Research evaluation

EVALUATION REPORT OF THE UNIT

BPL – Brain Plasticity Laboratory

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Centre national de la recherche scientifique - CNRS,

ESPCI Paris – Université Paris Sciences et Lettres – ESPCI Paris-PSL

EVALUATION CAMPAIGN 2023-2024

GROUP D

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High Council for evaluation of research and hignter education

In the name of the expert committee[1] :

Geneviève, ROUGON, Chairwoman of the committee

For the Hcéres[2] :

Stéphane Le Bouler, president par intérim

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:	Ms Geneviève ROUGON Institut des Neurosciences de la Timone - UMR CNRS 7289, France
Experts:	Mr. Philippe MARIN, Institut de Génomique Fonctionnelle, Hcéres expert Panel, (Vice-President) Mr. Bogdan DRAGANSKI, Centre hospitalier universitaire vaudois, Suisse, Hcéres expert Panel, (Expert) Ms. Ellouise Anderson LEADBEATER, Royal Holloway University of London, Royaume-Uni . Hcéres expert Panel, (Expert) Ms. Marion SILIES, Johannes-Gutenberg-University Mainz, Germany, (Expert) Mr. Simon SPRECHER, University of Fribourg, Suisse, (Expert) Mr. Torfi SIGURDSSON, Neuroscience Center Goethe Universität, Germany. (Expert) Ms. Helene MARIE, Institut de Pharmacologie Moléculaire et Cellulaire,Valbonne, France. (Representative of CNRS, Cons 25). Ms. Emilie PECCHI, Institut de Neurosciences de la Timone - UMR CNRS 7289 (Representative of supporting personnel).

HCÉRES REPRESENTATIVE

Ms. Nadia Soussi-Yanicostas

REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Mr. Bernard POULAIN (CNRS)

Mr. Costantino CRETON (ESPCI Paris-PSL)

CHARACTERISATION OF THE UNIT

- Name: Plasticité du Cerveau
- Acronym: PDC
- Label and number: num
- Composition of the executive team: composition of the executive team

SCIENTIFIC PANELS OF THE UNIT

SVE5 : Neurosciences et troubles du système nerveux

THEMES OF THE UNIT

The main scientific focus of Brain Plasticity Laboratory (BPL) is the investigation of the mechanistic understanding of key biological processes underlying brain plasticity. Their approaches are multiscale and multidisciplinary, combining both experimental and theoretical methodologies on organotypic cultures, Drosophila and rodent models. The composition of the unit has very significantly changed over the assessed five-year term. Two teams left, two are going to leave and they have been replaced by 4 newcomers.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The Brain Plasticity Laboratory (BPL) is a neuroscience research unit located at the Ecole Supérieure de Physique et de Chimie Industrielles (ESPCI Paris-PSL) in Paris. Neuroscience research at the ESPCI began with Pierre-Gilles de Gennes in 1995. The laboratory has been directed by Thomas Preat for the last two terms (2014–2018, 2019–2025). During the next term, the unit is going to move into a new building and will be directed by Philippe Faure, whose team joined the unit in 2021.

RESEARCH ENVIRONMENT OF THE UNIT

BPL is a key player in several research initiatives in the Paris area. On site, at ESPCI Paris-PSL, BPL contributes to a multidisciplinary environment at the interface of biology, chemistry and physics. The supervising authorities (CNRS, ESPCI Paris-PSL) support the laboratory by providing material and human resources, a building and help with administration and fund-raising. In its proximal environment, BPL is part of the Memolife 'Laboratoire d'excellence' (labex), initially funded by the competitive 'Investissements d'Avenir' program launched by the French government and now part of the PSL University major programs. This labex also includes teams of the IBENS (Institut de Biologie de l'ENS) and the CIRB ('Centre Interdisciplinaire de Recherche en Biologie' from the Collège de France). Beside grant support, the labex and the PSL University environment offer to BPL teams, access to cutting-edge technical facilities (e.g. light and electron microscopy, brain imaging, animal husbandry, transgenesis, genomics, proteomics, intensive computing centers, FabLab). At the level of the 'Région Île-de-France' BPL is part of the DIM C-Brains, whose aim is to structure and federate research and innovation in the fields of neuroscience and cognition.

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

Staff categories	Workforces
Professeurs et assimilés	1
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	7
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	13
Sous-total personnels permanents en activité	**27**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	9
Doctorants	17
Sous-total personnels non permanents en activité	**26**
Total personnels	**53**

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

Nom de l'employeur	EC	C	PAR
CNRS	0	8	10
ESPCI Paris-PSL	3	0	2
INSERM	0	2	1
SORBONNE UNIVERSITÉ	1	0	0
Total personnels	4	10	13

GLOBAL ASSESSMENT

The committee considers that the BPL unit is internationally well recognised for its high-profile publications, high successes in obtaining internationally competitive grants, with several members receiving invitations to meetings and prestigious prizes. The scientific production is overall outstanding (e.g. publications Nat. Comm., Nat. Neurosci., Neuron, Cell reports). Its scientific appeal and capacity to raise funding are exceptional (e.g. 2 ERC). Equipment is very diverse and state of the art. During the term, the BPL attracted two very talented senior teams and a promising early career junior group. The involvement in teaching is excellent. The unit being active in fundamental research has rather few possibilities to translation towards applications. Its interactions with public, private companies and industry are limited.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

In the previous report the committee recommended that some teams – seek further funding – increase the size of their teams to improve their chances to publish in higher impact journals and/or – be better coached. The composition of the unit in terms of affiliated teams has very significantly changed over the assessed five-year period. All the teams that were concerned either left (team 4 Brain Computer Interface; team 5 Pain and neural adaptation) or are in the process of leaving (team 2 Genes, circuits Rhythms and Neuropathology) the unit. A second recommendation was to improve communication between the different levels of employees. An effort has been made and the recommendation implemented by – setting up a retreat gathering all the personnel every two years – improving the governance structures such as the 'laboratory council' with representatives of each personnel category.

B – EVALUATION AREAS

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

Assessment on the scientific objectives of the unit

The committee considers that BPL teams have set excellent timely and highly competitive scientific objectives that are clear and ambitious. The seven teams constituting the unit are working in integrative neuroscience, studying brain plasticity, memory, decision-making, adaptation and learning and in some instances their alterations in diseases. The hallmark of the unit is to link genes and pathways to neural circuits and associated behaviours thanks to multi-scale and multidisciplinary approaches.

Assessment on the unit's resources

The BPL Resources are excellent. BPL had an excellent balance between permanent (25) and non-permanent (26) staff (end 2022) (21/4 2 October 2023) but with a lack of permanent staff for administration and animal facilities. Researchers are mainly from CNRS (7) and ESPCI (2). BPL is partly financed by CNRS and ESPCI (approximately 22% excluding salaries of permanent staff) and obtained an impressive number of competitive grants (>9.8 M€; ERC, ANR, Foundations). BPL will move in a renewed building and benefit from up-to-date equipment and Drosophila and rodent facilities.

Assessment on the functioning of the unit

The functioning is very good to excellent. BPL complies with the general mandatory rules of governance imposed by CNRS, ESPCI Paris-PSL and EU although some aspects could be improved. – Structures and new committees have been established in 2021 – The strategy and organisation are defined by the director and the deputy director after discussion with the scientific council composed of all the PIs in the unit. A statutory laboratory council had been created. Each team is scientifically and financially independent. Some improvements are necessary for gender equality and communication (e.g. identify a referent within BPL for Equality and. Parity, foster BPL spirit by stimulating interactions and social life).

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

Strengths and possibilities linked to the context

The committee considers that each BPL team has defined for itself a set of timely and ambitious scientific objectives in neuroscience fundamental research. The economic model of the laboratory is well-thought-out and mainly rests on the scientific and financial independence of the teams. A convergence towards the overall aim, which is to gain a mechanistic understanding of key biological processes underlying brain plasticity, had been increased by the competences of the newly recruited teams. (e.g. team 4 by studying memory acquisition, consolidation in rodents will complement team 1 studies on memory in Drosophila and team 3 studies that explore the relation between wakefulness and sleep in memory processing in freely moving mice and the newly established team 6. Each team has significant strengths and although at different levels, established, internationally recognised expertise as testified by their publications in top-rated journals (e.g. Nature Communications. Nature Neuroscience, Neuron, Cell Reports, Cell Metabolism) and the obtained competitive grants (e.g. 2 ERCs). BPL specificity is the use of a diversity in the models studied and the development of an integrative approach ranging from neurobiology to behaviour fostering causal links between the different levels of brain organisation and in some instance, alterations occurring in diseases.

Weaknesses and risks linked to the context

Although the teams acknowledged informal exchanges and some collaborations (e.g. between teams 5 and 3), this is not reflected by common projects and publications. Difficulties to establish interactions between teams working on different models and different integrative levels represent a risk and would require specific efforts. Size for the new young team (7) and the present lack of permanent position for its team leader as well as the lack of a permanent collaborator for team 4 are real threats. Mentoring for young investigators needs to be reinforced to increase their chances of success. Initiative of young scientists for communication and networking opportunities needs to be encouraged. For some teams, translational potential of the findings could be better considered such as translation towards clinics.

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 relocation of the BPL research unit to a new building on the ESPCI campus is scheduled for late 2023/early 2024. One of the most important opportunities is that the complete renovation of the building will increase the visibility and attractiveness of the unit and offers the opportunity to welcome the new teams (teams 6 and 7). The unit will also benefit from a new facility of 100 m2 for the Drosophila kitchen. It will allow teams to increase the number of rodents and to develop new experimental paradigms (team 5) in a very competitive field that is still underrepresented in France. BPL has established strong links with the neighbouring Neuroscience units (e.g. through the Labex Memolife). Teams also actively contribute to innovative teaching and initiation to research (e.g. by welcoming ESPCI engineer students).

Weaknesses and risks linked to the context

A risk that BPL will have to deal with concerns animal experiments. First, BPL needs additional personnel to manage the larger animal house. Second, the ongoing campus renovation might perturb (e.g. noise) the behavioural experiments. The unit management will have to take steps to mitigate them. Due to the limited number of technical staff half of the teams suffer from a deficit of technical support, however, partially compensated by access to local facilities. The potential offered by the ESPCI environment is not fully exploited although the move to a common building should help to optimise interdisciplinarity. Labex MemoLife is ending and support will depend on the success of the application to PSL major research programs (2025-2029).

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

BPL has set several structures and committees to ensure its governance and operation. A biennial retreat for all BPL members is held to facilitate communication across teams. Scientific animation is organised in the teams and at the level of the unit (internal seminars). The students also organise regular meetings. BPL is sensitive to the issue of gender equality. The ratio women/men is balanced when combining all career stages but with differences in the access to responsibilities. The recent recruitment of two women PI (teams 4 and 6) is improving the situation. PI of team 4 is involved in the ESPCI Equality program and the 'Cellule d'écoute et de veille' of PSLUniversity. BPL has an Information Systems Security Correspondent (ISSC) and a Prevention Assistant. The permanent staff working with animals has received training. A SBEA committee (animal welfare committee) meets every two months and a BPL researcher participates to the ethical animal committee CEEA59. For biological and chemical risks procedures are explained to each handler. Each new employee, attends a meeting with the Prevention Assistant and receives a CNRS guide to good scientific practice. In addition, a welcome booklet containing the rules of conduct is available on the BPL internal website. Several BPL members are trained as 'Sauveteur Secouriste'. Most papers are published in open access and all are deposited on HAL. A few measures have been taken for energy and resource savings and reduction of carbon footprint, (e.g. waste processing).

Weaknesses and risks linked to the context

The risks relate to the difficulty of finding qualified and stable staff to run both the management department and the animal facilities since the choice is to work with dedicated animal facilities staff instead of external staff (outsourcing the facility management). The regulations on animal experimentation that become more and more restrictive, places a heavy workload on researchers and induce long delays to obtain the requested authorisations. The unit did not mention additional possible actions to take in order to reduce carbon footprint (e.g. travel). Despite the function of the leader of team 4 in the ESPCI Equality program and the 'Cellule d'écoute et de veille' there is no identified referent within BPL for Equality and Parity.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The BPL attractiveness is clearly excellent to outstanding, as demonstrated by the quality and reputation of its fundamental research. The scientific reputation is attested by the exceptional success of the team leaders to obtain grants, honours and prizes. BPL attracted excellent senior and junior staff. ESPCI and PSL university provide an excellent international and multidisciplinary training environment with access to a new building state-of the art facilities and equipment.

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

BPL participates to the construction of EU research area and is attractive because of the recognition gained through its success in competitive calls for projects. Each of the teams present in the unit obtained international (e.g. an ERC advanced grants, an ERC Consolidator Grant, a Human Frontier Science Program (HFSP), and competitive French grants (e.g. one ATIP/AVENIR, 3′ Equipe FRM» labels (Teams 1, 6, and 5). Members were awarded prestigious prizes (e.g. Prix FRM, Prix de la Fondation NRJ, Fondation de France, Brain Star Award from the Canadian association for Neuroscience, CNRS bronze medal). Several members serve in national committees (e.g., CNRS, ANR, HCERES). Several researchers have been invited to international conferences (e.g. Gordon conferences, EMBO workshop, 13th International Conference on Brain Energy Metabolism). BPL attracts for their internships ESPCI engineering students with an original practical and theoretical training. Forty-two PhD students were hosted or are hosted (October/2023) in the unit as well as 29 postdocs among which ten obtained their PhD in the hosting team and twelve originated from foreign countries. Beside the interdisciplinary scientific environment and competences offered by ESPCI, BPL host two facilities particularly well suited for research involving Drosophila and mouse models. Top – to-the art technologies are mastered in the teams (e.g. in vivo and super resolution imaging, genetics, electrophysiology, fly and mouse behaviours).

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

BPL could be more pro-active in organising conferences despite the present difficulty of finding available amphitheatres, and the lack of a dedicated space due to the undergoing building renovations.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

Globally, the committee considers that the BPL scientific production in basic science is excellent to outstanding as several teams have published important discoveries. All residents and newly established teams have been involved in the research effort although with some differences. More than 30% of the publications are in high impact journals, however common publications have yet to emerge. PhDs and Post-docs are co-signing publications very often (>80%) as first authors. Most papers are published in open access and all are deposited on HAL.

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

From January 2017 to December 2022, research at BPL resulted in the publication of 80 peer-reviewed articles (105 if affiliated researchers that left the unit are taken into account). The experts noticed that the publications of the unit benefit from a visibility and novelty which stand well above the average and can be qualified as outstanding. There are around 25 papers as members first and last authors that appeared in elite journals of the discipline or multidisciplinary prestigious journals with large scientific readership such Nature (1), Cell (1), Nature Medicine (1), Nature Neurosci. (2), Neuron (4), PNAS (1), Nature Comm. (6), Cell metabolism (1), Nature Metabolism (1), Autophagy (2), Nature Biomedical Engineering (1), Science Advances (1) or Molecular Psychiatry (2). For instance, team 1 is a pioneer in the field of the interface between brain energy metabolism, and learning and memory introducing the use in vivo of a series of recently developed fluorescent genetically encoded metabolic sensors. Team 3 revealed the physiological basis of brain-body interactions in emotions, with the olfactory bulb transmitting regular breathing rhythm to the dorsomedial prefrontal cortex in mice, playing a specific role in freezing maintenance. The young leader of team 4 discovered before joining the unit a novel inhibitory pathway from the hippocampus to the thalamus which is essential for remote, but not recent, memory recall. Team 5 has developed performant photo-pharmacological methods for controlling neuronal ion channels and receptors with light in order to link changes in receptor activity in given neuronal pathways with alterations of neural circuits and ultimately of behaviour. The newcomer Team 6 has uncovered a key mechanism of stabilisation of nascent GABAergic synapses. BPL has generally made sensible choices concerning which journals to target, and has appropriate rules for authorship, typically allowing PhD students and post-docs to sign as first author. The scientific production of the 42 students and 29 post-docs is in general excellent and only 3/20 PhD students left BPL without yet having published their results. BPL clearly has been making efforts to comply with the need to respect fundamental principles of research integrity, ethics, and open science. The committee believes that BPL has a very good record in this respect. In addition, the lab has been following the CNRS's requirement to upload versions of all the publications to the HAL server with 95% of the BPL publications freely available in HAL. BPL teams have implemented means to guarantee reproducibility of results and their traceability.

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

The noticeable major weakness is the lack of common publications. The teams make the choice to find collaborations either national or international relevant to their needs outside the unit. The arrival of the new teams 5, 6, 7 might improve the situation but the committee suggests that the direction takes some actions to foster collaborative projects.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The committee considers that, globally, the BPL links with society are very good to excellent. Each team made efforts to communicate scientific knowledge to all audiences through various channels and formats. There is, however, a strong heterogeneity in team involvement. For team 3, such links were considered to be outstanding as the team collaborated with private companies in relevant domains and is strongly engaged with the general public. The newcomer Team 6 filled a patent with Inserm-transfer.

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

Each team is dedicated to effectively communicate its findings to a broader audience. This commitment to knowledge dissemination highlights their devotion to advancing the field of neuroscience and engaging with diverse communities (e.g. in team 3 a member maintains a public blog dedicated to sleep). In team 5 a member is an associate editor at Médecine/Sciences and works part-time with the team. This team also takes part in the program 'apprentis chercheurs addiction' (organised by the associations MILDECA, INSERM and 'Arbre des connaissances'), the aim of which is to host, one day a month, high-school students to participate in a research program on addiction. Team 2 PI gave a conference to Parkinson's patients (Drosophila, a small fly that offers a great hope for a better understanding of Parkinson's disease). Team 3 emphasises research with potential for real-world human applications. It developed partnerships with Dreem, which created an EEG headband for home sleep monitoring and with XII, which developed virtual reality for pain management. Both collaborations beneficiated of CIFRE (Convention Industrielle de formation pour la Recherche) fellowships. The team also collaborated with URGOTech on a cost-effective solution using the URGOnight EEG headband and a mobile application to make neurofeedback therapies more accessible. The newcomer team 6 filed a patent by Inserm-Transfert with an international extension (PCT/EP2022/059833), for the use of KCC2 enhancers in refractory epilepsy.

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

While some teams are doing research that is clearly important for society for most of them links with society and/or valorisation are clearly not a priority. This may be justified for researchers being primarily motivated by research, and tends to reinforce the idea that BPL is primarily concerned with fundamental research on normal or perturbed functioning of the brain.

ANALYSIS OF THE UNIT'S TRAJECTORY

For the next term (2025–2029), there will be a change of Director. The choice of the new director who joined BPL in 2021 was agreed by the entire personnel. He is experienced and is serving as adjunct director. He already fostered positive dynamics in the unit appreciated by the present director and all staff members. The scientific objectives have been set at the level of each team and discussed in the scientific council. These objectives are in line with the teams' past achievements and discoveries. They are set around three main axes: (1) understanding the mechanisms of memory and plasticity across different time scales (teams 1, 3, 4, and 6), (2) considering the individual and its adaptation to the environment (teams 1, 5, and 6), and (3) maintaining the necessary balance to preserve functions (teams 1, 3, 4, and 7). They rely on well-established research teams with excellent reputations, and two promising younger team leaders (teams 4 and 7). The complementary approach brought by team 6 who for example will study purinergic signalling in synapse stabilisation which has a role in the regulation of hippocampal synaptogenesis is involved in neuron-glia interactions and brain function will bridge the gap between analytical and integrative approaches. However, if the new recruitment of team 7 appears to be a good fit for BPL, topic-wise, the committee wonders why at this career stage he is already considered as a separate 'team' while not having stabilised his position and funding. The scientific environment within BPL is exceptional, with a distinctive combination of basic and theoretical approaches that fosters the development of integrated approaches. The technical developments set up by some teams are remarkable (e.g.' in vivo biochemistry' in Drosophila (team 1), photo pharmacological methods for controlling ion channels (team 5), new experimental paradigms to study behaviour (team 5) and enable to envision their large application and diffusion. There is also the possibility for BPL to hire an additional junior team after the move in the new building and the departure of team 2 to another institute. Hiring a team focusing on theoretical approaches would be a good addition to the present competences. The committee also encouraged extending the initiated collaborations between team 5 and team 3. A second major asset for BPL scientific environment beside the interdisciplinary offered by ESPCI is its membership of PSL university where Neuroscience is very well represented and BPL efforts to reinforce this community is considered very positively. Altogether this

environment strengthens the BPL opportunity to recruit high-level students with various backgrounds, a crucial point to maintain competitive research.
Altogether feasibility is excellent. All the teams but team 7 secured comfortable funding (e.g. ANR, FRM) for the coming years. As mentioned above, mastering by the teams of the top-to-the-art techniques for studying brain function (e.g. electrophysiology, functional imaging), for analysing complex behaviours, and for targeted control of brain activity (e.g. optogenetics, chemogenetics) support well the feasibility of their ambitious objectives.

Recommendations:

- The committee recommends that the new directorship considers whether the present strategy is sufficiently developed to maintain a unique identity within a competitive environment.
- When new recruitment will be done collaborative synergies should be considered as well as prior discussions with ESPCI to optimise welcome conditions.
- ESPCI interdisciplinary environment should be better exploited for collaborative purposes and the continuous fostering of innovative approaches (e.g. imaging).
- BPL should pursue a recruitment policy to bring in more young researchers into the unit.

RECOMMENDATIONS TO THE UNIT

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

The committee recommends to (1) try fostering more internal collaborations to improve the cohesion and maximise the potential of the Unit, (2) get an external opinion for strategy and decision processes from a Science Advisory Board (SAB), (3) explore possibilities to better share resources and take a better advantage of the scientific environment offered by ESPCI, (4) enhance quantitative analysis and modelling capabilities, which may still be relatively under developed, (5) foster BPL spirit by stimulating social life and inclusion of the newly recruited teams, (6) take into consideration the recent suggestions from the students relative to this point, (7) establish a committee and define future actions to take for reducing CO2 imprinting, (8) formerly identify inside BPL a representant to contact if problems of 'equality/harassment' arise, (9) set an 'annual interview' with the direct supervisor (n+1) also for non-permanent technical staff.

Recommendations regarding the Evaluation Area 2: Attractiveness

The committee recommends to (1) consider for future post-docs or candidates to a permanent position, profiles with a track record external to the unit, (2) explore ways to offer attractive packages to applicants, (3) reinforce visibility (e.g. websites, social media, invitations of external scientists for seminars, organisation of international conferences, symposia).

Recommendations regarding Evaluation Area 3: Scientific Production

The committee encourages – the very performant teams to carry on in the same way – the direction to coach young teams and mentor students and post-docs for their applications. – to increase the collaboration potential by making better use of their complementary approaches – devise a strategy for rapid dissemination of new methods and – larger contributions to reviews.

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

Opportunities in terms of translational research with a societal contribution could arise in particular with the new studies on brain pathologies (e.g. team 1 Alzheimer, team 4 psychiatric diseases, addiction…). BPL members should be actively encouraged to participate in scientific culture or dissemination events and go beyond relying on individual initiatives.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1 Energy & Memory

Name of the supervisor: Thomas Preat et Pierre-Yves Plaçais

THEMES OF THE TEAM

Research directions are dedicated to molecular, cellular and physiological processes for memory formation. Specifically, the two main axes of the lab are focused on metabolism and energy required for learning and on modelling Alzheimer's disease; both making use of the well-established mushroom body circuit in the fruit fly as model. The team has a long-standing and outstanding track record in both areas and pioneered particularly the connection between energy metabolism and distinct memory types.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report identified only a few weaknesses concerning the team and overall recognised its excellence. One point raised concerned the lack of funding for the disease axis. This line of research is supported via non-labelled CNRS funds and patronage funding, and to a certain degree this point remains present. An advantage of the comparably cheap fruit fly research is that the project can be maintained without major funding. It is stated that current applications to Alzheimer's disease foundations may provide a solution. In the long-term it may indeed be beneficial to gain financial support for this axis of the lab; or – alternatively indirectly link it to processes in the metabolism and energy project.

The second point was the establishment of a co-leadership structure, for which it was suggested that the lab should be subdivided into two domains. The two team leaders decided to move forward with a structure of a united lab with defined projects by each team leader. The consolidation of the newer team leader with a Director of Research CNRS promotion as well as successful publications of the two co-team leaders suggests that the strategy was successful.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Staff categories	Workforces
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**7**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	2
Sous-total personnels non permanents en activité	**4**
Total personnels	**11**

EVALUATION

Overall assessment of the team

Overall, the team is outstanding. It has an exceptional publication and research track record with an outstanding international reputation. The questions that they pursue are both novel and highly original. In the past years, they have been extremely productive and largely pioneered the field linking energy to memory. The team has been highly successful in attracting competitive funding including support by an ERC advanced grant as well as multiple ANR grants and grants by several other foundations. Scientific productivity was high at all levels within the team.

Strengths and possibilities linked to the context

Both co-leaders are well established in the field of Drosophila neuroscience with an outstanding international reputation, having presented their work at several national and international conferences (e.g. EMBO Workshop: Molecular and Developmental Biology of Drosophila, Greece, 2022; 26th European Drosophila Research Conference (EDRC). Symposium 'How context and internal state shape behaviour' Swezerland 2019). The co-PIs have published as co-corresponding authors on the most impacting publications of the team. Most relevant publications include contributions to Nature Comm, Cell Reports, Nature Metabolism, Journal of Neuroscience as well as collaborations in Cell and Nature. The investigations on energy metabolism and memory have been particularly intriguing because they highlight novel – and unanticipated – pathways and interactions of glia that are critical for distinct forms of memories. An intriguing connection that was hereby uncovered is the molecular form of energy-relevant metabolites and the role of glial cells. Recently they have contributed to the circuit dissection of the mushroom body when precise genetic tools became available to assess the function of individual cells within the mushroom body. The novelty and conceptual groundwork for this have been extremely strong and has received funding by the ERC as an Advanced Grant. As an exceptional acknowledgement, one team leader has recently been awarded Brixham Foundation prize and another has been awarded the CNRS Bronze Medal. Apart from the strong performance of the team leaders, the Assistant Professor within the team also published well and authored one article as a first author and two as co-corresponding authors. Along the same lines, the PhD students and postdocs have at least one first author or co-first publication, and most often at least one more article as second author, highlighting the productivity at all levels of the entire team. Beyond regular scientific productivity, the team has also participated at the 'Brain Week' or the Science Festival and participation at science awareness activities in high schools/college level. The team has also participated at press campaign of the Foundation for Medical Research (FRM) to highlight the relevance and impact of basic research for Alzheimer's disease in public, which has been recognised and broadcast on national television.

Weaknesses and risks linked to the context

The scientific excellence and productivity are strong, no major risks or weaknesses are apparent. The organisational change to a two-leader system appears established and the consolidation of the new team co-leader well advanced. Previous support by an ERC Advanced Grant certainly advanced research and the visibility of the work. Continued support by the ERC as well as the renewal of ERC funding is notoriously hard to achieve and the switch to a period without ERC funding may bring certain limitations. The current and continued publication record of the team, however, suggests that this period has not been harmful and potential future ERC grants may become relevant in the team's trajectory.

Analysis of the team's trajectory

The team is well established and the recent adaptations have been completed. The overarching line of research is dedicated to specific topics on learning and memory formation. Two parallel directions – energy dependence of memory and Alzheimer's Disease – are well established, with numerous publications in internationally leading journals. For both lines of research successful funding has been acquired. While metabolism became an attractive topic in various fields of biosciences over the past decade, the team took a pioneering role early on in establishing the fruit fly as model to link memory and energy, a decision that has paid off.

The core interest in linking metabolic energy with memory emerged from a pivotal Science publication in 2013, in which the team showed that starvation and feeding status is linked to memory performance; initially linked to dopaminergic input neurons. The continuation of this observation became a main line of research in the team and received funding by an ERC Advanced Grant. A major finding lies in the contribution of different types of glia to different memory phases and the use of distinct metabolites, which appear predominantly derived from glucose but differ for district memory types. Interestingly, several lines of preliminary results emerged to develop a comprehensive continued line of research mostly dedicated on molecular and metabolic pathways involved

in glia-neuron interactions and mitochondria regulating memory as future trajectories. The preliminary results support a role of fatty acids as metabolite as well as ROS as signalling molecule, specifically Hydrogen peroxide as signal from glia to neuron interaction.
Funding has been received by all of the three senior researchers, which provides security for the continuation of all lines of work. While it has been challenging to acquire funding for the AD projects in the past, recent financial support for this line of research is supportive of the approach and emphasises its validity, also highlighting that both lines of research in the team are successfully funded. The research strategy and topics continue along the same to lines – importantly the mentioned link between the two lines of research in the self-evaluation may further harbour synergies thematically and experimentally. On the molecular side, the link of Abeta42 to acetylcholine receptors in glia cells as well as the modulation of the fly Alzheimer Precursor Protein (APP) by certain metabolites has been elaborated.

Moreover, the consolidation of the Assistant Professor within the team, as senior researcher, will continue with the foreseen research direction habilitation (HDR) in 2024. In the long-term the possibly for a nomination for promotion as ESPCI professor might be envisaged.

RECOMMENDATIONS TO THE TEAM

The scientific directions are clear and the strength and potential risks of the respective lines of research are clearly recognised in the self-evaluation. The team has taken a pioneering role in linking metabolism, energy with learning and memory, thereby uncovered fundamental processes. It is clearly recommendable to continue to pursue a research plan along these lines and to build on previous expertise. The research plan clearly illustrates that the subsequent directions are well defined and that critical scientific questions will be addressed.

The interaction between the two lines of research may become relevant and foster synergies within the team. It would be recommended to enhance synergies, for example, as the emerging connections between APP and ROS. Publication track record is outstanding and given the current status of publications in preparation it is foreseeable that this trend will continue, continuation along these lines would also be critical for future competitive funding. While Drosophila is a powerful model system for genetic studies it is sadly often disregarded by funding agencies for biomedical research, a reason that may hinder more funding support for AD-line of research; here joint and collaborative projects with mouse or medical laboratories may increase the chances for successful applications.

Team 2 Genes Circuits Rhythms and Neuropathologies

Name of the supervisor: Serge Birman

THEMES OF THE TEAM

The team is known for its work on the dopaminergic neurons in Drosophila models, including for production of the first Th-Gal4 driver, and a brain dopamine-deficient mutant. In recent years, the research remit of the team has shifted towards an applied axis, seeking to identify synaptic pathways involved in neuroprotection, with a focus on Parkinson's disease and incorporating elements of ecotoxicology. This work combines imaging methods, behaviour and neurogenetics to study relationships between the dopaminergic system, activity, circadian rhythms and stress resistance.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous committee recommended wrapping up the ongoing projects of the team up to publication and notably the projects involving the permanent scientist who joined the team during the period. Following the recommendations, the team has published work relating to the former projects, including one study led by the scientist who had at the time recently joined the team (Lecompte et al. 2020 J Comp Neurol).
It was also recommended that specific efforts should be made to retain visibility to students following the retirement of a team member with teaching involvement; the group has trained nineteen students at Master-2 level or below, indicating success in this area.
The committee encouraged efforts towards communicating the advantages of Drosophila as an animal model to study endophenotypes of human diseasesThere has been some work in terms of outreach and communication with the public, including participating in a conference attended by Parkinson's patients. However, the team states that outreach has not been an important part of their activities.
Greater interaction with other teams within the unit was recommended. There is little indication that this has materialised, although external collaborations have been evident and are well developed.
The committee suggested allowing the line of research to adapt to the interests of individual new researchers, although not to the cost of the existing core. This is evident to some extent in the publication portfolio, where each PI is represented on at least one publication, although this work is yet to reach its full potential.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Staff categories	Workforces
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	0
Sous-total personnels permanents en activité	**3**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	2
Sous-total personnels non permanents en activité	**3**
Total personnels	**6**

EVALUATION

Overall assessment of the team

This is a very good team that is internationally recognised for its work on dopaminergic neurons using Drosophila models. Scientific production has been very good and includes significant work as lead (e.g., PLoS Gen) and collaborative contributors (e.g., Cell Rep). Its capacity to raise funding is excellent, evidenced by two ANR grants (one as coordinator) and other national sources (e.g., FRM, FDF as partner). The team has an excellent profile of external collaborative links and success in attracting a significant cohort of international students (12). However, the team would benefit from strategic consideration of the career trajectories of the newer senior researchers.

Strengths and possibilities linked to the context

The team is internationally recognised within its field and continues to cover both fundamental and applied research. From the perspective of scientific outputs, the team's performance has been very good during the period. Key publications include work in journals such as PLoS genetics (senior authorship) and Cell Reports (co-authorship), and both lead and co-authorship positions on other publications that include more field-specific journals. An exceptional contribution during the period has been a demonstration of a circadian-independent role for the gene Clock in protection against premature locomotor aging (Vaccaro et al. 2017, PLoS Genetics). The team has a good record of securing funding to cover its work, deriving from two ANR grants>300k€ (one as lead) alongside nine smaller national-level grants. The team leader has received invitations to present internationally at conferences in the USA and India (as well as nationally), contributes to editorial boards (e.g. Frontiers in Neuroscience, Neurodegeneration Section) and organised two symposia at international meetings, evidencing a strong international reputation. In terms of attractiveness, the team has an excellent record of successfully attracted visiting researchers at a junior level on a global scale (10 nationalities represented, excluding France), making for a multicultural environment that includes researchers from the global south. PhD students within the team usually produce at least one first-author paper from their PhD work. The team has also trained nineteen students at Masters level, indicating success in maintaining visibility to students. A particular strength is the team's record of international collaboration, with ten active collaborative projects during the period. Several of these have resulted in joint publications (e.g. Sun et al., Front Syst Neurosci 2018; Rahmani et al. Int J Mol Sci 2022), and others are evidenced through co-supervision of PhD students. This is clearly a very collaborative team, again evidencing a strong reputation at the national level.

Weaknesses and risks linked to the context

Although the team pursues several themes, the publication record during the period is unevenly spread between the permanent researchers. Two of the eight first/senior author outputs include other team members in a first/senior position, and so strategic consideration of the career trajectories of those researchers would be beneficial. Relatedly, the strategy of publishing several years of work in one paper is a risk for the PhD students. Although six of the eight PhD students trained by the team published as first author during the period, most did not publish more than once in the three years of the project. The team maintains over 1500 fly strains that must be cared for and distributed to other laboratories, but benefitted from the technical support of a single technician at 20% Full-Time-Equivalent. This potentially represents a considerable logistical and administrative burden for the researchers, who must distribute fly strains according to collaborative requests, alongside the high time investment required by maintenance. The team is strong in terms of international collaboration, but this is not yet represented in the acquisition of funding at international level. However, the team has successfully secured grants at the national level to maintain these collaborations. The gender balance within the team is a significant departure from benchmarked norms (female-dominated at all levels except the very top). It is not clear what has driven this situation. Engagement with the public is relatively low. The team states that communication to the public is not an important part of their activities, and although they have contributed to outreach events, the majority of engagement forums listed involved university students (with exceptions). This strategy comes at a risk of a missed opportunity to engage the public, particularly given the enormous applied interest of the team's work on Parkinson's Disease and the rarer Lesch-Nyhan disease. However, there has been an important contribution to workshops involving Parkinson's patients.

Analysis of the team's trajectory

The team will leave the unit at the end of this contract; therefore, the trajectory is not analysed.

RECOMMENDATIONS TO THE TEAM

The team is leaving the unit to merge with another team; therefore, no specific recommendations are provided.

Nonetheless, the importance of building new internal relationships in the team's new host institute is clear. These would allow the two CNRS researchers to build independent profiles and develop their interests to strengthen the team's research portfolio, which encompasses a strong base that could be emulated within the new research axes that are currently developing. More visibility of these researchers at international conferences would be a positive contribution in this direction.

Team 3 Emotion, Memory, Oscillations and Brain-Body states

Name of the supervisor: Karim Benchenane

THEMES OF THE TEAM

The team aims to investigate brain states, oscillatory modes and their role in memory processing through in vivo and ex-vivo approaches through monitoring breathing-related oscillations in the olfactory bulb whilst focusing on fear and aversive learning. The historical topics include sleep physiology with emphasis on non-Rapid-Eye-Movement (REM) sleep as a potential target for manipulation of reward and aversive memories. The new topics are emotion, aversive learning, stress, and brain-body interaction during wake and sleep. Here, physiological responses including freezing are studied in-depth in the rodent model including dedicated behavioural and electrophysiological techniques.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Following an 'outstanding' evaluation in 2018, the HCERES evaluators stressed the discrepancy between team size and the complexity of domains of expertise including the applied methods. This point was indirectly answered by shifting the research focus of the team that was bound to the development and implementation of new methods adapted to the team's size. Similarly, the recommended optimisation of expertise and resources, enhanced by the ongoing integration of a new ESPCI assistant professor, was mastered whilst refocusing the research topics of the team. The hiring of one young Chargée de Recherche (CR) through the CNRS will unequivocally strengthen the aimed cohesion.
The recommended collaboration with industry aiming at speedy transfer between the animal model and human was, particularly after the departure of the assistant professor, not followed further.
The recommendation for a senior scientist to obtain their HDR was followed with the appointment of the team leader as CNRS Director of research (DR2) in 2021 at 1st place in section 25.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Staff categories	Workforces
Professeurs et assimilés	1
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	**2**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	3
Sous-total personnels non permanents en activité	**4**
Total personnels	**6**

EVALUATION

Overall assessment of the team

This is overall an excellent team representing a mix between established and early career researchers with clear potential for major discoveries. The relatively low publication activity is partially compensated by the excellent scientific output in top journals. The team's funding is outstanding – besides several highly competitive grants (e.g. consolidator ERC) the team has ensured the transition of a PhD student to a CNRS permanent position. Despite this voluptuous funding, the team size remains an issue preventing the strong potential for translation of research achievements to clinically relevant domains. The funding of the next phase through competitive grants is not yet secured. The team has to be commended for their outstanding connections with industry, contributions to research evaluation (participation in various committees and boards) and teaching as well as for stepping up their activities in promoting science to the general public.

Strengths and possibilities linked to the context

The major strength of the team is the excellence of research in a niche topic with great potential translational and clinical relevance in humans. The team's expertise and methodological knowhow are innovation-oriented with a great portion of cohesion between senior members. The team has successfully integrated as new member an Associate Professor at ESPCI and has changed accordingly the research focus. During the evaluation period, the Associate Professor at ESPCI mastered the in vivo electrophysiology and optogenetic manipulation to enhance the interdisciplinary portfolio of the team. The cohesion is completed with the successful application of one early-career former member of the team for a CNRS position ((ranked 1st in section 26). The research focus changed to the investigation of emotion, aversive learning, stress and brain-body interaction during wake and sleep. The introduction of combined olfactory bulb gamma power analysis with hippocampus theta activity recordings allowing for robust and reliable sleep scoring, led to important new discoveries. Similarly, the differentiation of freezing subtypes in the U-maze contributed to the highly promising pharmacological pilot study with fluoxetine vs. diazepam to show unique effects of panicolytics vs. anxiolytics. This is considered as important for the team topic that will be led by the recruited CR potentially supported by an ANR grant (application in the 2nd step of evaluation). Equally promising is the current research activity in the field of cortico-subcortical interactions underlying social defeat stress and REM sleep.
This work resulted in a large dataset, two peer-reviewed publications (Nature Comm., PLOS Biology), three preprints on BioRxiv and five manuscripts at the preparatory stage. There are 6 co-authorships in the domain of sleep. During the evaluation period, the team relied on the continuation of the PIs ERC Consolidator grant (2016–2023), collaboration within two ANR grants (ASTROSLEEP (2013) and COCODE (2016)) and two Labex Memolife supports (2016). There was a decision not to apply to any further grants, but to focus on contributing to scientific evaluation in France – ANR as expert and vice-president of section 25 International Neuroscience. All the PhD students and Postdoc-secured employment after their time with the team. Placements included the private sector (start-up Cog-X, R&D at Cap Gemini, data scientist in a neurotech company, project manager at Merck pharmaceutical) and academic research (permanent CNRS position in the team, after a postdoc at UCL London, UK). The PI is an internationally recognised expert in his domain, well represented at various levels of national and EU-led research evaluation bodies. These and other activities are clearly contributing to enhancing the visibility and attractiveness of the team. The existing and future collaborations at the national and international level, additionally to the shared knowhow with other labs are a strong proof for the team's openness and commitment to transparent and collaborative science. The reputation of the team follows a rising trajectory – with participation on prestigious research committees and boards (GDR Neuralnet; ANR, elected member of the Scientific Council of the French Society for Neuroscience – 2016–2019– , both senior members serve at PhD committees and engage in teaching (organiser of Winter School on neuronal data analysis, workshops – Replays In Paris, College de France - 2019) and presenting their research in France (SFRMS 2020; Spring Hippocampal Research Conference 2019, 2023; Académie de médecine's Journee Claude Bernard 2021) and overseas (The Trieste Encounters on Cognitive Science – 2018; The Killam Lecture, McGill Canada; The Benesco Lecture – Switzerland). The team actively contributes to the unit's ethical protocols and data protection. One member of the team was appointed in 2018 as the new responsible for the mouse animal facility serves on the SBEA, and regularly organises meetings to evaluate ethical projects involving experiment on mice. The team emphasises research with potential for real-world human applications and collaborated with private companies: Partnerships include Dreem, which created an EEG headband for home sleep monitoring and XII, which developed virtual reality for pain management. Both collaborations received CIFRE funding. The team also collaborated with URGOTech. The team has an excellent diversity and gender balance track record – this should be supported and continued.

Weaknesses and risks linked to the context

The major weakness of the team is its low scientific publication activity. This counteracts the attempts to increase its visibility and attractiveness through collaborations, participation in research evaluation committees and scientific discoveries. This threatens the financial stability of the team, its potential for expansion. Given the transforming shift in the team's scientific focus, the maintenance and further development of new data acquisition and analytical techniques remains under the financial pressure that defines the team's size and teaching forces. The lack of a strategy for translation of animal research to humans poses a mid-to long-term challenges to the relevance of the outstanding scientific discoveries.

Analysis of the team's trajectory

The team has refocused its research on characterising the two types of freezing and their relation to panic and anxiety dissociation. The purpose is to study the underlying neurophysiological mechanisms, modulation profiles of various psychoactive drugs, and the neurophysiological impact of stress on sleep. These investigations are well focused and innovative. The committee recognises that the expertise and previous data in the field mentioned above (e.g. the team observed that freezing behaviour, previously considered a single homogeneous state, actually corresponds to two distinct types of fear depending on the situation) place the team in a very good position to competitively develop these projects. Interestingly, the team observed these two types of freezing in the social defeat stress task during which mice are exposed to mice used as aggressors. The techniques that will be used to characterise the two types of freezing by examining neurophysiological and bodily responses and their causal role (optogenetics to manipulate olfactory bulb oscillations and closed-loop stimulation to disrupt SWR) are stated to the art and mastered. The collaboration with the group 5 on the potential anxiogenic effect of nicotine is encouraged. The team also envisions to characterise the brain-body interaction in the different types of freezing by studying Corticotrophin-Releasing Hormone neurons via their chemogenetic manipulation, monitoring their activity in the behavioural tasks with calcium imaging and fiber photometry. The team will also evaluate sleep in stressful situations and their influence on the two types of freezing (supported by ANR Audiodreem) as well as the development and evolution of the two types of freezing in collaboration (supported by the submitted ANR BrainBody4Fear).
The team is well equipped technically and intellectually to perform the proposed projects. The team is recognised for its pioneering brain computer interfaces, with several methods such as the rewarding electrical stimulation protocol as well as the sleep scoring used by other teams. The main risks lay in the discrepancy between the workforce of the team and the ambition of the projects and its ability to obtain additional grants.

RECOMMENDATIONS TO THE TEAM

The team should focus on enhancing its publication activity that will be the premise for successful grant applications. As in the previous evaluation, also in 2023 the team size remains an issue – both in terms of maintenance and further development of highly specific and complex techniques, but also a decisive step determining publication activity. Successful competitive funding can partially compensate for the lack of CNRS funding for an engineer needed for supervision of the students. The national and international collaboration should be strengthened – the current joint supervision with colleagues from Canada, the planned activities with Marseille and Denmark, additionally to the fact that there are international students, increase the visibility and attractiveness of the team. As previously recommended, the links to industry should not be negated – the translation of the obtained promising results in the animal model to humans should be a priority.

Team 4 Cerebral Codes and Circuits Connectivity

Name of the supervisor: Gisella VETERE

THEMES OF THE TEAM

The young ATIP/AVENIR team investigates the neuronal substrate of memory acquisition and consolidation using mice as model organism. The projects are divided in two main fields of interests: 1) The process of consolidation of long-lasting memories; 2) The nature of memory engram cells in the brain. To address these two topics, they use cutting-edge techniques to probe neuron and neural network activities during memory processing such as optogenetics, graph theory analysis of networks, in vivo calcium imaging, electrophysiology, and computational modelling.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

This team integrated into the unit in August 2018 and was thus not evaluated by the previous HCERES committee.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Staff categories	Workforces
Professeurs et assimilés	1
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**2**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	3
Sous-total personnels non permanents en activité	**4**
Total personnels	**6**

EVALUATION

Overall assessment of the team

This is an excellent young dynamic team with strong potential. Transition of the team leader to independence is ongoing with own funding (860 Keuros since setting up team), international recognition (47 invited conferences) and team's international workforce. This positive trajectory warrants validation in next years by last and 1st authorships of the team leader and workforce, respectively. Attracting other senior scientists for supervision duties could be a plus. Building national/international networks to obtain funding and increasing translational relevance of findings towards the clinics should be considered.

Strengths and possibilities linked to the context

The PI research contribution is exceptional as demonstrated by her previous publications as first author with two publications in Nature Neuroscience and one publication in Neuron, its strong international recognition with two international awards by the PI (Brain Star Award 2017; Aspirational Neuroscience Prize 2019) and the numerous

invitations to the PI to give seminars around the world (47 invited seminars including in international conferences such as SFN, FENS, etc.). These publications generated a large body of international highlights, online articles and blogs for scientific and general public (e.g. 'Editor's choice' in Science, Faculty 1000, scientific american article, etc.). The team leader also organised a symposium as a satellite meeting of FENS 2022 focusing on her topic. Between 2017 and 2022, the team leader published 4 first-author original research articles, three of which were published in top 5% of journals in the field (2 Nature Neuroscience, 1 Neuron). The PI also co-authored two other articles. Overall, during the evaluated period (2017–2022), the publication out represents 66.66% of publications as first author. This production totalled about 280 citations. The production is exceptional, although stemming from the PI's previous work as a post-doc. The PI also published a book chapter in Italian. Since the team's creation, the PI obtained competitive funds (total of 860 K Euros) (ANR JCJC, ANR as co-PI, NARSAD, Emergence de la ville de Paris) and the ATIP/AVENIR label (but funding declined due to the ANR JCJC). Most funds were obtained as single PI, except for one ANR where she is co-PI with other French teams. One post-doc obtained a MSCA fellowship and the three PhD students obtained their own fellowships. The team's ability to raise funding is thus excellent. The PI was able to attract post-doc, PhD, Master and visiting students from different countries creating a highly international environment. The first PhD student just graduated after obtaining a 4th year by the FRM, but the first author publication is still being prepared. A first manuscript with a post-doc of the team as first author and the PI as last author is on Biorxiv and under revision. These trainees had the opportunity to present their work as posters at international meetings (e.g. SFN and FENS). The PI is involved in local committees such as the Equality program at the ESCPI to promote gender balance and the 'Cellule d'écoute et de veille', a group acting at PSL to facilitate reporting of sexist, sexual violence, harassment and discrimination. The PI also has heavy teaching duties at the ESPCI from Licence to Master level.

Weaknesses and risks linked to the context

While there is a strong positive dynamism of research in the team, it has yet to be valorised by last-authorship publications of the ongoing research by the PI and first authorship by the workforce. It is expected as the research is now effective for about 4 years (albeit the COVID sanitary crisis), but publication as last author will be the challenge in the couple of years to come. The funding capacities are secure for only a couple of years of the new contract. The PI is not yet part of national or international networks (only one ANR in collaboration with other French teams). This diminishes the potential to obtain additional funding. The research is highly fundamental, but could be of relevance to different diseases e.g. post-traumatic stress disorder and schizophrenia (as mentioned in the document). Yet, the PI does not mention any collaborations with the clinics. This diminishes the translational potential of the findings. As the PI is professor is the only senior permanent staff in the team and holds teaching duties, this provides a risk for highly efficient supervision on a daily basis in the lab. Yet the PI seems to manage supervisory activities quite well maintaining this delicate balance between teaching and supervision as attested by the large body of preliminary data and ongoing manuscript preparations as last author presented during the visit.

Analysis of the team's trajectory

The trajectory of this young team is on a positive ascending slope. The research will continue to be funded, at least for a few years, by two ANRs. State-of-the-art technologies to perform detailed analysis of neural networks dynamics in vivo in behaving animals are now mastered and routinely used by PI and workforce. These include use of miniaturised microscopes to analyse calcium dynamics in substructures during behavioural analysis, optogenetic tools including the Fast Light and Calcium-Regulated Expression (FliCRE) tool to tag and reactivate neurons that were active during specific behaviours, deep learning and graph theory to analyse large neural networks. The ongoing projects belong to two main aims: 1) to study the network dynamics during long-term memory consolidation; 2) to study the engram dynamics during memory acquisition. These are addressed in five ambitious projects piloted by different members of the workforce. With the current workforce and grants obtained, the projects are well developed. As each one is complex in its questions and hypotheses to be tested, it seems like the PI's workforce is diluting its energy on all projects at the same time, which could complicate their finalisation within a reasonable timeframe. The first team's project is finalised as a manuscript deposited on BiorXiv and currently under revision for publication. Finalising results into peer-reviewed publications will be the major challenge facing the team in the coming years. There is, at present, limited collaborations with local teams, be it within the unit, at ESPCI or within the city. Also, the young PI is not yet well integrated in larger French or international consortia. PI is currently the only permanent team member having to supervise all aspects of projects. PI will continue to participate in teaching activities to disseminate knowledge, but little contribution to dissemination to society is foreseen.
The committee recommends that the PI focuses on the most advanced projects to ensure efficient completion and transformation into high-impact publications. In future, focusing on fewer key projects that are most strongly related to the theme of the team would help to enhance overall scientific impact and visibility. This is important to ensure future career paths of the workforce and attractiveness to new students and post-docs. Also, we recommend building additional French and international networks to obtain new funding to maintain recruitment and increase visibility, including to lay public. Research performed is relevant to memory-linked disorders. The PI could take advantage of this to increase translational relevance of findings with links to the

clinics or complementary work on human tissues. This should help valorise work. While the committee acknowledges that it is very difficult to attract permanent staff, the PI, with help of the direction, should discuss all possibilities to stabilise the team with additional permanent personnel.

RECOMMENDATIONS TO THE TEAM

This is a dynamic young team that holds all the cards to transform this positive energy into impactful publications. It will be important for the PI to publish the original research obtained in these last years as last author soon to finalise this transition to independence. The fact that the PI holds both a team leader and professorship position is commendable but makes it a challenge to be forthcoming on all fronts. The PI should try to attract senior researchers to the team to help her in day-to-day supervision of activities regarding the research. The development of national and international networks (e.g. Europe) will be essential to obtain additional funding. We recommend looking towards the clinics for collaborative work to validate the findings obtained in rodents.

Team 5 Neurophysiology and Behaviour

Name of the supervisor: Philippe Faure et Alexandre Mourot

THEMES OF THE TEAM

The overall research theme of the team is how nicotine modulates reward, aversion and decision-making in mice through its effects on the midbrain dopaminergic (DA) system. A particular emphasis is placed on understanding inter-individual variability in behaviour and how it relates to nicotinergic and DAergic circuits. The team also aims to understand how these circuits could underlie nicotine addiction and how they are affected by stress. To address their scientific questions, the team uses state-of-the art methods including in vivo and ex vivo electrophysiology, optogenetics, behavioural analysis and computational modelling as well as 'photopharmacology'. The team has made important contributions to the development of this a cutting-edge tool.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Since the team joined the BPL in 2021, it was not evaluated in the previous report

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Staff categories	Workforces
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	**6**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	5
Doctorants	8
Sous-total personnels non permanents en activité	**13**
Total personnels	**19**

EVALUATION

Overall assessment of the team

This is an excellent to outstanding team with an international reputation. The team has an excellent to outstanding scientific performance during the evaluation period and has further consolidated its position as a leading authority of nicotinergic modulation of the dopamine system at the electrophysiological and behavioural levels. The team has incorporated new members, has graduated PhD students and many existing members have advanced to higher career stages.

Strengths and possibilities linked to the context

The team has been scientifically very productive during the evaluation period, publishing sixteen peer-reviewed articles with group members as first and/or last authors, with several of these in high-impact journals including Nature Biomedical Engineering, PNAS, eLife, Neuron, Nature Comm and Molecular Psychiatry. Their discoveries regularly published in high impact international journal deal with how nicotine differentially affects projection-defined dopamine neuron subpopulations to influence anxiety (Neuron, 2021), the elucidation of how nicotine

affects individual decision-making strategies (Nature Comm, 2021), how interindividual differences in behaviour are related to differences in dopaminergic activity (Nature Comm, 2018) and how nicotine's effects on dopamine neurons might mediate stress susceptibility Molecular Psychiatry, 2018). The team has also continued to develop and apply the method of 'photo-pharmacology' involving the activation of nicotinic receptors by light (Elife, 2018), which will likely be of great value to the larger neuroscience community. In addition to their high-impact publications, the team's international visibility is also demonstrated by participation in international conferences including the Gordon Research Conference and a keynote presentation at the Dopamine meeting. Team members have also received numerous scientific awards at the national and international levels (Prix de La Recherche for neuroscience researchers, Nemko Prize in Cellular or Molecular Neuroscience). The team co-leaders have acquired approximately EUR 3 million in funding between 2017 and 2022, mostly from within France (ANR, FRM) but also from prestigious international programs such as the HFSP. The current team is highly diverse, with all career levels (master's student, PhD students, Post-doc and PI) well represented. It is also very international, with many members from outside France (Netherlands/Italy, Sweden, USA and Switzerland) and the ratio of male and female group members is overall good (12 females, 14 male). The team also appears to be highly collaborative, as demonstrated by the large number of co-authors (13 to 22) on the papers published by the team. The self-evaluation carefully details how the team ensures the training of its members and helps with their career advancement. Several team members at various career stages have advanced their career during the period and 6 PhD students have defended. Each PhD student has published an average of five articles, which is an impressive number and indicates that the students are productive and contributing scientifically. The team members also take an active part in teaching in various programs at different institutions (Sorbonne University, Paris Cité University, ENS, Paris Tech and Pasteur Institute) as well as in public outreach (hosting of high school students, popular articles in scientific information media).

Weaknesses and risks linked to the context

This is a very strong research team and no major weakness and risks could be identified, especially with regard to the science. However, a few areas of improvement are worth mentioning. The team has made several important discoveries during the evaluation period relating dopamine neuron activity to behaviour, using the juxta-cellular recording method (Torquet et al., 2018; Morel et al. 2017). The advantage of this approach is that it allows unambiguous identification of dopamine neurons. The disadvantage, however, is that recordings are (by necessity) performed outside the behavioural tasks and thus the relationship between dopaminergic activity and behaviour can only be tested at the team level using measures of spontaneous activity (as opposed to measuring task-related activity in the animals while they perform the behavioural tasks). Given the high relevance of the team's research topics to human psychopathology (addiction and vulnerability), a lack of collaboration with clinicians can be seen as a potential weakness. Overall, the number of male and female team members is quite well balanced; however, the PIs are mostly male.

Analysis of the team's trajectory

The team's success in the evaluation period in terms of scientific output, the impact within the scientific community and acquisition of funding rises 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 nonetheless compelling and clearly builds on their scientific and technical achievements from the previous years. Particular focus will be placed on social behaviour and how the social environment mediates individuality and confers vulnerability to psychiatric illness. The role of nicotine and its associated circuits will continue to be investigated in this context using new tools and refined versions of tools already existing in the team. On the one hand, the team plans to further develop their 'photopharmacology' approach to more precisely control the activation of nicotine receptors in the brain; on the other hand, they plan to develop new behavioural arenas that allow mice to display more naturalistic behaviour while at the same time allowing precise monitoring of these behaviours. This is a very exciting research trajectory; the importance of studying behaviour not only under the highly constrained conditions of typical behavioural tasks but also under semi-naturalistic conditions is becoming increasingly more appreciated in neuroscience. However, such an approach poses two challenges that the team will need to overcome. One of these concerns the quantification of naturalistic behaviour, which can be extremely high-dimensional and should be analysed as such to capture its richness. Equally complex is the issue of how to relate such high-dimensional behaviour to neuronal activity. Although the team possesses considerable data analysis skills and has recently recruited a computer engineer, it is not clear whether these resources alone will suffice for these new analytical challenges or whether the team will need to seek collaborations with experts in for example machine or deep learning within the local community. The second challenge will be to record neural activity from behaving animals in the complex environments that the team plans to use, which may not be compatible with tethered recordings (e.g. tunnels) or the presence of other mice. Thus, the team might face a trade off in the richness of the behaviour they can study and in how much detail they can simultaneously record neuronal activity. However, given the team's outstanding publication record to date, there is a high likelihood that it will be able to overcome these obstacles and generate interesting scientific findings. Overall, the team's trajectory is realistic in terms of its expertise and workforce. The

team has funding until 2025 and its outstanding track record in securing grants during the evaluation period gives hope that they will be successful in acquiring additional funds during the next period.

RECOMMENDATIONS TO THE TEAM

The team's scientific trajectory builds on its strengths and achievements in the current evaluation period. At the same time, the research direction is novel and exciting, with its emphasis on social behaviour and interindividual variability. New methods established by the team for examining neuronal activity during the evaluation period, such as fibre photometry, should be put to use for examining the activity of dopaminergic neurons during behaviour. Given the potentially novel analytical challenges posed by this research direction, the team should consider collaborations with experts in machine and deep learning within the Paris scientific community. Given the high translational relevance of the team's research (addiction and vulnerability), collaborations with clinical researchers should be considered, which might increase the team's visibility and funding opportunities.

Team 6 The dynamic synapse

Name of the supervisor: Sabine Levi

THEMES OF THE TEAM

Team 6 will be created at the beginning of the next contract by a PI who previously co-headed a team focusing on the mechanisms of formation and plastic regulation of central synapses at the 'Institut du Fer à Moulin' (IFM). The new Team 6 will explore the mechanisms underlying the development, stabilisation and plasticity of GABAergic and glutamatergic synapses. It will focus on the role of adenosine A2A receptors and WNK signalling, which have previously been identified by the team as key regulators of GABAergic transmission. To achieve its objectives, the team uses a multidisciplinary and multiscale approach combining biochemistry, electrophysiology, calcium and chloride imaging, as well as state-of-the-art imaging techniques including 3D single particle tracking and super-resolution microscopy.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous committee recommended the team to maintain its productivity moving forward and specially to highlight its success and team profile with the generation of additional high-profile reviews.
The team significantly improved its productivity, capitalising on its previous research and the launching of new research programs, with the publication of several articles in wide readership generalist journals such as Science, Nature Comm and Cell Reports). The team also published five review articles (TINS, Neuropharmacology, Frontiers…) and one book chapter, to increase its visibility in its research fields.
The committee also encouraged the team to pursue its research efforts on KCC2 and the regulation of inhibitory synaptic development and plasticity given its high level of expertise in these areas.
The PI has followed this recommendation by deciphering 1) a key mechanism of stabilisation of nascent GABAergic synapses (Science 2021), 2) the role of GABAA receptor lateral diffusion and phosphoregulation of gephyrin in synaptic scaling (Battaglia et al., eNeuro 2018), 3) the impact of conformational changes of GABAA receptors induced by channel opening or desensitisation on the diffusion/stability of GABAA receptors at synapses (Merlaud et al., iScience 2022).
The recommendations of the previous committee have been entirely followed by the team.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Staff categories	Workforce
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
Sous-total personnels permanents en activité	**2**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	1
Doctorants	4
Sous-total personnels non permanents en activité	**6**
Total personnels	**8**

EVALUATION

Overall assessment of the team

This is an excellent to outstanding team which has been successful at all levels. Its scientific production and technical achievements are outstanding. The team has published remarkable work identifying a key mechanism underlying the stabilisation of nascent GABAergic synapses and highlighting the role of the chloride-sensing WNK signalling pathway in the regulation of GABAergic synapses. The fund-raising capacity of the team is impressive, with 3 M€ secured from various competitive European and national calls during the previous contract. Overall, the team has a high international reputation and appeal and has been successful in attracting talented early career scientists from France and abroad.

Strengths and possibilities linked to the context

The team has made seminal discoveries in the field of formation and stabilisation of GABAergic synapses during development and the regulation of mature synapses. For instance, it has shown that if GABAA receptor- and A2 adenosine receptor-dependent signalling pathways act synergistically to stabilise GABAergic synapses, A2A receptor activation is sufficient. This led the team to propose that A2A receptors act as detectors of active GABAergic synapses to regulate their fate towards stabilisation or elimination. The team also identified the chloride-sensing WNK signalling pathways as a master regulator of GABAergic synapses in mature neurons. The team proposed that it might be a therapeutic target for the treatment of brain pathologies as epilepsy and psychiatric disorders. The team has published 24 original papers (including 10 in position of responsibility) and five review articles that totalled 580 citations over the assessment period. Some of them were published in wide readership or historically recognised journals specialised in Neuroscience with high quality standard requirements, such as Science, Nature Comm, Cell Reports, Neuropsychopharmacology, J Neurosci, J Physiol, iScience, etc. The team also filed one patent with an international extension for the use of KCC2 enhancers in refractory epilepsy. This is an outstanding production in the qualitative and quantitative points of view. The team has been successful in securing funding (near 3 M€ over the evaluation period) from European (2 ERANET) and national origins (5 ANR, FRC, FFRE) and received an FRM Team label in 2022. The international visibility and appeal of the team are evidenced by i) the large number of invitations to give conferences at national and international meetings (e.g. European Synapse Meeting, NeuroFrance 2021, Cajal course on Advanced Techniques for Synapse Biology 2019, Gordon Research Conference), ii) the participation of the PIs in editorial boards (eNeuro, Neuropharmacology) and various institutional committees (Scientific Council of the UFR 'Life Sciences' at Sorbonne University, Scientific Board of FFRE, chair of the HCERES visiting committee of GIN), and iii) their participation in scientific committees of DIM C-BRAINS and of the next FENS forum. Furthermore, the team is part of the Labex BioPsy. The team has been very successful in attracting students at all levels, as well as postdocs from various countries (e;g., Japan, India, Hungary, Austria, Spain). All PhD students and postdocs published at least one article as first author. The team's scientists are strongly involved in teaching. The PI participates in several master courses (Sorbonne, Paris-Cité) and in the prestigious Cajal course on advanced synapse biology techniques in Bordeaux. With regard to research outreach activities, the team's work was highlighted by INSB-CNRS, INSERM brief#52, journal of the French Society of Neuroscience, Médecine Sciences (article and cover) and by the national press (La Provence 2021) and TV (Interview in Le Magazine de la Santé, France 5, 2020). The team was also committed to hosting high-school students for their observation internship.

Weaknesses and risks linked to the context

The presence of a permanent technical staff to ensure the essential lab manager function in the team during the next contract is uncertain. This is certainly a weakness for such a team with three permanent scientists, including the PI and two associate professors with heavy teaching duties. In spite of the high-translational potential of the research theme of the team (for instance, the team's work suggests that the WNK signalling pathway as well as the NKCC1 and KCC2 transporters might be therapeutic targets in epilepsy and psychiatric disorders linked to the dysfunction of GABAergic transmission), its interactions with the clinics and pharmas/biotechs are limited. Increasing such interactions would certainly provide the team new opportunities of funding. The research outreach activities of the team are currently somewhat limited.

Analysis of the team's trajectory

The team has been highly successful over the past five years in terms of scientific production and funding and the challenge for the newly created team is certainly to maintain such a high level of productivity and funding in the future years. For that purpose, it is important that splitting the original team does not lead to a loss of expertise and technical skills in the newly created team.

The team's project for the next contract period is structured around three well-defined objectives, namely i) the role of adenosine A2A receptors expressed in neurons and microglia in glutamatergic synaptogenesis; ii) the role of WNK signalling in the regulation of KCC2, NKCC1 and GABAA receptors; and iii) the atypical role of NKCC1 acting as a scaffold for SPAK, the main effector of WNK, to regulate the activity of NKKC1, KCC2 and GABAA receptors. It will capitalise on a large corpus of preliminary data of the team suggesting a broad involvement of A2A receptors located in neurons and microglia in synapse stabilisation and pruning, respectively, and the key influence of KCC2 and NKCC1 in GABAergic transmission. It strongly relies on the expertise of the team in state-of-the-art imaging techniques, including single particle tracking and super-resolution microscopy and a multidisciplinary strategy from molecules to functional and behavioural studies in mice. It will also benefit from a strong workforce of PhD students (4) and the recruitment of two associate professors scheduled at the beginning of the next contract. Importantly, funding from various sources are secured at least until 2025, including an important 'FRM team' funding that recently started, which secure postdoc and engineer positions for the next term.
The expertise and workforce available in the team are solid guarantees for the success of the project on the mid to long term. There is also no doubt that the project will be impactful, especially if the team engages collaborations with other teams in the unit to capitalise on their complementary knowledge of behavioural tasks (anxiety, memory, etc.) and of the Drosophila model to test the physiological relevance of hypotheses from in vitro models.
The committee also recommends that the team initiates interactomics studies based on biotin proximity labelling approaches to identify in a more global manner SPAK/NKCC1 interactors and phosphoproteomics studies to identify novel WNK/SPAK substrates at GABAergic synapses, taking advantage of the great expertise in these approaches and state-of-the-art mass spectrometry facilities available at the Biological Mass Spectrometry and Proteomics team.

RECOMMENDATIONS TO THE TEAM

The committee recommends that splitting the current team will not result in a loss of expertise and technical skills. In this regard, it strongly recommends that the engineer who is currently working in the team will also move to the BPL laboratory to continue to provide the team her technical support to prepare hippocampal cultures and perpetuate its unique knowhow in the field.
The committee also recommends for the team to establish collaborations with other teams within BPL to benefit from their complementary expertise in physiological and behavioural studies, and to be more proactive in establishing collaborations with clinicians as well as pharmaceutical companies, given the translational potential of its research.

Team 7: Maintenance of the nervous system & behaviour

Name of the supervisor: Raouf Issa

THEMES OF THE TEAM

Team 7 very recently joined the unit and does not have team members yet. He aims to ultimately understand how neuronal function is maintained post development. The team leader (PI) is planning to follow two lines of research, with the overarching goal to understand how neurons maintain their function. In the first project, the PI wants to build on his previous, postdoctoral work and investigate early-acting regulator on neuronal function. In the second projects, the PI proposes to study the role of autophagy-related genes in a neurodegenerative disease model.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The PI integrated into the unit very recently, in January 2023, and was not evaluated by the previous HCERES committee.

Overall assessment of the team

The team has not formed yet, and the PI has just started, so there will be no assessment in this report.

Strengths and possibilities linked to the context

The PI of team 7 has an excellent track record from his postdoctoral work, as evidenced by high-profile publications (e.g. Issa et al. Current Biology 2019, Issa et al. PNAS 2022). This leads to high potential to obtain competitive funding, and he recently obtained a Marie Curie grant.

Weaknesses and risks linked to the context

The PI of team 7 has not attracted a permanent position yet. (His own position is only funded until September 2024). Recent applications to the ERC or the ATIP were unsuccessful and leave his future at the BPL uncertain.

Analysis of the team's trajectory

The objectives as presented in the report and in the oral presentation, remain rather vague. Furthermore, the two proposed projects are not clearly connected or linked. Whereas the first project appears to be a more logical continuation of his previous work, the presentation clarified that the second project is what the PI obtained his current funding (Marie Curie) for.
The future of this team is uncertain, and to start a team at the BPL without having secured competitive funding or a position can be considered high risk. Although the PI had some successes (an A rating at the ERC, resulting in Tremplin-ERC funding of 113 k). At this career stage, it is essential for the young PI to get maximum support from his more senior colleagues, in order to potentially succeed at future grant applications.

RECOMMENDATIONS TO THE TEAM

The committee strongly advises the PI to seek mentorship from his colleagues at the BPL. Even if not a formal requirement from the Marie Curie fellowship, good mentorship can provide guidance on how to navigate the uncertainty.

CONDUCT OF THE INTERVIEWS

Date(s)

Start: 24 octobre 2023 à 8 h 30

End: 25 octobre 2023 à 18 h 30

Interview conducted: on-site or online

INTERVIEW SCHEDULE

October 24, 2023
8:30 a.m.-8:50 a.m. Closed session with the committee

8:50 a.m.-9 a.m. Presentation of the committee

9 a.m.-9:40 a.m. Presentation of the unit with major achievements and Project/trajectory by the director Mr. Thomas PRÉAT (ex-post) and Mr. Philippe FAURE (Project/trajectory) 20 min presentation + 20 min discussion with the committee)

9:40 a.m.-10:20 Presentation of Team #1: Neurophysiologie et Comportement. PI: Mr. Philippe FAURE et Mr. Alexandre MOUROT (20′ presentation (ex-post & Project/trajectory) + 20′ questions)

10:20-10:40 coffee break

10:40-11:20 Presentation of Team #2: Énergie et Mémoire. PI : Mr. Thomas PREAT & Mr. Pierre-Yves PLAÇAIS (20′ presentation (ex-post & Project/trajectory) + 20′ questions)

11:20-12:00 Presentation of Team #3: Connectivité des codes et circuits cérébraux. PI: Ms. Gisella VETERE (20′ presentation (ex-post & Project/trajectory) + 20′ questions)

12:00-1 p.m. Private meeting of the visiting committee (Debriefing)

1 p.m.-2 p.m. Lunch

2 p.m.-2:40 p.m. Presentation of Team # 4: Mémoire, Oscillations et état de vigilance. PI : Mr. Karim BENCHENANE (20′ presentation (ex-post & Project/trajectory) + 20′ questions)

2:40 p.m.-3:10 p.m. Presentation of Team #5: Gènes Circuits Rythmes et Neuropathologies. PI: Mr. Serge BIRMAN (15′ presentation (ex-post & Project/trajectory) + 15′ questions)

3:10 p.m.-3:50 p.m. Presentation of Team #6: Synapse Dynamique. PI: Ms. Sabine Levi. (20′ presentation (ex-post & Project/trajectory) + 20′ questions)

3:50 p.m.-4 p.m. coffee break

4 p.m. – 4:20 p.m. Presentation of Team # 7: Maintenance of the nervous system & behaviour. PI: Ms. Issa RAOUF. (10′ presentation (Project/trajectory) + 10′ questions)

4:20 p.m.-6:30 p.m. Private meeting of the visiting committee (Debriefing)

GENERAL OBSERVATIONS OF THE SUPERVISORS

Arnaud TOURIN
Vice-president for research and outreach

+33 1 80 48 59 13
arnaud.tourin@psl.eu

Paris, February 2, 2024

M. Eric SAINT-AMAN
Director
Research Evaluation Department
HCÉRES

Reference : DER-PUR250024148 - PDC - Plasticité du cerveau

Dear Director,

The supervising bodies of the *Brain Plasticity Laboratory* warmly thank all the Committee's experts for their evaluation work. They have no comments to make on their report.

Yours sincerely.

Arnaud Tourin

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2 rue Albert Einstein
75013 Paris, France
T.33 (0)1 55 55 60 10

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