit where he/she will be responsible for the technological transfer. This can be an excellent opportunity for the team to make part of its equipment more user friendly and accessible to the community.

The team has applied to different ANR grants for the next period but up to now the results of the demands are not known. If these demands are not fruitful, there is a risk for the maintaining of the development of the highly innovative microscopes of the team.

## RECOMMENDATIONS TO THE TEAM

The committee encourages the team leader to improve integration within the SPPIN environment by adapting the technological developments to the unit's biological applications. For instance, the laser metrology project, although very interesting and innovative, currently has no applications within the unit.

The team leader is highly involved in various projects, something that limits his time to focus deeper on the projects, adapt them to the biological questions and make technological transfer (duplicating system and expertise transfer) either to the Core Unit of the SPPIN or to the microscopy facility of the UAR Biomedtech.

The team's situation is relatively fragile, as there is a risk that the team leader will continue to be the only permanent member of the team. A new professor position is open in 2024, with the team leader as a candidate. In case of success, particular attention should be paid to keeping his current associate professor position in the unit and the team, to strengthen the manpower for R&D.

**Team 6:** Synapses of Affective Behaviours

Name of the supervisor: Marco Diana

## THEMES OF THE TEAM

The team's scientific interests are focused on how molecular mechanisms contributing to the processing of inhibitory and excitatory inputs in neurons are integrated into neural circuits and determine affective, emotional behaviours. In particular, they have been interested in studying the Medial Habenular nucleus, a circuit implicated in fear conditioning, aversion, anxiety depression and addiction. The team is also interested in associative thalamic structures, such as the periventricular thalamus and the parabrachial nucleus. Such structures are interesting because they have a simple anatomical organisation, with no local interneurons so that all synaptic inputs are of extrinsic origin.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

This is a new team created in 2022 by two researchers coming from the Quai Saint Bernard site in the Sorbonne, in the NPS unit. There were no recommendations to take into account.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	0
<b>Sous-total personnels permanents en activité</b>	<b>2</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	0
<b>Sous-total personnels non permanents en activité</b>	<b>1</b>
<b>Total personnels</b>	<b>3</b>

## EVALUATION

### Overall assessment of the team

This small team (one researcher and one lecturer) only joined the SPPIN in late 2021 from the NPS unit at Sorbonne University. There are then no publications with the SPPIN as an affiliation, but this is not unexpected given that a lot of time will have been taken up with the move. That said, it is clear that the team leader has an impressive track record including several noteworthy publications in the past, including a paper published in Science in 2019 that he signed as last author.

### Strengths and possibilities linked to the context

The team leader's previous publication track record is encouraging and suggests that he is capable of doing cutting-edge research.

### Weaknesses and risks linked to the context

The integration within the SPPIN has yet to be validated.

## Analysis of the team's trajectory

The team was a component of the Neuroscience Paris Seine (NPS) unit with the team leader being an autonomous senior researcher before its arrival at SPPIN in 2022. It first demonstrated the existence of novel excitatory glycinergic NMDA receptors containing the unconventional GluN3A subunit, which are mandatory for the emergence of conditioned aversive states in adult mice (Otsu et al., Science, 2019) extending the spectrum of physiological functions associated with the typically inhibitory neurotransmitter glycine. The team relocation was motivated by the development of state-of-the-art optical techniques at the SPPIN (2P, miniscopes, fiber photometry) that could greatly expand the research carried out by the team. The team is well funded with 4 ongoing ANR grants (CHOLHAB, CerebelleMO, ParObesity and HABEMOOD) that will provide around 1,100 K€ of funding lasting until 2027. The team has ongoing international collaborations with laboratories in Hungary, Australia, Switzerland, as well as national collaborations with laboratories in Strasbourg and Paris-Cité University. There is also a new ECOS Sud project involving Argentina (HABEraSER). There were no PhD students at the time of report, but one M2 student and one postdoc. The team envisions to stay relatively small, with one more technician or researcher if possible, and 3–4 PhDs/postdocs in total. Globally, the team's trajectory looks very promising.

The team is highly involved in teaching (close to 200 hours/year for 2 PIs) with administrative duties (international mobility co-chair of the Master Bip) and proposing innovative tools for education (creation of 8 teaching modules including practical ones on electrophysiology).

## RECOMMENDATIONS TO THE TEAM

The committee encourages the team leader to optimise his integration within the SPPIN environment by building collaborations with other researchers on-site. This could involve co-supervision of students, and the possibility of making use of some of the innovative technological approaches developed in the unit. It would also be important to include the SPPIN as an affiliation even for research that was carried out in the previous laboratory.

**Team 7:** Molecular Biology of Neuronal Transport

Name of the supervisor: Nicolas Panayotis

## THEMES OF THE TEAM

This new team created as the result of an international call for a junior group, follows three lines of research, building on the PI's previous work at the Weizmann Institute, Israel: *i)* deciphering the role of importins in CNS functions, using advanced imaging techniques, RNA-seq, and translationalomics, in cellular and mouse models, *ii)* characterising the role of MeCP2 transport in the context of two neurodevelopmental disorders, Rett and MeCP2 Duplication Syndrome, and *iii)* developing novel photoinducible tools to control nuclear transport of transcription factors.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was created very recently and there are no recommendations from a previous report to be taken into account.

## WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	0
<b>Sous-total personnels permanents en activité</b>	<b>0</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	0
<b>Sous-total personnels non permanents en activité</b>	<b>1</b>
<b>Total personnels</b>	<b>1</b>

## EVALUATION

### Overall assessment of the team

The team has just been created, so there will be no assessment in this report.

### Strengths and possibilities linked to the context

Not applicable.

### Weaknesses and risks linked to the context

Not applicable.

### Analysis of the team's trajectory

The PI has an excellent track record from his postdoctoral work at the Weizmann Institute, as evidenced by high-profile publications (e.g. Cell Reports 2018; Science 2020; Cell Reports Medicine 2021) and a patent

(WO2018/207178 filed). This leads to a high potential to obtain competitive funding. The trajectory is excellent and very promising. However, the project seems overambitious for a young team with multiple lines of research, costly experiments, and requiring many transgenic mouse lines, which may put this young team at risk. The project suffers from a lack of focus on one specific line of research. In addition, the PI has not yet obtained a permanent position, and at the time of the evaluation it is unclear how and for how long the PI can be funded. Although the PI had a success in securing a 'Fondation de France' grant (249 k€), it is essential for a young PI at this career stage to get maximum support from the institute, especially to succeed in future grant applications.

## RECOMMENDATIONS TO THE TEAM

The SPPIN offers a mentoring program, which is an important asset for a young PI starting his team. The PI should secure a permanent position by applying to various programs (CNRS, Université, Chaire Prof Junior, Chaire d'excellence...).

The committee also recommends the PI to focus on one line of research in order to publish rapidly and secure long-term funding.

**Team 8:** Orientation & Coordination  
 Name of the supervisor: Desdemona Fricker/Michael Graupner

## THEMES OF THE TEAM

The team will investigate spatial orientation and motor control, starting from the encoding of internal and external stimuli up to the adaptation of behaviour to ongoing events. *In vitro* techniques such as slice electrophysiology will investigate cellular mechanisms, and *in vivo* techniques such as multi-electrode extracellular electrophysiology, and calcium imaging during awake behaviour will reveal how network activity gives rise to behavioural responses.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

This will be a new team starting in January 2025. So, there are no recommendations from a previous report.

## WORKFORCE OF THE TEAM: in physical persons at 1/1/2025

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	0
<b>Sous-total personnels permanents en activité</b>	<b>2</b>
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	0
<b>Sous-total personnels non permanents en activité</b>	<b>1</b>
<b>Total personnels</b>	<b>3</b>

## EVALUATION

### Overall assessment of the team

The team will join the SPPIN in January 2025, so there will be no assessment in this report.

### Strengths and possibilities linked to the context

Not Applicable.

### Weaknesses and risks linked to the context

Not Applicable.

### Analysis of the team's trajectory

This promising team will join the SPPIN in January 2025 to develop an ambitious research project that perfectly fits with the SPPIN objectives. It will be led by one DR and one CR CNRS scientist, accompanied by a Professor emeritus. The team members have strong expertise in state-of-the-art neuronal recording methods as well as

computational methods critical for data analysis. For their installation as an independent team in the SPPIN, they will need support in terms of lab space, access to facilities, and technical support.

The envisioned research program is very ambitious, as it involves the recording of populations of neurons during awake behaviour, but it seems sound and timely. In their current laboratories, the two PIs are already developing the methodological tools that will be necessary to carry out their projects. The scientists are already in the SPPIN building and have been collaborating for several years, in particular in frame of a PhD codirection. One of the scientists already has experience in co-directing a team at INCC. The transition should thus be smooth, enabling the researchers to continue ongoing experiments and start new ones without a significant gap in their activity.

The future team leaders both have an HDR, and are currently supervising six PhD students, so that there will potentially be a large workforce. Additionally, one professor emeritus will participate in the projects.

The experiments planned will be highly time-consuming, with groups of experimental subjects being trained during several weeks. In addition to performing the experiments themselves, this will require the development and maintenance of complex ad hoc setups combining behaviour and recordings. The data analysis will undoubtedly also involve a lot of software development. At the present, the team is projected to start without any technical support. The workload of the permanent researchers, who are the only ones who possess the extensive know-how necessary for completing the projects, could be very heavy.

Past research projects have focused on different topics, namely spatial navigation and motor coordination. Bringing together those two themes could be very challenging.

## RECOMMENDATIONS TO THE TEAM

The team would strongly benefit from the presence of a technical assistant or an engineer to help with experiments, development and maintenance of the setups and/or data analysis.



## CONDUCT OF THE INTERVIEWS

### Date

**Start:** 18 janvier 2024 à 9 h

**End:** 18 janvier 2024 à 18 h 30

**Interview conducted: on-site or online**

### INTERVIEW SCHEDULE

**Research Lab Visit program**  
**Saints Pères Paris Institute for the Neurosciences (SPPIN)**  
**Date of the visit: January 18–19<sup>th</sup>2024 (on site)**  
**Present Lab director: Martin Oheim**

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**HCÉRES Scientific advisor:** Mr. Giovanni Stevanin

**Research committee:**

Mr. Maxim Cazorla (Marseille), Expert

Mr. Antony Czarnecki (Bordeaux), Expert (CoNRS25 representative)

Ms. Valérie Ego-Stengel (Saclay), Expert

Mr. Orestis Faklaris (Montpellier), Expert (PAR representative)

**Mr. Philippe Marin (Montpellier), Expert Panel Hcéres (President)**

Ms. Sara Morley-Fletcher (Lille), Expert (CNU69 representative)

Mr. Simon Thorpe (Toulouse), Expert Panel HCÉRES

Observers:

Ms. Kim Charvet, Chargée de mission à CNRS-Biologie

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**January 18<sup>th</sup>**

**8:30-8:50**

Welcome coffee (closed-door): Visiting committee with the HCÉRES advisor (Room Sabatier A)  
 Saints-Pères Paris Institute for the Neurosciences (SPPIN – CNRS UMR 8003)  
 45 rue des Saints-Pères, 75270 Paris cedex 06

**8:50-9 :00**

Presentation of the evaluation process to the unit by the HCÉRES advisor (ROOM R229)

**9:00-10:00**

Presentation of the unit scientific outputs and strategy, presentation of the Core unit by the lab director (30' presentation + 25' discussion)

**10:00-10:30**

*Coffee break (room Sabatier A)*

**10:30-12:15**

Presentation of the scientific programs and research results by group leaders (15' presentation + 14' discussion, R229, 5' with team leader alone)

Team 1: Biophysics of the Brain (Martin Oheim)

Team 2: Cerebellar Neurophysiology

(Céline Auger/Brandon Stell; Future: Thibault Collin/Brandon Stell)

Team 3: Motor-Neurons & Neuromuscular Junctions

(Future: Pathophysiology of the spinal cord)

(Boris Lamotte-d'Incamps and Daniel Zytnicki; Future: Nicolas Guérout)

**12:15-1:30 p.m.**

Lunch and debriefing (closed-door with the committee and HCÉRES advisor) (ROOM E368)

**1:30 p.m.-2:40 p.m.**

Presentation of the scientific programs and research results by group leaders (15' presentation + 14' discussion, R229, 5' with team leader alone)

Team 4: Membrane dynamics (Bruno Gasnier;

Future: Christine Anne-Longin & Bruno Gasnier)

Team 5: Singular Imaging (Marc Guillon)

**14:40-15h40**

Presentation of the scientific programs of new teams

(8' presentation + 7'discussion R229, 5'with team leader alone)  
 Team 6: Synapses of Affective Behaviours (Marco Diana) arrived late 2021  
 Team 7: Molecular Biology of Neuronal Transport (Nicolas Panayotis) arrived 2023  
 Team 8: Orientation & Coordination (Desdemona Fricker/Michael Graupner) arriving

<b>3:40 p.m.-4 p.m.</b>	Coffee break (Room Sabatier A)
	<b>Meetings with the various categories of personal</b> (ROOM R229)
<b>4 p.m.-4:30 p.m.</b>	Discussion with engineers, technicians and administrative personnel (in French)
<b>4:30 p.m.-5 p.m.</b>	Discussion with PhD students and post-docs
<b>5 p.m.-6:15 p.m.</b>	<b>Visit of the unit and its facilities</b>
<b>6:15 p.m.-7:15 p.m.</b>	Private meeting of the visiting committee (closed-door at room E368)
<b>7:30 p.m.</b>	Evening dinner and discussions (only committee members and HCÉRES Scientific advisor)

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### January 19<sup>th</sup>

<b>8:30-9:00</b>	Welcome coffee (closed-door): Visiting committee with the HCÉRES advisor (ROOM E368)
	<b>Meetings with the various categories of personal</b> (ROOM E368)
<b>9:00-9:30</b>	Discussion with the representative of the managing bodies (closed-door) & local representatives
<b>9:30-10:00</b>	Discussion with scientists (without previous and novel team leaders)
<b>10:00-10:30</b>	Discussion with previous/new team leaders
<b>10:30-11:00</b>	Coffee break
<b>11:00-11:30</b>	Discussion with the director (closed-door)
<b>11:30-1:30 p.m.</b>	Lunch and debriefing (closed-door with the committee and HCÉRES advisor) (ROOM E368)
<b>1:30 p.m.</b>	End of the visit and Departure from Paris

## PARTICULAR POINT TO BE MENTIONED

A good atmosphere and a generally good state of mind were noted by all categories of personnel, despite the fact that the unit was scattered throughout the building.

## GENERAL OBSERVATIONS OF THE SUPERVISORS

Le Président

Paris, le 18 avril 2024

HCERES  
2 rue Albert Einstein  
75013 Paris

**Objet : Rapport d'évaluation de l'unité DER-PUR250024315 - SPPIN - Saint-Pères Paris institute for neurosciences.**

Madame, Monsieur,

L'université Paris Cité (UPCité) a pris connaissance du rapport d'évaluation de l'Unité de Recherche SPPIN - Saint-Pères Paris institute for neurosciences.

Ce rapport a été lu avec attention par la direction de l'unité, laquelle n'a pas fait état d'erreurs factuelles, par la vice-doyenne Recherche et le doyen de la Faculté des Sciences d'UPCité (cf courrier du Doyen Cazayous qui identifie deux inexactitudes à corriger), par la vice-présidente Recherche d'UPCité et par moi-même. L'ensemble des acteurs d'UPCité remercie le comité pour son travail d'évaluation

**Présidence**

**Référence**

Pr/DGDRIVE/2023

**Affaire suivie par**

Christine Debydeal -  
DGDRIVE

**Adresse**


85 boulevard St-Germain  
75006 - Paris

En exprimant ma confiance sur le fait que la trajectoire de l'unité tirera pleinement profit de l'écosystème de la recherche au sein de l'université Paris Cité maintenant stabilisée, je vous informe ne pas avoir d'observations d'ordre général à exprimer sur le rapport provisoire.

Je vous prie d'agréer, Madame, Monsieur, l'expression de ma considération distinguée.

[www.u-paris.fr](http://www.u-paris.fr)

Édouard Kaminski



Référence  
MC/NE/EB/2024-025

**Faculté des Sciences**  
**Université Paris Cité**  
5 rue Thomas Mann  
75013 Paris

Objet : DER-PUR250024315 - Évaluation HCERES de l'UMR 8003 SPPIN- Retour Tutelle Université Paris Cité

Chères et Chers Collègues,

Nous souhaitons par ce courrier remercier les membres du comité de visite pour le temps qu'ils ont consacré à l'évaluation de l'UMR SPPIN, ainsi que pour leur écoute et le travail considérable qu'ils ont accompli.

La Faculté des Sciences est fière de compter l'UMR SPPIN parmi ses unités de recherche et rappelle la grande qualité de la recherche menée par tous les membres du laboratoire.

Après lecture du rapport provisoire d'évaluation de l'UMR 8003 SPPIN, la Faculté des Sciences souhaite répondre à deux observations faites dans le rapport.

1 - On page 10 of the report it is written: "*There is no human resource contact person to provide information to the staff employed by the University.*"

We invite the laboratory to turn to the university to benefit from all the possibilities in this field. Human resources advisors are available at UFR Biomedical.

At the level of the Faculty of Sciences, the HR department, its director Sébastien Ramesh and Marie Brajeul advisor career mobility and professional development are available.

More generally, the university is mobilizing to support agents who can obtain information on BIATSS promotions via the following link <https://intranet.u-paris.fr/recrutement/concours-itrf/> or follow courses for competitive entrance examinations offered by the Gestion Parcours et Compétences Department.

2 - On page 11 of the report it is written: "*For instance, the turmoil created by the fusion of Paris Descartes and Paris Diderot universities resulted in a loss of an Excellence chair package and the recruitment of the SPPIN's candidate at Pasteur institute.*"

Institut Pasteur is part of the Université Paris Cité. This candidate has therefore been recruited by our establishment. The Chairs of Excellence were set up during the probationary phase of the Idex (2019-2021) and made possible by the merger of the two universities. Notice that, candidates prefer to choose a permanent position over a temporary one, however "excellent".

En vous priant, chères et chers collègues, d'accepter nos chaleureuses salutations.

Maximilien CAZAYOUS  
Doyen  
Faculté des Sciences  
Université Paris Cité

Nathalie EISENBAUM  
Vice-Doyenne recherche Faculté  
des Sciences  
Université Paris Cité



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