



agence d'évaluation de la recherche
et de l'enseignement supérieur

Department for the evaluation of
research units

AERES report on unit:

Neuroscience Paris-Saclay Institute

Neuro-PSI

Under the supervision of the following
institutions and research bodies:

Université Paris-Sud

Centre National de la Recherche Scientifique - CNRS

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research units

*On behalf of AERES, pursuant to the Decree
of 3 november 2006¹,*

- Mr. Didier HOUSSIN, president
- Mr. Pierre GLAUDES, head of the
evaluation of research units department

On behalf of the expert committee,

- Mr. Serge SCHIFFMANN, chair of the
committee

¹ The AERES President "signs [...], the evaluation reports, [...] countersigned for each department by the director concerned" (Article 9, paragraph 3 of the Decree n ° 2006-1334 of 3 November 2006, as amended).



Evaluation report

This report is the result of the evaluation by the experts committee, the composition of which is specified below.

The assessment contained herein are the expression of independent and collegial deliberation of the committee.

Unit name: Neuroscience Paris-Saclay Institute

Unit acronym: Neuro-PSI

Label requested: CNRS - Université Paris Sud

Present no.:

Name of Director
(2013-2014): Mr Philippe VERNIER

Name of Project Leader
(2015-2019): Mr Philippe VERNIER

Expert committee members

Chair: Mr Serge SCHIFFMANN, Université Libre de Bruxelles, Belgium

Experts: Mr Boris BARBOUR, École Normale Supérieure, Paris (representative of CoNRS)

Mr Bruno BONTEMPI, CNRS, Université de Bordeaux

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Scientific delegate representing the AERES:

Mr Laurent GROU

Representatives of the unit's supervising institutions and bodies:

Mr Etienne AUGÉ, Université Paris-Sud

Mr Bernard POULAIN, INSB-CNRS



1 • Introduction

The 3-day visit took place from February 17th to 19th 2014. The overall organization of the visit was very satisfactory and the director and his collaborators should be complimented for their involvement. The time reserved for interviewing the director and department directors was appropriate and, thanks to the availability of the proposed director Mr Philippe VERNIER throughout the rest of the visit, all important aspects of the research unit's present and future organization were discussed in depth. The written information provided prior to the visit was adequate, and each department and team's oral presentation constituted a very useful complement. The discussions with the Director alone and together with the three department directors, as well as the discussion with the funding bodies occurred in front of the entire experts committee. For the discussions involving the technical staff, the PhD students/postdocs and the staff researchers, the experts committee splits into three separate groups. The unit presentation by the director and the three department's presentations by their corresponding leaders were open to all unit members and all team members did attend the presentation of their leader. Each team leader was given 15 minutes of presentation followed by a 15 minutes discussion with the entire experts committee in presence of all team members, who were all free to answer both scientific and organizational questions. The final report presented here is based on the reports that were sent in and was approved by all the experts of the committee.

History and geographical location of the unit

The Neuroscience Paris-Saclay Institute, or Neuro-PSI, will constitute a new unit - a mixed unit between CNRS and the future Université Paris-Saclay - that emerges from a large-scale and ambitious project based on the objective to establish a multidisciplinary and internationally recognized Institute of basic Neuroscience research in the south-Paris area. During the five-year project (2015-2019), all participating teams of Neuro-PSI will be relocated, with a plan scheduled to begin in 2017. Teams will leave their current locations (see below) to move into a new building located on the Saclay-Plateau, in close proximity to the highly reputable brain imaging and cognitive science institute Neurospin, the goal being to create one of the largest and most interdisciplinary Neuroscience research centers in France. Thanks to the efforts of the proposed director and other team/department leaders, and the support from the university and CNRS, the construction of the new building is guaranteed and secured financially. In the present proposal, by the time the full move to the Saclay Plateau is completed, Neuro-PSI is expected to be constituted of 4 departments, "Development & Evolution", "Molecules & Circuits", "Cognition & Behavior" and "Unit Neuroscience, Information and Complexity", each incorporating 6 or 7 teams coming from different existing structures. Most of the teams currently belong to three different units, the unit "Neurobiology and Development" (N&D, Dir. Philippe VERNIER) and the unit "Neuroscience, Information and Complexity", (UNIC, Dir. Mr Yves FRÉGNAC), forming together the Institute of Neurobiology Alfred Fessard (INAF) on the CNRS Campus in Gif-sur-Yvette, and the Center of Neuroscience Paris-Sud (CNPS, Dir. Mr Serge LAROCHE) located at the Université Paris 11 in Orsay. It should be noted that following the suggestion of a newly appointed Scientific Advisory Board (SAB), several existing teams in these structures have been deeply reorganized, mainly by merging some of them and/or by refocusing the activity of their researchers. Three additional teams from other existing structures will join the Neuro-PSI project, one from the Institut de Biochimie et Biophysique Moléculaire et Cellulaire (IBBMC) located in Orsay, one from the Laboratoire d'Enzymologie et de Biologie Structurale (LEBS) located in Gif-sur-Yvette and a last one from the Curie Institute in Orsay. Only the two former teams decided to be part of the project from its beginning and were part of the evaluation process; the third one will join the project later in 2017 and was therefore not evaluated by this committee. Moreover, it is also worth mentioning that from the 4 departments that will ultimately constitute Neuro-PSI, only 3 of them will be part of the project from the beginning of the contract, since the UNIC unit is expected to join only later at the time of relocation in 2017. Consequently, the UNIC teams were not submitted to the present evaluation process. Altogether, this means that the next five-year period will be divided into two phases in terms of geographical location and organization:

During Phase 1 (2015-2017), Neuro-PSI will be composed of 3 departments encompassing 19 teams that will remain dispersed in different buildings on different campuses.

During Phase 2 (2018-2019), Neuro-PSI will be constituted of 4 departments with 26 teams, all relocated in the new Neuro-PSI building on the Saclay Plateau nearby NeuroSpin.

In addition, three existing technological platforms, presently attached to the N&D unit in Gif-sur-Yvette, will be part of Neuro-PSI and will relocate to the new building. This will also be the case for the different animal facilities existing at INAF and CNPS in Gif-sur-Yvette and Orsay, which will be grouped in a common animal facility building on the Saclay Plateau.



Management team

The Neuro-PSI unit will be headed by Mr Philippe VERNIER, current director of the N&D unit, who was designated by all team leaders who will be part of the project. A board of directors will be constituted by the directors and deputy-directors of the 3 (Phase 1) and then 4 (Phase 2) departments. This board will be consulted by the director for decisions on all management issues (general laboratory policy, priorities for staff recruitment, laboratory budget, purchase of large equipments). The director will be assisted by an administrator who will be recruited very soon as the CNRS has confirmed its willingness to open a new position for a high-level administrative profile to support the new unit. This administrator will be in charge of the management of all infrastructures including platforms, finance, informatics and communication as well as human resources. As mentioned above, the director and board of directors will also take advice from an external SAB for scientific matters. It will help the Institute to promote scientific excellence by refocusing research lines if needed and by elaborating criteria and decision processes leading to recruitment of new teams in the future. As already established in some of the existing units, dedicated team leaders will bear scientific responsibilities for technological platforms and facilities. It is noteworthy that a procedure to appoint a new director at the end of the next five-year period will be rapidly settled, since Mr Philippe VERNIER and the specific SAB organized prior to this AERES visit, insisted on their desire to see turnover in this key position.

AERES nomenclature

SVE1-LS5 Neurobiology

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	25	28
N2: Permanent researchers from Institutions and similar positions	43	48
N3: Other permanent staff (without research duties)	26	27
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	5	5
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	50	49
N6: Other contractual staff (without research duties)	7	9
TOTAL N1 to N6	156	166

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	48	
Theses defended	69	
Postdoctoral students having spent at least 12 months in the unit	57	
Number of Research Supervisor Qualifications (HDR) taken	20	
Qualified research supervisors (with an HDR) or similar positions	43	49



2 • Assessment of the unit

Neuro-PSI is a new unit that groups a large number of teams - 19 at the beginning of the project - working on diverse animal models (zebrafish and various other aquatic animals, *Drosophila*, *Xenopus*, chicken, rodent, songbirds) with the aim of creating an innovative Institute gathering a critical mass in Neuroscience and enabling a “*multi-scale analysis of brain functions and their dynamics, ranging from molecules to the organism’s behaviour and cognition and from embryos to adults*”. The aim of the unit is to play a major local role, since it will ultimately regroup on a single campus on the Saclay Plateau all the forces in the field of Neuroscience in the Paris-South area creating strong visibility at the national and international levels. All levels of analysis will be represented with the aim of creating strong interdisciplinary interactions and to reach for excellence. As presented, the scientific project is of very high quality and relies on impressive human and funding resources that have been already engaged to achieve its objectives. The experts committee therefore expresses a particularly positive general opinion of this project of unit creation and was impressed by the enthusiasm of all proposed participants to the project. Because Neuro-PSI is a future unit that does not exist yet, some aspects and especially the scientific outcome of the last period could only be assessed as the sum of the individual outcomes of the existing teams or units. As a whole for the 19 teams that will constitute Neuro-PSI, the overall quality of the research is very satisfactory, with several outstanding teams. Over the last five-year period, these teams published more than 500 papers in international journals with a significant number (33) published in leading or highly recognized journals. The future organization of the unit regarding both its departmentalization and assignment of researchers and leaders is attractive, even though many aspects still remain to be refined to reach the ultimate goals of efficiency, cross-fertilization, interdisciplinarity and excellence. Appropriate procedures have to be settled for several issues to make sure that scientific excellence will be and remain the guiding aim of Neuro-PSI. The detailed assessments - below in point 3 - provide a more detailed view of these issues.

Strengths and opportunities related to the context

- A highly attractive federative project with the aim of merging several pre-existing research units and teams into a coherent and efficient association of teams allowing an extensive *multi-scale analysis of brain functions* using appropriate animal models and state-of-the-art technologies.
- A high and general enthusiasm of all participants and high cohesion of the team leaders regarding the project’s objectives.
- The ability to obtain strong support from the funding bodies, CNRS and university, such as for the construction of the new building, which is guaranteed and secured financially.
- A very high overall quality of the research in teams constituting the new Neuro-PSI, with several outstanding groups.
- The ability of a majority of Neuro-PSI teams to obtain funding for their research. Several projects are supported by international programs and one team has obtained a prestigious ERC advanced grant.
- The existence of state-of-the-art imaging and behavioural analysis platforms.
- The capacity of several teams to establish solid and fruitful partnerships with other units and platforms on their present campus.
- The high involvement of most Neuro-PSI team members in teaching at the master and PhD levels and training of PhD students.

Weaknesses and threats related to the context

- Some heterogeneity in the scientific outcome with some teams exhibiting a productivity that could be substantially increased in quality.
- A significant heterogeneity in the quality of the scientific projects in some departments. A lack of focus (or refocusing) was apparent in some of the recently reconstructed teams.
- The risk that the rather rigid organization in separate departments could prevent deep and fruitful collaborations and natural interactions between teams and researchers from different departments.
- The lack of recruitment of new groups in the present form of the project and the lack of clear procedures to attract and recruit new groups in the future.



- Some heterogeneity in the ability to obtain funding, with some teams being threatened by an absence of external funding.
- Some heterogeneity in the number of students/post-docs per team and the potential negative impact of a no-student situation on the future of a team.
- Some heterogeneity in teaching activities, with several teams constituted mostly or exclusively of full professors or assistant professors, resulting in overwhelming teaching duties in these teams.
- An important deficit in communication and information transfer to the technicians, engineers and administrative staffs regarding the re-organization of the current units in a merged Neuro-PSI and the future move of the Institute to the Saclay Plateau.
- Understaffing of some shared services as the computing services and the animal facilities.
- Structural difficulties of the move to the Saclay Plateau for lecturers who will have to commute frequently between the Saclay Plateau and Orsay where teaching will continue to take place.
- Some heterogeneity in PhD student supervision with, in some cases, limited contact with the doctoral schools.

Recommendations

The institute should recruit new highly performing young teams - from France or abroad - in the near future. The experts committee strongly recommends to design and implement concrete strategies to reach this objective.

In view of its more structured and homogenous organization in terms of research themes and projects, the experts committee recommends to take, as much as possible, the department "*Development & Evolution*" as a template for the final organization, structures and team design of the *Molecules & Circuits* and "*Cognition & Behavior*" departments.

The experts committee strongly recommends a very active organization of events, seminars, transdisciplinary brainstorming discussions, and specifically a retreat across the department's frontiers.

The experts committee strongly recommends the establishment of transparent rules for the appointments of new team leaders and of the next unit director and in order to avoid, as much as possible, internal inheritance; the experts committee also recommends giving a strong voice to external expert advices (i.e. SAB) in the recruitment process.

The experts committee strongly recommends the establishment of transparent, clear and fair rules for space attribution, attribution of technicians, engineers and administrative staff to specific teams or technological platforms, financial allocation of the recurrent funding from the CNRS and university, and creation of a solidarity fund.

The experts committee recommends the development of a strategy for mentoring young team leaders, to avoid dangerous 'no grant' or 'no student' situations.

It is recommended to take into account the position of the teaching staff by adequately integrating these teacher-researchers into teams and projects.

The experts committee strongly recommends organizing information meetings to clearly explain where and how the technicians, engineers and administrative staffs will be assigned in the future Neuro-PSI.

The obligatory meetings of the "Conseil du Laboratoire" should be programmed with a minimum of one to two meetings per year.

Support of the common facilities, and especially the animal facilities, should be secured by opening new positions or, if not possible, by reassigning current staff members to the facilities.

Student access to computing facilities and journal access should be made more uniform, as should safety training. The unit should aim at enabling each student to attend international meetings.

The arrival of foreign students and post-docs would be greatly simplified by the creation within the Neuro-PSI Institute of an international office to ease their interactions with the universities and CNRS.

It is recommended to use English as the default language for all scientific seminars, lab meetings, etc.



To improve PhD student supervision and to identify any problems as early as possible, the experts committee recommends designating an informal tutor-advisor to each PhD student within the Institute and to promote the organization of PhD "scientific days" or retreats self-organized by the PhD students.



3 • Detailed assessments

Assessment of scientific quality and outputs

Because Neuro-PSI is a future unit that does not exist yet, regarding the assessment of its scientific quality and outputs, it can only be considered at the time of the visit as the sum of its different individual constituents. The project and strategy for the coming five-year period including its scientific quality and relevance are discussed in criterion 6 of this report.

As a whole, the 19 teams that will constitute Neuro-PSI exhibit an excellent scientific outcome with projects and achievements in a wide range of topics from molecules and development to cognition and behaviour which are explored using numerous animal models and state-of-the art technologies. These have led to high impact discoveries, such as the roles of miRNA in hindbrain embryogenesis, the nuclei involved in the emergence of activity of the respiratory rhythm generator, the spreading from cell to cell of misfolded protein aggregates in Parkinson and Huntington diseases, and the molecular mechanisms of circadian rhythms. With a total working force of about 220 members, these teams published more than 500 papers in international journals. A significant number (33) of these articles were published in leading or highly recognized journals ($IF \geq 10$): Nature 1x, Nat Neuro. 5x, Nat Cell Biol 1x, Nat Comm 3x, Nat Meth 1x, Nat Rev Neurosci 1x, Nat Rev Mol Cell Biol 1x, Plos Biol 2x, Mol Psychiat. 1x, J. Clin Invest. 1x, Genome Res 1x, Genome Biol 1x, Dev Cell 1x, Curr Biol 3x, PNAS 10x, including articles issued from collaborations. However, this general overview cannot mask a significant heterogeneity in quality among the teams. While several groups have undoubtedly reached an outstanding level of publication, other teams exhibit a productivity that could be substantially increased in quality and an international visibility that could be significantly improved as well.

Even if there is some heterogeneity amongst the teams, as a whole the publication level is very satisfactory with around 100 publications per year, a very good proportion of papers in high level journals and a large part of these publications with a member of the Neuro-PSI teams as first or last author.

By developing technological platforms, some of the teams, especially from the N&D unit in Gif-sur-Yvette, have established strong partnerships with other laboratories on their campus. In the same unit, several technological platforms have been settled with the support of national and international funding, either inside the unit, and under the supervision of specific team leaders (AMATRACE or TEFOR), or independently outside the unit as it is the case for AMAGEN.

Assessment of the unit's academic reputation and appeal

The very high impact and attractiveness of some teams, but not all of them, are reflected by their numerous invitations to national and international meetings and symposia as well as by the fact that some team members have been actively involved in the organization of several of these meetings. The teams actively contributed to international programs as shown by their presence in EU Marie Curie networks, EU- FP7, and HFSP programs, and one PI was recently awarded a prestigious ERC advanced grant. In addition to these richly funded programs, funding of the Neuro-PSI teams is, in general, very satisfactory, with many teams being supported by several ANR grants (about 50 ANR in total for the 2008-2013 period) and grants from diverse foundations for a total income of about 4 million € per year during the last five-year period. It might become more difficult for some teams to maintain or increase their level of funding and mentoring on this particular aspect is highly recommended. As stated below, the heterogeneity in the capacity of the teams to raise external grants could be slightly and temporarily buffered by creating a solidarity fund, which could be fuelled by a small percentage of the total income generated by all teams of the institute.

Although this capacity is rather heterogeneous, most of the teams were able to attract a substantial number of PhD students and post-docs both from France and abroad. The strong involvement of members in teaching both at master level at the Universities Paris 5, 6, 7 and 11 and in different doctoral schools contributed to such a good PhD student recruitment level.

Assessment of the unit's interaction with the social, economic and cultural environment

Several teams from different existing units developed inventions that have been patented. As a result, a total of 11 patents have been registered. Beside this effort of economical valorisation, technological platforms have been developed through the support of national and European grants and are open to external users.



Assessment of the unit's organisation and life

The proposed organization of the Neuro-PSI consists of three different departments, essentially determined on the basis of scale of analysis, which are themselves composed of 6 to 7 teams. The three departments are named "Development & Evolution", "Molecules & Circuits", and "Cognition & Behavior". The assessment of this proposed organization and the questions arising from the plan for the future organization and life of the unit are detailed below in the strategy and five-year plan assessment paragraph.

Assessment of the unit's involvement in training through research

All teams take part in teaching and training through research both at the Master and PhD levels and through doctoral schools, with several members acting as director, president or organizer of teaching departments, Masters or Doctoral Schools. Although all current units take part in both types of teaching and training programs, the CNPS is composed of a high number of full professors and assistant professors (about 50 % of the permanent researcher staff) who have therefore very high teaching duties covering all academic levels (Licence-Master-PhD).

Globally in the 19 teams during the five-year period 2008-2013, 66 PhD theses were completed and defended and 46 PhD theses are in progress. Although the experts committee was impressed by the overall enthusiasm expressed by PhD students and postdocs concerning their research projects, several complaints were however expressed that illustrate the current heterogeneity in their training, supervision and support. More specifically, a substantial number of students reported variable provision of computing and journal access services, poor animal facility support, and some inequality regarding the opportunity to attend international congresses as well as unequal access to shared equipment and platforms.

Assessment of the strategy and the five-year plan including unit's organization and rules

The general objective of the present project of creation of the new unit called Neuro-PSI is to gather a critical mass in Neuroscience to allow a "multi-scale analysis of brain functions and their dynamics, ranging from molecules to the organism's behaviour and cognition and from embryos to adults". By establishing this institute on the Saclay Plateau next to NeuroSpin, and near several reputed High Schools such as the École Polytechnique, the aim is also to favour highly interdisciplinary research at the interface between neuroscience and physics, mathematics and cognitive sciences. The experts committee was very impressed by the high quality of the scientific project and the human and funding resources that have been already engaged to achieve these objectives. If successful, with the right teams at the right place, such an institute should undoubtedly become a leading Neuroscience Center not only in France, but also worldwide. The experts committee was also impressed by the enthusiasm of all proposed participants of the project, with a specific mention to the director who was obviously highly instrumental in establishing the project with the help of the department's directors. As far as it was understood, the project is a genuine bottom-up project that emanates as a federative project from the researchers themselves. The confrontation of several models and related experimental approaches is presented as an essential element of the function, dynamics and visibility of the future unit with a strong willingness to favour transdisciplinary features, and especially a solid interface with mathematics, physics and engineering. However, this laudable desire still appears rather artificial and fragmentary in the reports and projects of most evaluated teams.

To achieve the ultimate goal of interdisciplinarity and excellence in Neuroscience of Neuro-PSI, the proposed strategy is to constitute three departments (that will later on be joined by a fourth one), essentially determined on the basis of the scale of analysis, and which are themselves composed of 6 to 7 teams at the starting time of the project. The three departments are named "*Development & Evolution*", "*Molecules & Circuits*" and "*Cognition & Behavior*". The rationale to form structured departments instead of a single large Institute constituted of its 19 teams was extensively debated within the experts committee. Although it was understood that this will favour a simplified organization regarding sharing of some equipments and animal models, the concern of the experts committee was that this potentially rigid organization could prevent deep and fruitful collaborations and natural interactions between teams and researchers from different departments. This could be especially true since during phase 1, before moving to the common building in 2017, departments will be separated geographically and will grow used to functioning independently with very limited interactions. Therefore, the experts committee strongly recommends to the director and department directors to very carefully and actively organize, both in time and space, events, seminars, transdisciplinary brainstorming discussions, retreats across the departments' borders during Phase 1, a strategy that should continue during Phase 2 when all the teams will be under the same roof. Secondly, the experts committee strongly questioned both the process that led to the constitution of the departments and the criteria for deciding to put a specific team in one department instead of another. This is especially the case for the departments "*Molecules & Circuits*" and "*Cognition & Behavior*" for which it appears that the decision was mostly - but not only- based on



geographical criteria instead of strong scientific projects and excellence criteria. As a consequence, the experts committee feels that these two departments suffer from two major weaknesses. First, there is a significant heterogeneity in scientific projects with some teams being very remote from the main proposed topics and even from the suggested level of analysis and methodological approaches. Second, and more importantly, there is also a substantial heterogeneity in the scientific productivity and project quality of their teams, with some teams obviously being outstanding while others suffering from lower visibility and output as well as unstructured projects. One partial reason for this could be that, following the reorganization of some existing teams, integration lacked refocusing team members on the projects for which their expertise is highly complementary. In comparison, the department "*Development & Evolution*" appears much more structured and homogenous in terms of themes, projects, organization and scientific production, most likely because all teams are already been to working together via the development of common technological platforms. Thus, the experts committee recommends to the unit's director and the directors of the "*Molecules & Circuits*" and "*Cognition & Behavior*" departments to take, as much as possible, this department as a template for their final organization, structure, and team design. As far as the department "*Development & Evolution*" is concerned, it has to be additionally noted that the team "*Signalling and Neural Development*" (A-H. Monsoro-Burq) currently located at the Curie Institute in Orsay, is supposed to join Neuro-PSI on the Saclay Plateau during Phase 2. This is a young and dynamic team, with excellent track record and very good potential for future achievements. The team will certainly benefit from its incorporation in the new institute and it will bring additional approaches that are complementary to those used by current institute members. Considering the "*Cognition & Behavior*" department's organization, the geographical situation of one team in Saint-Etienne, 500 km from the Institute, was strongly questioned by the experts committee.

A major issue that arises both from the director's presentations and the experts committee discussions is related to the evolution of the future Institute. The experts committee is strongly convinced that, to reach its goal of excellence, the Institute will have to recruit excellent new young teams - from France or abroad - in the near future and that its organization must take this need very carefully into account. This is especially important because several team members and team leaders will retire within the next few years. These departures will impact the teams and the departments, which will have to go through a deep reorganization. Although the director is aware of this fact, the experts committee was concerned that concrete actions were not or will not be sufficiently designed and implemented to reach this objective. As a representative example, space organization in the new building must absolutely take this requirement into account since as explained by the funding bodies, the total working surface planned for the new building will not exceed the sum of the presently available surfaces in the different units. The experts committee urges the director, the department directors and the funding bodies to give the highest priority to this issue.

During the course of the evaluation process, meetings with the staff Researchers, the technical staff and the PhD students/postdocs gave rise to several issues regarding the management and task organization of engineers and technicians, the supervision of PhD students and post-docs and the involvement of staff researchers. It is noteworthy that the future organization of animal facilities emerged from all staff meetings as a major concern. These concerns are summarized below:

Neuro-PSI hosts 50 researchers who are not group leaders, among which 12 have teaching positions. Most of them were present at the dedicated meeting. The principal preoccupation of the researchers was the current merger of several units and the forthcoming move to the Saclay Plateau. The overall feeling about the relocation was genuinely positive. It appeared that nearly all of them saw it as an exciting opportunity and were keen to contribute to and benefit from it. Against this positive background should be set worries about the structural difficulties of the move for lecturers, who will have to commute frequently between the Saclay Plateau and Orsay, where teaching will continue to take place. This additional burden could be made worse in the event of transport difficulties. The teaching staff also expressed understandable unhappiness about the fact that they are evaluated only on their research (in competition with full-time researchers) despite their heavy teaching loads. This is a very important issue that was clearly apparent during the oral presentations of teams composed of a majority of members holding teaching positions. In its future organization, it must be recommended to Neuro-PSI, first, to carefully take into account the positioning of the teaching staff by adequately integrating these teachers-researchers into teams and projects with full-time researchers and, second, by ensuring, whenever possible, a better distribution of teaching loads.

Globally, PhD students and post-docs expressed an overall positive view of their positions with a general feeling of a positive atmosphere in all current units. However, they also manifested different complaints, which should be taken into account in the future organization of Neuro-PSI. First, it seems that support from several facilities is at the least heterogeneous and at the most, rather poor. It is therefore recommended to support the students, regarding informatics, library, information on safety protocols and equitable attendance to international meetings. There is an urgent need for an international office for foreign PhDs and post-docs to ease their interactions with the universities and CNRS offices where all administrative documents and interactions are in French. This must



be developed at the internal level in the Neuro-PSI Institute. The way the PhD students are supervised appears highly heterogeneous and in some cases rather insufficient with limited contact with the Doctoral Schools. The following recommendations could be proposed to improve this supervision. An informal tutor-advisor for the PhD students should be designated within the Institute as an additional but local reference in addition to the supervisor. Mentoring for self-organization and initiative must be proposed to students and post-docs as well as possibilities of early career promotion, and finally, PhD "scientific days" or retreats self-organized by the PhD students must be considered. In addition, it was stated that much of the official scientific communication was held in French, excluding many of the international students. It is therefore recommended to use English as the default language for all scientific seminars, lab meetings etc. Lastly, it seems that PhD students were not sufficiently informed about the new project and relocation of all teams onto the Saclay Plateau. This should not be considered as a real downside since most of them will most probably not be concerned by the relocation. However, it must be noted that the students do not see the Saclay Plateau in its present form as an attractive site for student-life.

The technicians, engineers and administrative staff were highly concerned by the whole project and were very numerous at the meeting. To put it bluntly, the experts committee was stunned by the extraordinarily high level of anxiety regarding the creation of the new Institute, and the move to the Saclay Plateau. From their point of view, this anxiety is related to the low amount of information that they received/assimilated from the director, the department directors and the team leaders, and from the funding bodies. Moreover, it even appeared that the information they received was often contradictory depending on whether it came from inside or outside the units. Whatever the reality of this situation is, the experts committee strongly recommends the board of directors TOGETHER with the funding bodies rapidly clarify the details of the situation and explain where and how the technicians, engineers and administrative staffs will be assigned in the future Neuro-PSI, both during the first phase of the project and at the starting point of Phase 2, a critical time when the relocation to the new building will take place. Strikingly, it appears that, presently, at least within the INAF, there are no official laboratory meetings, which include the presence of at least one designated person from the technicians, engineers and administrative staffs. The experts committee reminds the unit's director that the presence of delegates is mandatory and the experts committee highly recommends to organize such meetings ("Conseil de Laboratoire", "Assemblée générale") in the new Institute with a minimum of one to two meetings per year. In addition to this main concern, two very important issues must be addressed. The first one concerns the experimental facilities; all of these appear to be understaffed currently and this situation might worsen in the future Institute. This is particularly the case for the computing service support and for the animal facilities. All technicians, engineers and administrative staffs share this view, as do all users, researchers, PhD students and postdocs. A clear and thorough re-organization of these common facilities, and especially of the animal facility, is absolutely mandatory upon moving. Obviously, these structures will constitute a vital support for the whole institute and must run efficiently. It appears rather clear that either opening of new positions or, if not possible, re-assignment of current staff members to the facilities will be necessary and the directors are therefore strongly encouraged to create sufficient shared technological platforms to optimize human resources and proper functioning. It is also recommended to more carefully monitor and standardize the careers of technicians, engineers and administrative staffs. The experts committee also recommends consideration of the best method to ensure quality of opportunity regarding the slim promotion prospects for technicians, engineers and administrative staff; the staff felt that promotions are more frequently awarded within teams as compared to within technological platforms.

From all the points raised above concerning strategy, five-year plan and the unit's organization, the experts committee has made several additional critical recommendations. It is absolutely mandatory to establish transparent, clear and fair rules for space attribution, assignment of technicians, engineers and administrative staffs to specific teams or technological platforms, financial allocation of the recurrent funding from the CNRS and university, and constitution of a solidarity fund. Moreover, strategies for mentoring of team leaders to avoid dangerous 'no-grant' or 'no-student' situations will need to be considered carefully and implemented. Rules concerning different aspects of governance must also be clarified and clearly stated regarding the following issues: identification of respective administrative and scientific duties of the director, department directors and the administrator, recruitment of new teams, appointment of new team leaders and appointment of the next director. For the latter two questions, the experts committee strongly recommends avoiding internal inheritance, as much as possible, and recommends, both for team leaders and the unit's director, to seek expert external advice (for instance from a SAB). At the present time, the project appears to require more maturation regarding all these points and rules must be fully elaborated in the coming two-year period before the move to the Saclay Plateau. Making these procedures explicit is likely also to ease integration of the UNIC department.

In conclusion, the experts committee was very pleased with the quality of the science of the future Neuro-PSI and with the high potential and ambition of the project for the next 5-year period. The experts committee has no doubt that the unit's director and the department directors are very committed to making the project a success, but there are still a series of issues that must be addressed and resolved in order to generate a fully mature institute ready to achieve its ultimate objective of excellence in Neuroscience at both the French and international levels.

4 • Team-by-team analysis

Team 1: Zebrafish neurogenetics

Name of team leader: Ms Laure BALLY-CUIF

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	3
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	2
N6: Other contractual staff (without research duties)	3	3
TOTAL N1 to N6	9	11

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	2

• Detailed assessments

Assessment of scientific quality and outputs

The zebrafish neurogenetics team joined the N&D unit in 2010. The aim of the team is to understand the molecular mechanisms that underlie neurogenesis and the functional organisation of the brain using zebrafish as a model. The team is internationally recognized, vibrant and has constantly pushed the boundaries to develop new concepts as well as tools to answer new questions. The main focus in the last 5 years was the control of both embryonic and adult neurogenesis, and the relationship between adult neurogenesis and behavioural output. Using a combination of molecular and cellular approaches in vivo, live imaging and a newly-established platform for behavioural studies in zebrafish, the group has identified the mechanisms that:



I) control the balance between cell cycle exit and lineage commitment versus continued proliferation involving a microRNA;

II) regulate adult neurogenesis in the pallium, including the identification of radial glia cells as bona fide neural stem cells, and multiple roles of Notch signalling in controlling quiescence and amplification.

In addition, the team has established a platform to measure fish behaviour and made use of this platform to establish a link between deregulation of adult neurogenesis and reward behaviour. The quality and quantity of the primary research publications (32) resulting from this work is outstanding, including papers in *Developmental Cell*, *Nature Neuroscience*, *Development* and *J. Neuroscience*. Among these outputs the *Nature Neuroscience* paper from 2008 has already more than 100 citations and promises to be influential. In addition, the team has contributed to 6 reviews and 6 book chapters, demonstrating international recognition and influence of their work. In summary, the broad scope of scientific topics in developmental neuroscience and the impressive scientific output distinguishes this laboratory as outstanding.

Assessment of the team's academic reputation and appeal

The team is clearly attractive and visible as evidenced by PhD students and postdocs recruited from international locations. The group leader is a national and international leader in her field. The group leader has continuously attracted grant funding including the chair of excellence of the ANR (2008, 2010) and a recent ERC advanced grant, a highly prestigious award. The group leader has established a network of international collaborators of excellent reputation and coordinated large EU grants; these are large networks with many teams and the PI's leading role is evidence for her international recognition.

Likewise, the group leader's service on many evaluation committees speaks for her being recognized as excellent scientist; these include the ANR Neuroscience committee, INSERM evaluation committee in Neurosciences and being an elected member and Vice-President of the CNRS evaluation committee in Cell Biology, Development, Evolution and Reproduction (section 22).

The group leader is consistently invited to speak at national and international conferences including one plenary lecture and received 15 invitations for seminars at various institutions across Europe. The group leader is co-organizer of international conferences and is invited to contribute reviews to well-known journals. Overall, the international academic reputation and visibility of the team is without any doubt outstanding.

Assessment of the team's interaction with the social, economic and cultural environment

The group leader is a member of board of trustees of French Society of Developmental Biology, which is evidence of a commitment to the community. The group has established collaboration with Sanofi-Aventis to screen for drugs modulating adult neurogenesis.

Assessment of the team's organisation and life

This is a well-structured team organised into three main topics, each containing scientists at different levels. There is a common theme and overarching aim that unites the three topics and maximizes interactions and resource sharing within group. At this point the team is somewhat isolated due to its location outside of the department, reducing the possibility for local scientific interactions. However, this should change dramatically with relocation to the new site when the entire unit moves to the Saclay site.

Assessment of the team's involvement in training through research

The team has a good number of PhD students, well embedded into the team structure. The group leader is director of an international PhD programme, which attracts international students, encourages mobility. This is evidence for her commitment to teaching and training future generation of scientists. In the past the team has attracted excellent international members; of the postdocs trained five are now independent or have moved to different lab (1).



Assessment of the strategy and the five-year plan

The future strategy of the team clearly builds on past achievements and is a logical extension, but also a move towards new avenues. The team has moved from more developmental questions of brain patterning and neurogenesis to adult neurogenesis, the molecular control of neural stem cell properties and homeostasis and behavioural studies. Specifically the team wishes to address:

- I) the cellular dynamics and heterogeneity of neural stem cell pools;
- II) the molecular control of neural stem cell activation;
- III) the coordination of neural stem cell behaviour at population level;
- IV) neural progenitor subtypes;
- V) changes in neural stem cell homeostasis under pathological conditions.

To this end they have developed new transgenic zebrafish tools, imaging technology and a behavioural analysis platform and will combine experimental analysis with modelling approaches.

Conclusion

▪ Strengths and opportunities:

This is an overall very promising, interdisciplinary topic with excellent potential for a successful continuation of productive research and future funding. The team is at the leading edge in the field, the future strategy is very strong, presenting a well-focused and ambitious plan, which exploits recent findings and embarks into new territories. There is good expertise in the team with recent strategic recruits and appropriate collaborators. Clearly the team is moving towards new questions and to an even more interdisciplinary concept.

▪ Weaknesses and threats:

At this point, one weakness is the physical isolation of the team in its current location, although this has clearly not affected its productivity. However, this will change dramatically in the future when the entire department and indeed unit will move to a new building on the Saclay plateau. The productivity however can be affected by the lack of infrastructure, especially for animal facilities on which the team depends heavily.

▪ Recommendations:

This is a very strong team of international reputation and with an excellent strategic plan for future research. It will be crucial for the continued success of the team to integrate it into the new location in Neuro-PSi, close to technical platforms and to provide sufficient professionally run infrastructure to support the team's animal research.



Team 2: Neural Crest: Development and Evolution

Name of team leader: Ms Sophie CREUZET

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)	1	
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	3
N6: Other contractual staff (without research duties)		1
TOTAL N1 to N6	5	5

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions		1

• Detailed assessments

Assessment of scientific quality and outputs

Over the last five years, this small team which includes the team leader, one post-doc, 2 PhD students and one Emeritus professor, has made a series of important contributions related to the role of the cephalic neural crest in cranio-facial skeletal formation. Its members have established that the combinatorial activity of three transcription factors of the Six family (Six1, Six2, Six4) is required for neural crest derived craniofacial skeletogenesis. In a collaborative work, the team also showed that the tumour suppressor LKB1 is involved in the delamination of cephalic neural crest cells, and that its inactivation leads to severe facial defects. These results are novel and influential in the field, well in line with the past history of the team leader and the outstanding scientific trajectory of its Emeritus professor.



During the 2008-2013 period, the publication record is very good overall, with a total of 9 articles, including research papers in excellent (1 PNAS) or specialized journals in the field (Cell Mol Life Science, Developmental Biology). However, none of them appeared in outstanding journals and only a limited number were published with the team leader as senior author. A higher level of excellence could be made accessible if a couple of additional manuscripts, which are still under revision are published, one of which being under revision in Nature Communications. The team also contributed to one review and 4 book chapters.

Assessment of the team's academic reputation and appeal

While the team should be considered as quite established and with an outstanding reputation, it is undergoing a generational change under the direction of a young principal investigator who was previously part of the team. This is an important transition but also an excellent opportunity to continue with the trend of significant contributions achieved in the past. Indeed, the team has provided seminal contributions to the field of neural crest development that made it into textbooks. There is no doubt that the new team leader possesses the knowledge, expertise and potential to generate important scientific advances in the field but her international recognition and that of the team will need to grow further. She needs to achieve full independence, and develop her own plans that should be more ambitious, both in terms of scientific production in top-rated journals and project width. The experts committee believes that she has all the qualities to succeed: she has published in excellent journals before, has a very good capacity of fund raising, and is actively participating in teaching and student training. Moreover, she benefits from an effective network of national and international collaborations. Members of the team were invited as speakers to 20 national/international meetings and seminars, gave 24 presentations and co-organized 2 meetings, which highlights the attractiveness of the team. The funding level appears to be adequate for the moment with a grant obtained from the Fondation pour la Recherche Médicale and a NIH grant in collaboration with another member of the Institute in the "Molecules Circuits" department.

Assessment of the team's interaction with the social, economic and cultural environment

The team is involved in vulgarization activities and has received funding from a private company. Its activity in this respect is noticeable, especially considering that the team is still small.

Assessment of the team's organisation and life

The team leader needs to consolidate her independence in order to build a solid and dynamic team.

Assessment of the team's involvement in training through research

The team leader has successfully supervised two PhD theses. Two other PhD students have undertaken their projects, supporting the very promising training qualities of the team. The team leader also participated to 4 PhD committees and was actively involved in some teaching duties at the Master level at the Université Paris-Sud but also abroad.

Assessment of the strategy and the five-year plan

The team proposes to address four different lines of research in chicks tailored to exploring the cellular and molecular mechanism enabling the neural crest to control brain morphogenesis and sensory development. The first line, basic science-oriented, represents the logical continuation of an ongoing external collaboration with Albert Bonniot Institute in Grenoble. It aims at deciphering the influence of energetic stress such as hypoxia on the neural crest cell polarity, migration and differentiation. This is an interesting and possibly innovative topic in the field of cephalic neural crest development that is worth pursuing. The remaining three research lines seem to constitute a twist of the team towards a more biomedical-oriented type of research. Particularly timely is the investigation of the molecular pathways underlying neural tube defects, which are congenital anomalies and constitute a common type of birth defects in humans. The second line of research will attempt to link ontogenic scenarios to exome sequencing in the context of neurological disorders. Capitalizing on the previous identification by the team leader of signalling molecules involved in the growth and properties of the retina, the complex problem of eye development and its deregulation responsible for ocular malformations will also be addressed by combining embryological techniques and gene expression profiling.



Although somehow related, these research lines are quite diverse and the team should consider defining better or prioritizing what they want to pursue. The written description of the projects is sometimes confusing. For example, in aim 3 it is proposed to “further explore the role of cephalic neural crest in the nuclear translocation of Foxg1 and the synaptic stability”. Why alluding to synaptic stability ? What is the team going to explore in this field ? Similarly, it is proposed to link “the ontogenic scenario with the exome sequencing in the cohort of patients”. Again it is unclear what the team wants to pursue here. What exactly will be the role of the team in patient exome sequencing ? The last aim related to “Coloboma to Cyclopia: deciphering the morphogenetic role of cephalic neural crest in ocular development” is also puzzling since it takes advantage of an extreme model in which eye defects may be secondary to alterations not directly related to cephalic neural crest.

Conclusion

▪ Strengths and opportunities:

This is a small team that is undergoing a generational change with a creative young team leader. The team has a very good publication track record and was successful in generating important findings in its field using innovative methodological approaches. The team is expected to continue to produce significant advances in their field of research.

▪ Weaknesses and threats:

While the proposed research project is challenging, the major risk lies in the numerous issues that will need to be tackled and the perhaps underestimated potential pitfalls that could be difficult to address and resolve given the small size of the team. It could be worth delineating some axis with clearer aims and concentrating on one or two axis first to ensure the highest international visibility in the field of the team leader. Dispersing in too many different aspects of neural crest function might be at this stage counterproductive and prevent publications in outstanding journals.

▪ Recommendations:

The team leader is encouraged to be fully independent from her former mentor and to clearly define her personal scientific interests. This will help to take full recognition and visibility for the publications of the team and for the work they will carry out. Also, while achievable, the ability to recruit additional permanent researchers in the team is not yet demonstrated and should be considered a priority in the coming years. This strategy could help consolidate the team and ensure that it will gain the attention and visibility of the international community that it deserves.



Team 3: Morphogenesis of the chordate nervous system

Name of team leader: Mr Jean-Stéphane JOLY

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	3
N6: Other contractual staff (without research duties)	2	2
TOTAL N1 to N6	11	11

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	7	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The group is formed of 11 persons, namely 3 staff scientists, 3 post-docs, 1 PhD student and 4 engineers and technicians (3 permanent positions including an IR and 1 CDD). The group has a strong background in evolution and development with a particular focus on the evolution of transcription regulation using ascidian and medaka as models. On that topic, they produce papers on a regular basis with the team leader as last author in journals with increasing impact factor, including *Developmental Biology* (2008, 2009) *Plos One* (2009), *Dev Neurobiol* (2010), *Plos Genetic* (2010), *PNAS* (2013). More recently they joined the field of neural stem cells biology using the Zebrafish brain as main model, taking advantage of the leading input of their close collaborators and of the state of the art technical platforms available on site. They found in the peripheral midbrain layer (PML) of the Zebrafish embryo a population of slow-amplifying progenitors (SAP). They identified several SAP markers, which are co-expressed in the retina suggesting that midbrain and retina progenitors might derive from ancient sister cell types. These data were recently



published in *Development* (2013). They are now defining the contribution of the PML to the optic tectum using imaging and lineage analysis; finally they obtained data indicating that proteins involved in DNA/RNA metabolism and ribosome biogenesis could play an important role in SAPs. These novel and original data are the basis of their research project. Overall the group has a very good production with 19 original articles and 3 reviews, the PI being last author on 7 papers. However, the number of publications appears unequal in the team, some of its members displaying a low publication record despite their full time dedication to research.

Assessment of the team's academic reputation and appeal

Academic reputation and appeal are excellent. The group leader was the coordinator of numerous international and national projects: -European FP7 CISTEM project, -“Grand Emprunt” Infrastructure d’Avenir TEFOR (Zebrafish and drosophila TALEN and PHENOTYPING services), EFOR network aimed at promoting functional research on model organisms in France, ANR “Chorregnet” (2005-2008) and “Chorevonet” (2009-2013), ACI (2012). The group leader served as expert for reviewing several grants (e.g. NSF, NIH, Canadian research Agency, ANR, etc.) and articles (e.g. *Development*, *PNAS*) and the group leader was member of the CNRS section (2010-2011), ANR blanc (2009-2011). The group leader has been invited speaker at numerous international (10) and national (13) meetings and is regularly invited to give seminars (10) in France and abroad. In the last five years, they attract 6 post-docs, 3 are currently in the lab.

Assessment of the team's interaction with the social, economic and cultural environment

In 2013, the group leader was the main author on a patent on the in vitro production and use of TALEN proteins for genome modifications. The group leader supervised the elaboration of 7 movies on model systems for the EFOR network and coordinate a special issue of *Biofutur* on model organisms.

Assessment of the team's organisation and life

The ability of the team to raise national (ANR, ACI, FRC) and international (FP7) funds allowed reinforcing the group with post-docs and technician.

Assessment of the team's involvement in training through research

Five PhD students have been trained during the period; one of them has now a position in UCSC and a second one has a position in IMAGIF. The team leader also did teaching (around 15h in 2008 and 6h in 2012) and was member of 12 PhD thesis and 3 HDR juries. He also participates to Master 2 yearly juries.

Assessment of the strategy and the five-year plan

The scientific project is focused on three fundamental questions concerning NeSCs (Neuroepithelial stem cells) biology. The first one aims to identify the important genetic components for NeSC function. According to the data mentioned above they plan to analyse the function of selected genes essential for ribosome biogenesis. The second aim is to determine how NeSCs homeostasis is regulated in abnormal situations (modified nutritional context, chemical ablations or viral infections). Third, they plan to decipher how transcriptional regulation is achieved in NeSC by characterizing a putative regulatory element involved in boosting specific gene expression in NeSCs, by in silico searches and chromatin marks analyses. As a whole this research project is good but not precise and focused enough, the readout of experiments and the specific objectives are not always clearly stated. Moreover studying neural stem cell biology in Zebrafish brain might be very competitive, except if the PML constitutes a “niche”, a situation which remains to be proven.

Conclusion:

- **Strengths and opportunities:**

The scientific environment with the leading input from their close collaborators and the state of the art technical platforms available on site.



- **Weaknesses and threats:**

A rather broad and unfocused project in a very competitive field. The group leader was a coordinator of a European grant until 2012, and of an ANR “blanc” (2011-2014) but the team might be in trouble in the near future since they will have no grant after 2014.

- **Recommendations:**

To focus on specific questions (for example the project on ribosome biogenesis seems promising if it can be pushed to the mechanistic) that will give a clear advantage in term of originality and will allow the project to be funded and to give rise to excellent publications.



Team 4: Stem Cells and Neurogenesis in the Retina

Name of team leader: Ms Muriel PERRON

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	4	4
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	4
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	13	13

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	4	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	5	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	3

• Detailed assessments

Assessment of scientific quality and outputs

The team has worked on the molecular mechanisms regulating the growth and differentiation of the *Xenopus* ciliary margin for many years, making important contributions to this field. Recently, the team has focused on the Shh, Wnt and Hippo pathways, obtaining interesting results that have been well received by the scientific community. Some of these results were published in very good journals of the field (Stem Cells and Development), whereas others constitute a good body of evidence upon which the PI has elaborated part of the plans for the next few years (Dev. Neurobiol., J. Neurosci.). Nevertheless, the team should be more ambitious in terms of global output given their size and connections (see below). The recent incorporation of the CERTO team and the collaborative environment of the unit raise these expectations.



Assessment of the team's academic reputation and appeal

The team is rather large, with established members, a good number of students and postdocs, technical help and several ongoing international collaborations, placing the team in a good position to compete in the international field. The group leader is already well consolidated and internationally recognized for the work in the *Xenopus* CMZ and the team has been able to recruit students and postdocs from abroad, which is indeed a sign of high reputation. The team leader is also often invited to important international meetings (e.g. Gordon Conferences) and to deliver seminars in different countries. The group leader has been also involved in organizing international meetings and acts as a reviewer for journals and international granting agencies. Her appointment as a deputy director of the Evo-Devo Department reflects her commitment to the unit and the appreciation of her colleagues. The recent incorporation of the CERTO (Centre d'Études et de Recherches Thérapeutiques en Ophtalmologie) lab members is seen as a good opportunity to strengthen the work of the team and opens new avenues of research in neurodegeneration with the inclusion of the mouse as a novel model system for the lab.

Assessment of the team's interaction with the social, economic and cultural environment

The group leader has been recruited as scientific director of a laboratory supported by the Retina France association: CERTO. This is certainly a sign of the team's involvement with the social environment. The team is also involved in scientific networking with other private companies and receives support from the Belgian Government. The team is also involved in popularizing science and participates in related activities.

Assessment of the team's organisation and life

As mentioned, the team is large but with a well-balanced proportion of experienced and more junior researchers. Organization seems working well with good integration of all members including those of the CERTO.

Assessment of the team's involvement in training through research

The more senior members of the team are fully involved in training in several directions. During the period here revised, three PhD theses have been accomplished and others are on the way.

Assessment of the strategy and the five-year plan

The proposed research lines represent the logical continuation of the recent research of the lab. The team has invested in technology and focused on new pathways (Hippo), so they should soon get a tangible return for their activities. The plan of undertaking part of their research in mice, translating what they have and are learning in the frog to the field of retinal degeneration and regeneration is very appealing. However, here the team should be aware that they enter a new and very competitive arena, full of experienced and well-funded labs. Their plans in this direction need therefore to be more precise and clear-cut than those presented in the written and oral presentation of their future directions. Although full interaction between the team and the CERTO members should benefit the scientific output of the team, the group leader needs to differentiate what are the goals of the Neuro-PSI team and what are those of the CERTO members. The group leader should also consider the time/gain costs of the different collaborations she has established (aim 4). For example, what will be the advantage of establishing a model for Usher syndrome in *Xenopus*, when there are already several mouse and zebrafish models ?

Conclusion

▪ Strengths and opportunities:

This is a well-consolidated team with a good productivity.

The team is internationally recognized.

The five-year plan is in general very positive with aspects that represent the logical continuation of the present research of the team.

The team has been well funded so far.



- **Weaknesses and threats:**

Some aspects of the five-year plan are less clear and possibly overlapping with the goals of the CERTO.

- **Recommendations:**

The team is encouraged to be more ambitious in the future in terms of productivity, especially considering the size of the team.

The group leader needs to organize her time carefully between the two activities so that the PSI team will not suffer from dilution in a larger group.

Funds for the future need to be secured.

Team 5: Forebrain development and evolution

Name of team leader: Ms Sylvie RÉTAUX

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	5	5

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

- Detailed assessments**

Assessment of scientific quality and outputs

The team is composed of a permanent researcher (DR1), 2 post-docs, 1 PhD student and 3 technicians. The group leader is the unique permanent scientist. The general objective of the team is to decipher the mechanisms that drive forebrain evolution in vertebrates. The roles of midline signalling systems, regionalisation, patterning and neuronal differentiation are studied in original animal models including lampreys - a macroevolution model to gain insights in the ancestral characteristics of the vertebrate forebrain - and *Astyanax mexicanus*, a microevolution model fish that exists as a “normal” surface morph and cave dwelling morphs, that lack eyes and have developed sensory systems and behaviours that are essential for survival in dark environments.

During the last five years, the team has obtained significant results on mechanisms regulating the development of the pallium - that include variations in transcription factors and cis-regulatory modalities in specific cells, the Cajal



Retzius cells and the germinal zone progenitors - and on the implication of midline signalling systems (Hedgehog, FGF, Wnt) in forebrain anatomy, with changes in non-coding regulatory sequences. The team made major contributions to the establishment of resources and tools for a microevolution model, the blind cavefish *Astyanax mexicanus*. Using this model, they identified changes in morphogen signalling causing important anatomical modifications consistent with the hypothesis that cavefish lost their eyes for other advantageous traits; they document changes of adaptive behaviour and identified an increase in a group of neurons involved in this behavioural shift.

These results have led to the publication of 14 original articles and 7 reviews, signed by a team member as first or last author, in good (e.g. Plos One, J of Neurobiol, Zebrafish) to excellent journals (e.g. Cerebral Cortex, PNAS, Development, Current Biology, J Comp Neurol). 5 other original articles have been published in collaboration with other teams. Relative to the limited size of the team, this production is excellent.

Assessment of the team's academic reputation and appeal

International visibility is excellent. The group leader participates in an international project (European FP7 CISTEM, partner). She co-organized two international meetings and one symposium in an international meeting and is regularly invited to conferences (8) and seminars (7). The group leader is Academic Editor for PlosOne and was guest Editor for special issues of Seminars in Dev Biol and "EvoDevo in Extreme Environments". In the last five years, the team had 6 post-docs, including 1 Japanese, 1 Chinese and 1 American and a visiting professor coming from Marist College (USA) illustrating the international reputation of the group. The group leader has been a member of the Conseil National des Universités, Section 69 (Neurosciences). The ability of the team to raise national (ANR, FRC) and international (FP7) funds allowed attracting post-docs from France and abroad (Japan, China, USA).

Assessment of the team's interaction with the social, economic and cultural environment

The team leader is writing in vulgarisation journal (Biofutur) and teaches at "Université du 3^{ème} âge".

Assessment of the team's organisation and life

The team is rather small with the group leader as the unique permanent scientist. The recent recruitment of a talented engineer allowed a fruitful re-organization of the team.

Assessment of the team's involvement in training through research

Three PhD students have been trained during the period. All these students were "moniteur" (teaching assistant, 64h/year). One got a position of Assistant Professor. The team leader also did teaching (around 15h/year) and was member of 10 PhD thesis juries as well as member of the Master2 and Doctoral School yearly juries.

Assessment of the strategy and the five-year plan

The scientific project focuses on the evolution of the cavefish, a domain where the group is in a leading position. It is built up on the team's achievements of the past years that include resources and tools. A first group of questions that will be addressed relate to the morphogen-dependent mechanisms that drive eye loss, modified forebrain development and adaptive social and feeding behaviour in cave dwelling fish. This project in direct line with the recent data obtained by the group is supported by an ANR (ASTYCO, 2011-2014). A second group of questions concerns the molecular evolution of *Astyanax*, including the nature and number of genes involved in adaptive changes, a comparison of independently-evolved cave dwelling morphs, and the impact of coding sequence changes on morphological and behavioural adaptation to life in cave. This project is also supported by an ANR (BLINDTEST, 2013-2016) and will be performed with two partners. Finally, on a slightly longer term, they propose to expand their study to the cis-regulatory sequences that clearly have to be considered to elucidate the molecular evolution in blind cavefish. This is an outstanding project considering the originality and quality of the proposal.



Conclusion:

- **Strengths and opportunities:**

The team is at the forefront in its field and very well integrated in the international scientific community. They developed numerous indispensable tools and raise grants to work in excellent conditions, that should keep them world leading in the field.

- **Weaknesses and threats:**

The group leader is the unique permanent researcher. Given her future role of head of the Department Evo-Devo of the future Institute, she should really aim to attract another permanent researcher to stabilize the team.

- **Recommendations:**

The experts committee recommends that the team continues to perform this excellent and very exciting research.

Team 6: Development & Evolution of Neurotransmission

Name of team leader: Mr Philippe VERNIER

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	3	4
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	6	6

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

This is a relatively small team with two permanent researchers, one technician, two postdoctoral researchers and one PhD student. The overall aim of this group is to understand the organisation of monoamine neurotransmitter systems in the vertebrate brain, how this organisation changes during evolution and relates to behavioural output. The broad scope of research that investigates very diverse aspects of dopaminergic neurons (evolution, molecular identity, anatomy, function) is unique. The group leader's lab has shed light on the evolution of tyrosine hydroxylase genes involved in dopamine synthesis, on the classification of dopaminergic receptors, and on the genetic specificity and function of dopamine-producing neurons. The group leader has a disproportionately heavy administrative duty, which appears to impact somewhat on the research productivity. Despite this, the team's publication record is overall good (BMV Biol. Mol. Cell. Neurosci., J. Comp. Neurol.), and it has made very good contributions to the understanding of the anatomical organisation of the monoamine system in different chordate species. Papers are published in Mol.



Cell Neuroscience and J. Comp. Neurology, both respectable journals in the field. This work has revealed an unexpected complexity of the dopaminergic system and highlighted important organisational differences during evolution. More recently, the team has used genomic approaches to study the evolution of dopamine receptor D1 genes, and recently published these data in a higher impact journal (Mol. Biol. Evol.). These studies reveal a significant divergence of coding and regulatory sequences, which may underlie the evolution of different life styles. In addition, the team has produced several major reviews, including contributions to an encyclopedia co-authored with another leading figure in this field. In summary, a very good output that has formed the basis for future papers with far-reaching influence.

Assessment of the team's academic reputation and appeal

The group leader is not only director of the new Neuro-PSI, but is also involved in a large number of other public activities including being President of the French Society for Neuroscience, participating in many national and international evaluation committees, advisory boards and councils of foundations and co-organising many international meetings. This is clearly evidence for the Pls dedication and commitment, but also for his recognition in the scientific community in general and neuroscience in particular. The team is part of the zebrafish brain atlas initiative, an important international project, demonstrating the high quality of their work and that they are respected internationally. The group has attracted a few international postdoctoral researchers, and more recently an internationally renowned neuro-anatomist and evolutionary biologist, was a guest researcher in the team. This has clearly born fruit as evidenced by joint papers, reviews and contributions to an encyclopedia. The team has attracted external funding throughout, including larger cooperative grants. Overall, the group leader visibility and reputation is excellent.

Assessment of the team's interaction with the social, economic and cultural environment

The team has some involvement in articles for the general press, participation in TV/radio programmes and outreach activities.

Assessment of the team's organisation and life

This is a relatively small team with 2 “chargés de recherche” (class 1) and a few more junior researchers; this makes for a fairly focused group with complementary expertise. This is good given the large administrative engagement of the group leader and helps the group to focus, but also maximises involvement and interaction with other groups in the center. The new Neuro-PSI site will provide access to major resources, especially behaviour facilities and open up the possibility for asking big questions and more interdisciplinary research, some of which has already begun.

Assessment of the team's involvement in training through research

The group leader is involved in various doctoral programmes including being vice-director of one programme in Paris 11 as well as a programme at Masters level. The team has successfully supervised two PhD theses during the evaluation period, and currently trains one more student. This is very appropriate given the high level of administrative burden of the group leader.

Assessment of the strategy and the five-year plan

The team tackles evo-devo questions mainly with respect to the neurotransmitter systems and the development of new approaches and collaborations, which will now allow developing exciting new projects and branching out to ask behavioural questions. The 5-year plan is concise and focused on development, evolution and functional characterisation of dopaminergic system mostly in fish, but a few other models are also used for comparison. The group will concentrate on three populations of dopaminergic neurons. First, it will investigate the origin and function of dopamine neurons that control locomotion using transgenic lines combined with molecular analysis, optogenetics to modulate activity patterns and assess how this influences swimming behaviour. Second, they will characterise preoptic-hypophyseal DA neurons and their molecular signature to elucidate their role in the control of the neuroendocrine system that regulates reproduction. Third, to shed light on the evolution of cognitive functions the team will study dopamine function in the pallium using a comparative approach combining axonal tracing, electrophysiology and behavioural tests.



The plan is adequately based on the strength of the current group and combines descriptive, morphological and anatomical approaches with transgenic fish for imaging, which are being developed in collaboration with other teams as new tools. In addition, the group will venture into new territory and study locomotion behaviour and cognitive functions. This clearly follows a current trend and is an area with a promising future. The choice of the fish as a model system is good because of its relatively simple brain, good imaging technology and because behavioural tests are quite straightforward to set up.

Overall, the team will benefit from moving to the new site with excellent potential for new interactions. The new site will offer better links with imaging and behavioural approaches, and access to appropriate platforms for these studies. This will be an important move for the group, which is currently rather isolated, and will provide excellent facilities to make their projects work.

Conclusion

▪ Strengths and opportunities:

The team forms a small group of researchers with complementary expertise. A recent boost in publications, the development of new tools and consolidation of exciting collaborations pave the way for a strong research programme. The team has assembled all the elements to move into new directions and to address important questions related to the development and evolution of monoamine systems.

▪ Weaknesses and threats:

The group leader is extremely active in the scientific community outside his research group, having been appointed, in addition to many other duties, as the director of Neuro-PSI. While this clearly speaks for his leadership qualities and the respect he has in the community, it may impact on his own group.

▪ Recommendations:

In summary, the team has developed a strong research agenda for the next years based on previous data, newly developed technologies and new collaborations. They have put together an exciting programme to address important questions with respect to the organisation and function of the dopaminergic system, and how changes in its organisation relate to behavioural changes during evolution. The group will benefit from the Neuro-PSI project providing access to crucial technological platforms, strengthening of ongoing collaborations and forging new ones.

Team 7: Pharmacology and Biochemistry of the Synapse

Name of team leader: Mr Hervé DANIEL

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	5	5
N2: Permanent EPST or EPIC researchers and similar positions	2	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	8	7

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	5	3

• Detailed assessments

Assessment of scientific quality and outputs:

The core of this group is composed of one professor and 2 assistant professors (maîtres de conférences). During the period under review the core members of the group were joined by 2 CNRS researchers and a professor with quite different experience in protein biochemistry; all are nearing retirement. The main expertise of the group is in molecular and cellular studies of the cerebellar cortex. In this review period, they have focused on the function of presynaptic metabotropic receptors (mGluRs), specifically mGluR4 expressed on parallel fibres. The group has an on-going collaboration on the (successful) development of specific drugs for this class of receptors, whose lack of pharmacology has previously hindered their study. The central results of the group were:

1) the demonstration of an unexpected signalling mechanism of mGluR4s via the PKC pathway, rather than via modulation of PKA;



II) the interaction of mGluR4 with proteins of the presynaptic complex (a successful internal collaboration between the two parts of the group);

III) the demonstration of functional P2X purinergic receptors in Bergmann glia (in addition to the known P2Y receptors).

The core group published 11 articles of which 7 had group members in 'positions of responsibility' (first and/or last author). These articles appeared in good specialist journals (notably J. Biol. Chem., J. Physiol (Lond), J. Neurophysiol.). Although outside of this committee's expertise, it is of note that the protein chemists contributed a significant output of their own (30 articles). Overall, the experts committee felt that the work of the group was understandably focused, given the limited resources of the group, yet answered clearly posed questions with high-quality experiments that produced genuinely original results of benefit to their scientific community.

Assessment of the team's academic reputation and appeal:

The group has recognised experience in the cerebellum, in part through the leader's work with former colleague. They maintain very good national collaborations on metabotropic receptors and this has also been the source of the group's recent ANR funding, but no running funding has been obtained for the immediate future except the recurrent funding they receive from the university. They also have an international collaboration with the University of Innsbruck.

Assessment of the team's organisation and life:

CNRS researchers that will retire in the near future recently joined the team with different expertise. New team's organisation will be required.

Assessment of the team's involvement in training through research:

The core group members all have teaching positions and have assumed heavy responsibilities in the administration of teaching. In the group as a whole, 4 PhD students graduated during the period under review (including protein chemists).

Assessment of the strategy and the five-year plan:

The project has two main parts: the study of presynaptic mGluR4s at parallel fibre synapses, itself subdivided into physiological investigations and pursuit of the search for interacting proteins, and measurements of potassium and water balance involving Bergmann glia in a dystrophin model. The exploitation of novel pharmacological agents specific for the mGluR4s is the logical extension of the current collaboration. A significant part of the project is predicated on what appears to be an mGluR4 effect that does not involve modulation of calcium channels. The authors hypothesise that this is mediated by calcium-independent protein interactions rather than via the PKC pathway previously identified. Although it is likely that work of quality comparable to the historical production will eventually result, expert committee members expressed some reservations about parts of the project as presented. In particular, they felt that it would be difficult and time consuming to identify directly (as opposed to indirectly) interacting proteins. Controlling for altered trafficking/localisation of mGluR4s could pose additional problems. A positive point was the desire of the group to acquire new techniques (ion-selective micro-electrodes, membrane-penetrating peptides, optogenetic techniques, proximity ligation assay), although validation of some may again prove time consuming.

Conclusion:

▪ Strengths and opportunities:

Expertise in the cerebellar circuitry; continuity of subject matter; good collaborations.

▪ Weaknesses and threats:

The limited funding and human resources, imposing the need for focused projects of sometimes limited scope, may impair the ability of the group to compete effectively.



- **Recommendations:**

Leverage of external expertise through collaborations, both to develop new techniques and to attempt to raise funds is one possible avenue to develop the group, as its members presumably realise.

Team 8: Hindbrain Integrative Neurobiology

Name of team leader: Mr Gilles FORTIN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	7	7

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs:

The hindbrain integrative neurobiology group is a middle-sized team (3 scientific staff, 2 post-docs, 2 PhD students and 2 technicians). The main focus of the team is the development of the neuronal circuits involved in the control of respiration. They use the mouse embryo as a model system together with innovative molecular genetic tools, optic stimulation and imaging to delineate the functional connectivity of the developing circuits controlling respiration. The group has published 15 original papers and 5 reviews during the period 2008-2013. The team leader signed two major papers as last author in Nature Neuroscience (2009, 2010) and team members set up numerous collaborations that give rise to regular papers in excellent to prestigious journals J. Neurosci. (2009, 2010, 2011), Development (2011), Nature (2013). Overall, the experts committee was very impressed by the outstanding group's achievements.



Assessment of the team's academic reputation and appeal:

The group has provided fundamental insights in the development of rhythm generators in the vertebrate central nervous system. This work has been recognized and commented upon in prestigious journals (e.g. 2009 Nature Neurosci, 2010 Nature Neurosci, 2010 Cell). The group has been represented at many international conferences and meetings, been very successful in funding and established important collaborations both nationally (e.g. IBENS, Université Paris Descartes) and internationally (e.g. Salk Institute, FMI Basel, Karolinska Institute). In 2011, the group leader received the CNRS Scientific Excellence award and is member of numerous scientific committees (e.g. CDS8 ANR Biologie Santé, Faculty of 1000 section Neuro-Development, Fondation Recherche Santé Respiratoire). In the last five years, 4 PhD students, 2 post-docs, and 3 visiting scientists were supervised underscoring the attractiveness of the group that benefits of an outstanding reputation in the field. The ability of the team leader to raise numerous grants (ANR, FRC, DIM, FRM team accreditation) allowed attracting post-docs.

Assessment of the team's interaction with the social, economic and cultural environment:

The team leader diffused his scientific achievements through international and national tribunes.

Assessment of the team's organisation and life:

This is a small but highly efficient team that was able to raise substantial national (ANR, FRM, FRC) funds.

Assessment of the team's involvement in training through research:

The group is involved in teaching in two master modules, in supervising PhD students (two finished and two on-going) and has participated in four thesis committees.

Assessment of the strategy and the five-year plan:

The research program is a natural continuation and based on the team's discoveries of the organization of the retrotrapezoid nucleus (RTN) and the preBötC oscillator. It is divided into three parts:

- I) foolproof evidence for the requirement of the RTN for CO₂ chemoreception and for the dysfunction of the RTN being causal to the congenital central hypoventilation syndrome;
- II) establish the functional connectivity of the RTN;
- III) establish the anatomical connectivity of the RTN and other respiratory neurons.

The proposed research will be carried out using state-of-the art methodology including molecular genetics, optogenetics, optical wavefront engineering based microscopies and trans-synaptic tracing. The proposed research promises very high impact, still being realistic and focused.

Conclusion:

▪ Strengths and opportunities:

The group is in the forefront in its field and eager to adopt new techniques and to collaborate with very competent groups.

▪ Recommendations:

The experts committee recommends that the group continues to aim high, adopt new techniques and find interesting collaboration both within, and outside, the unit.

Team 9: Functional Brain Imaging and Behavior

Name of team leader: Mr Jean-René MARTIN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1
N6: Other contractual staff (without research duties)		1
TOTAL N1 to N6	4	4

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	1

- Detailed assessments**

Assessment of scientific quality and outputs:

The “Functional brain Imaging and Behaviour” team, headed by Mr Jean-René MARTIN, uses the fruit fly *Drosophila* to analyze neuronal mechanism underlying behaviour, with an emphasis on ageing and longevity, locomotor activity and olfactory signalling. The group leader has during the recent years established a novel optophysiological approach in *Drosophila*, i.e., functional optical calcium imaging using a bioluminescence sensor. This approach complements existing optical calcium imaging techniques based on fluorescence, an achievement for which he is highly recognized within the scientific community. This technical approach has particular advantages, e.g., with respect to long-term measurements and recording of spontaneous neuronal activity in the brain of living fruit flies. Mr Jean-René MARTIN’s research has a great opportunity to further advance use of this application in order to fully exploit the potential of this method. The group leader’s lab uses this tool to investigate neuronal activity in olfactory neuropils in the *Drosophila* central brain. As a second key topic the lab investigates the role of a small



nucleolar RNA in longevity and ageing, a topic of high relevance and with great future potential. The group has published eight original publications since 2008 in decent scientific journals of good quality (e.g., J. Exp. Biol., PlosOne, BMC Neurosci.). The team leader has summarized the bioluminescence imaging technique in form of a review and has edited a book on genetically encoded functional indicators, which is acknowledged as a good publication record both with respect to output and scientific quality.

Assessment of the team's academic reputation and appeal

The team is, when compared with other teams of the Department of Molecules and Circuits, relatively small, with two permanent team members and a small number of non-permanent researchers. The group leader has continuously attracted noticeable grant funding from various sources. Despite the small size of the lab, the team is internationally well known for the invention of aquaporin-based calcium imaging using bioluminescence in *Drosophila*. The group leader is throughout the scientific community working with *Drosophila* neuroscience very visible and well known through active participation at relevant international conferences. The group leader also edited a book on optical imaging techniques and genetically encoded sensor proteins, underscoring his reputation as an expert in this field. It is expected that the group continue to provide substantial contributions to both the optical imaging field and the research topic of behavioural neurobiology in the future. Overall, the international academic reputation, appeal and visibility of the lab are very good.

Assessment of the team's organisation and life

The group is small, but clearly structured and organised into two main topics, each containing scientists at different levels (permanent researchers, PhD students and master students). A strong level of interaction within the group is certainly ensured by the relatively small and manageable size of the group.

Assessment of the team's involvement in training through research

The team has over the last years continuously trained a number of PhD and master students. The group leader is also strongly involved in teaching at the Université Paris-Sud in various courses and modules, which certainly facilitates the attraction of students.

Assessment of the strategy and the five-year plan

The 5 years research plan includes a number of highly interesting and very detailed points. The future strategy of the team clearly builds on the one hand on past achievements in developing optophysiological techniques and is a logical extension. On the other hand, the team moves towards new avenues in investigating molecular mechanisms influencing ageing. The two main topics encompass in particular physiological functions of the mushroom body (cholinergic transmission, the role of biogenic amines, nocturnal and spontaneous activity of neurons) analysed using optical imaging techniques, and the role of a particular snoRNA in longevity and ageing. The high importance and relevance of these research topics are beyond any doubt. With respect to the promising future prospect of these research projects it is to be expected that more lab members can be recruited that can efficiently follow up the two extensive research topics. The future location of the lab in the new Neuro-PSI building will certainly facilitate the interactions of the lab. In particular, the group leader's efforts to make the calcium imaging feasible for other researchers, e.g., in the context of circadian rhythms investigated by collaborators in the institute, or the investigation of snoRNA in mice, can be expected to be fruitful. Overall, the research plan and future research strategy is evaluated as very good.

Conclusion

▪ Strengths and opportunities:

The research plan builds on good achievements in the past and combines both further advance of innovative technology with the development of promising new topics of research. This concept provides a high potential for continuing and enhancing productive research and future funding. The team is well established in the particular field of research with good expertise in the lab, and the future strategy implies very promising original and innovative aspects. The planned new location of the laboratory will certainly provide more opportunities for collaborative interactions.



- **Weaknesses and threats:**

One weakness is the small size of the lab, which attenuates the progress of scientific achievements and output. More collaborative interactions to fully exploit the innovative technology established by the team will be helpful. However, a stronger embedding of the team might be achieved in the future when the entire department and the entire unit will move to a new building on the “Saclay’s plateau”. Both the productivity and the collaborative interactions will probably profit from the new location.

- **Recommendations:**

This is a research team of international reputation with a convincing strategic plan for future research. It will be crucial for the continued success of the team to expand the number of scientists to achieve the targeted goals. It is recommended that the team will be well supported to enable the continuation and progress of the valuable research projects by funding. It is also recommended that a reasonable integration of the group in the new Neuro-PSI building will be provided.



Team 10: Protein misfolding and aggregation in neurodegenerative diseases

Name of team leader: Mr Ronald MELKI

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	6	6
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	5	6
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	11	12

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	3	4

• Detailed assessments

Assessment of scientific quality and outputs

The “Protein misfolding and aggregation in neurodegenerative diseases” team is presently part of the “Laboratoire d’enzymologie et biochimie structurales” (UPR 3082 - CNRS) located in the CNRS campus of Gif-sur-Yvette. The team will thus now leave its present structure to join the new Molecules & Circuits Department of Neuro-PSI. The team is composed of 5 permanent researchers (1 DR1, 3 CR1, 1 CR2) including the group leader, 2 technicians (AI), 1 post-doc fellow and 2 PhD students. The objective of the team is to decipher the molecular mechanisms and roles of protein misfolding and aggregations in neurodegenerative disorders such as Parkinson’s, Huntington’s and Alzheimer’s diseases. Between 2008 and 2013, they originally and remarkably demonstrated through very fruitful collaborations with Brundin and Kopito groups that alpha-synuclein assemblies in Parkinson and huntingtin (Htt) assemblies in Huntington, spread from cell to cell as observed with PrP in the Creutzfeld-Jacob disease. Related to this discovery, they also aimed at identifying important players in the aggregate formation, mechanisms of cell to



cell spreading - endocytosis, axonal transport, toxicity - and functional characteristics of each oligomer species. Different tools have been developed to scrutinize amino acid sequences that have coevolved with polyQs and to probe polyQ/Htt assembly into fibrils. A recent and significant result is the isolation of two strains of α -synuclein with different structures, toxicities and propagation properties. Thus, this is a very active and creative team that developed a large array of molecular, structural and functional technologies. As a result, both the quantitative and qualitative quality of the team's publications is outstanding. The team published 26 original articles and 8 reviews, signed by a team members as first, last author or corresponding author in good/very good (e.g. PLoS One, Faseb J, J Biol Chem, Biophys J) to excellent journals (e.g. Ann Neurol, Nature Commun, Angew Chem Int Ed Engl). The team leader is co-corresponding author of a review in Nat Rev Mol Cell Biol (IF = 37). 20 other original articles have been published in collaboration with other teams, several of them in excellent (e.g. Ann Neurol, PNAS, PLoS Pathog) and top (e.g. J Clin Inv, Nat Cell Biol) journals.

Assessment of the team's academic reputation and appeal

International visibility is excellent and demonstrated by the number of invited conferences (21 in France and 7 in Germany, UK, USA and Germany) and seminars in renowned Research Institutes (20). The team leader has taken part to the organization of 5 international meetings. Since 2008, he is a member of a scientific committee of the French National Institute for Agricultural Research (INRA). He has participated to 3 AERES experts committees. He is director of IFR115 (2010-2013) and deputy director of UPR 3082 (2013-2014). The team is attractive as indicated by numbers of PhD students having achieved or presently running their thesis in the lab. The impact of the team and the PI is major in the field of protein misfolding and aggregation and is illustrated by the important collaborations with leading groups worldwide that have been initiated based on the team's expertise and leading to top level publications (e.g. Nat Cell Biol, PNAS, J Clin Invest, Nat Rev Mol Cell Biol). This impact is also demonstrated by the high number of citations that these recent paper already received as 153 citations for the Nat Cell Biol 2009, 142 citations for the J Clin Invest 2011, and 131 citations for the Nat Rev Mol Cell Biol 2010). The group leader was and is well funded by national (5 ANR grants (2 as coordinator), FRM FdF) and international grants (HFSP 5FP7, Era-net-neuron, Galileo program). The team has been granted the prestigious Bettencourt Schueller Foundation award "coup d'élan à la recherche" (boost for the research).

Assessment of the team's interaction with the social, economic and cultural environment

The team is involved in some activity of scientific and medical vulgarization.

Assessment of the team's organisation and life

The group is very well structured with scientists at different levels of their scientific careers and a network of very efficient external collaborators.

Assessment of the team's involvement in training through research

Six PhD students have been trained during the period. The team leader did some teaching (around 6 to 10h/year), contributed to workshops and was member of 8 PhD thesis juries and 7 HDR committees.

Assessment of the strategy and the five-year plan

The new project is in line with the previous achievements of the group. Five objectives will be addressed by using a combination of cell biological, biochemical and biophysical methods and will focus on alpha-Syn and htt. These objectives include the definition of the structure-function relationship for the resulting aggregates, the identification and characterization of the interactions of molecular chaperones involved in fibrillar assemblies, the interaction of the aggregates with the neuronal/cell membrane compartments, the identification of cell surface partners and routes used to penetrate cells and spread from one cell to another, the characterization of in vitro, in vivo and human alpha-Syn strains. Altogether, the project seems very exciting and timely since:

I) it is based on technologies that are available in the team and for which the team exhibits a high level of expertise or an impressive network of efficient collaborations;

II) it addresses cutting-edge questions in the field of cell to cell spreading of protein aggregates, which is very original, recent and concept-challenging regarding neurodegenerative diseases and to which the group has been a main contributor.



Conclusion

- **Strengths and opportunities:**

This is an outstanding and productive team with a great creativity. The team leader is a world-class expert on this topic. The team makes significant conceptual advances in the field on a regular basis and has proposed, together with collaborators, a challenging and very exciting new model for neurodegenerative mechanisms. They use advanced methodological tools that combine all levels of analysis. The project is excellent and will address a large series of questions for several types and subtypes of aggregates. The experts committee will be impressed if the team would succeed in every sub-project that is proposed.

- **Recommendations:**

This is a strong and mature team. Its visibility in neuroscience is excellent. In light of the originality of the project, there is no doubt that the high level of publication will be maintained in the near future.


Team 11: Molecular Genetics of Circadian Rhythms

Name of team leader: Mr François ROUYER

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	4	4
N3: Other permanent staff (without research duties)	4	4
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	11	10

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	3

- Detailed assessments**

Assessment of scientific quality and outputs

The “Molecular Genetics of Circadian Rhythms” team uses the fruit fly *Drosophila* to analyze neuronal and molecular mechanisms underlying circadian rhythms and sleep/wake cycles. This field of research encompasses a large number of laboratories around the world, and the group leader is well embedded in this scientific community as a leading investigator. The outstanding scientific output and its quality are evident by a large number of publications (10 original publications are listed since 2008), often in journals of high impact (e.g., Nature Neuroscience, Plos Biology, Journal of Neuroscience). The excellent quality of the research is also reflected by the scientific novelty of the reports and the very careful analysis of detailed open questions, e.g. regarding the thorough analysis and dissection of distinct clock neurons and the discovery of novel genes involved in controlling circadian clocks. Most publications are genuine papers originating from this group. Two review articles in the prestigious journal “Nature” complement the publication record. Key findings of the group are the identification of several gene products



controlling the function of oscillating clock genes and the characterization of light input to circadian clock neurons. This influential and substantial contribution of the group to the understanding of circadian rhythms at diverse levels of analysis, ranging from molecular mechanisms over neuronal connections to behaviour, together with the impressive scientific output distinguishes this lab as outstanding.

Assessment of the team's academic reputation and appeal

The team is, when compared with other teams of the Department of Molecules and Circuits, of a reasonably large size. Since the group leader has managed to hire a number of scientists over recent years, both at the PhD student and postdoctoral level, the team is evidently attractive. This is underscored by the continuous approval of grant funding from various sources (nine research grants since 2008). The group is internationally very well-known and recognized as a leading lab in the field of research on circadian rhythms. The high esteem of the group leader research is underlined by a large number of international collaborations and many invitations to international conferences. Moreover, the group leader is the author of the chapter “circadian timing” of an international textbook on neurosciences, which also demonstrates his international visibility and reputation as a leading expert in this field. In summary, the academic reputation of this lab is undoubtedly outstanding.

Assessment of the team's interaction with the social, economic and cultural environment

The group leader is actively participating in research management and policy, e.g., as a board member of scientific organizations, as a deputy director of the CNRS unit UPR 3294, and as a member of the steering committee of the Neuro-PSI project.

Assessment of the team's organisation and life

The group is a very well-structured team of scientists at different levels of their scientific careers (permanent researchers, third party-funded postdocs, PhD students and undergraduate students). There is a common topic (circadian rhythms in *Drosophila*) as an overarching aim that unites the various levels of research and ensures interactions and resource sharing within the group.

Assessment of the team's involvement in training through research

The team has a number of PhD students significantly contributing to the research activities. The lab has also hosted a remarkably large number of students for internships. Moreover, the group leader has participated in a noticeable number of PhD thesis and HDR committees and is strongly involved in teaching at the Université Paris Sud, the Université Paris Diderot and the ENS Paris. The strong involvement of the unit in training through research is clearly noticeable.

Assessment of the strategy and the five-year plan

The 5 years research plan is along the lines of the group previous and successful work. However, novel and state-of-the-art approaches are also proposed to be included (e.g., optical imaging in collaboration with team 9, establishing an ubiquitin biotinylation system, or the use of the GRASP technique to pinpoint synaptic contacts between neurons). The research plan is very well substantiated by a large number of specific points to be addressed. The overall scope is impressive and encompasses topics at various levels of analysis, ranging from the deciphering of intercellular cascades controlling circadian oscillators, over a dissection of neuronal networks of clock neurons and light-induced input to circadian clocks to determining targets of clock neuron outputs. All of the proposed research endeavours are convincing and solid with respect to scientific relevance and technical feasibility. Overall, the research plan and future research strategy is evaluated as outstanding.

Conclusion

- Strengths and opportunities:

The research plan covers various aspects of a common theme with excellent potential for a successful continuation of productive research and future funding. The team is at the leading edge in the field, the future strategy is solid, with a well-structured plan that builds up on recent achievements, but also includes novel approaches. There is good expertise in the team and an excellent network of international collaborators.



- **Weaknesses and threats:**

There are no obvious weaknesses or threats, besides the risks that always exist if new technologies are to be established. However, the move to the new Neuro-PSI building will certainly help to profit from expertise and equipment of other groups, e.g., in the fields of optical imaging technology and of transcriptomics/proteomics.

- **Recommendations:**

This is a research team of very high international reputation and with a totally convincing strategic plan for future research. The research strategy makes full use of the new potential advantages that the new Neuro-PSI will offer with respect to interaction and sharing of platforms and resources. It is strongly recommended that the team will be maximally supported to guarantee continuation and progress of the indeed outstanding research projects.



Team 12: Transduction and Developmental Neuropharmacology

Name of team leader: Mr Martial RUAT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	2	3

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team is composed of a permanent researcher (DR2), 1 engineer (IR1), 1 post-doc and 1 PhD student. The main objective of the team is to understand how developmental signals are produced and influence brain functions. The team uses genetic and pharmacological tools to analyse alterations of these signals, such as those linked to human mutations responsible for brain tumours and other diseases. During the last four years, the team has obtained significant results on the role of Hedgehog (hh) signalling in brain function and on the transduction pathways involved. Other results are related to the roles of calcium sensing receptors in the brain. These results have led to the publication of 9 original articles and 6 reviews, signed by a team member as first or last author, in good (Mol Pharmacol, Differentiation, J Med Chem, Cell Calcium, etc) to very good journals (J Neurosci, Stem Cells, TIPS). 13 other original articles have been published in collaboration with other teams, some of them in excellent journals



(Circ Res, Ann Rheum Dis, Arthritis Rheum, J Clin Invest). Publications are well cited. Relative to the limited size of the team, the overall production is excellent.

Assessment of the team's academic reputation and appeal

The team leader is actively engaged in the community as member of the executive committee of the future Neuro-PSI and deputy director of the Molecules & Circuits department of Neuro-PSI. He has been a member of the CoCNRS (section 25, Neurosciences, 2008-2012) and participated in 3 AERES experts committees. International visibility is demonstrated by the number of invited conferences (18, 8 for the team leader) and seminars in renowned research institutes (15). In addition, the team leader took part to the organization of 2 international meetings and 4 symposia in other international colloquia. The team's ability to raise funds has been limited to 3 national grants (ANR, LCC).

Assessment of the team's interaction with the social, economic and cultural environment

During the last four years, the team has deposited 7 patents, with international extensions for 6 of them. Molecules described in some of these patents are sold by different companies (Tocris, Santa Cruz, Sigma, Merck Millipore, etc.). This is clearly a strong activity of the group, and in fact this group is the most successful team within the unit in this respect. This clearly demonstrates the team ability to attract commercial interest, to market their compounds and is also evidence for the strong pharmacological approach of this team.

Assessment of the team's organisation and life

This is a small team, however the project presented is rather large and, given the number of team members, may require some focus. There are good collaborations and connections outside the team. The group will benefit from a larger center and more interactions across disciplines when NeuroPSI is established; some collaborative efforts have already been made across departments with the help of IDEX.

Assessment of the team's involvement in training through research

Four PhD students have been trained during the period. One of the previous team members has now established her own independent group. The team leader has some teaching responsibility (around 6 to 10h/year) and was a member of 16 PhD thesis juries and 2 HDR committees. Given his background he should have good potential to promote interdisciplinary teaching.

Assessment of the strategy and the five-year plan

The strategic plan has two clear parts: pharmacology of shh modulation and the biological role of shh signalling in the adult brain. In principle, this is a good combination of approaches with great potential, because the work lies at the interface of biology, stem cells, disease and drug design. In particular, synthetic biology could be very interesting, should be highly fundable and is useful with respect to possible therapeutic application in neurodegenerative disease.

However, the 5-year plan does require some re-thinking and re-structuring, and lacks some focus given the size of the team. The strategy is roughly divided into two main topics:

- I) the role of shh in adult neural stem cells;
- II) development and functional assessment of novel shh pathway modulators.

Thus, this small group proposes to tackle a large question in a field where the investigator has less expertise (adult neural stem cells) than in drug design approaches, which is the strength of the team. The adult stem cell field is highly competitive, as is the involvement of shh signalling, and has already attracted attention of large groups. With the departure of one team member with biological background, the team leader should consider taking advantage of the strong stem cell focus of the Development & Evolution department and/or re-evaluate future plans to retain competitiveness and to continue to be successful. The molecular screens proposed may generate very interesting data, but lack a clear biological hypothesis and need to be followed by a very clear strategy for prioritisation of genes for validation and further investigation so that novel principles can be discovered.

The second aspect of the project aims to generate or functionally evaluate new modulators of shh signalling to manipulate canonical and non-canonical signalling, respectively. The non-canonical pathway is poorly understood and



virtually no downstream effectors have been identified; however this pathway seems to be independent of transcriptional activation downstream of *shh*. Design of specific smoothened agonists and antagonists will be very useful to disentangle the function of these pathways, if indeed they are different, and will clearly help to move the field forward. The team has indeed developed molecules that bind Smoothened, but do not appear to affect downstream transcriptional events. However, the team leader does not present a clear strategy to characterise the downstream events of non-canonical signalling or a strategy to ascertain that this is indeed how these drugs work. This requires as a first step the assessment of signalling read-outs. This is essential before embarking on large-scale experiments to assess the function of this potentially new pathway in adult neural stem cells or in different parts of the brain.

The new location will open up access to new facilities and new scientific stimulation and provide excellent opportunities at the interface of basic research, medically relevant problems and chemical biology, translational research, industry. The team needs to exploit this aggressively to attract more funding and members. It seems that they have already begun to do this in the context of IDEX.

Conclusion

- **Strengths and opportunities:**

Renowned expertise of the team leader in the pharmacological field, ongoing collaboration with chemists.

- **Weaknesses and threats:**

Small team in a very competitive field.

- **Recommendations:**

A team with very good past activity and potential, but it needs to step up to acquire more funding, become internationally competitive and produce top quality papers, and in particular adjust projects in a very competitive field. If this can be done the combination of molecular, drug design approaches with biological questions is extremely promising and should attract considerable funding and interest from industry. Be more active in international networks. Acquire more funding to attract post docs. Focus and adjust the project to the team's size and to more precise questions.


Team 13: Molecular Neuroendocrinology of Food Intake

Name of team leader: Mr Mohammed TAOUIS

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	3	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	10	9

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	4	4

- Detailed assessments**

Assessment of scientific quality and outputs

The main interest of the team, which presently belongs to the CNPS at Orsay, stems on elucidating how inappropriate endocrine and metabolic environments during early life durably impair hypothalamic neuronal organization and its resistance to leptin and insulin. This is an important research topic in the field of food intake with high societal relevance. The most significant team achievements concern the elucidation of how the anorexigenic cytokine CNTF contributes to the neuronal leptin resistance and the impact of leptin blockade during early life on long-term hypothalamic leptin sensitivity.

Over the 5-year period between 2008 and 2013, the team, which is composed of 8 permanent researchers (1 professor, 2 assistant professors, 2 researchers, 1 technician and 2 assistants engineers), has published 35 articles and 3 reviews with half of the paper co-signed in major position by team members. This is overall good but does not



reach the expected level of excellence to face the international competition in the field of food intake. Despite its solid expertise and potential, the research output of the team has been rather modest given its size, with all publications appearing in specialized journal (e.g. Diabetes, Endocrinology). The team leader, professor at the Université Paris-Sud is heavily involved in teaching and has been very active in this context (co-director of a Master M2 and responsible for several teaching modules). Despite his heavy teaching load, he was successful in keeping his publication record at a very good level. However, the number of publications appears very unequal in the team, some of its members displaying a low publication record despite their full time dedication to research.

Assessment of the team's academic reputation and appeal

The team leader is dynamic and actively involved in both teaching and research activities. He established a broad network of national and international collaborations whose research expertise is complementary to the work done in the team and which is expected to be stimulating for the whole team. Team members have been invited as speakers to a substantial number of national and international meetings as well as seminars (total of 21 over the last 5 years) and actively involved in the supervision of PhD students. Two PhD students will be involved in the future research projects. Team members have been successful in raising grants (ANR, Fondation pour la Recherche Médicale) but most of them will end in 2015 and getting additional funding will be crucial to ensure completion of the coming 5-year projects. The team was also involved in the organization of 3 conferences and meetings.

Assessment of the team's interaction with the social, economic and cultural environment

The team is involved in vulgarization activity.

Assessment of the team's organisation and life

Regular meetings are organized within the team to coordinate the scientific research among researchers, PhD and post-doctoral students. Management and life of the team seem to be adequate to enable proper functioning and interactions.

Assessment of the team's involvement in training through research

The team involvement in training and teaching is overall impressive. Six PhD thesis were defended in the team throughout the 2008-2013 period and 3 others are underway. Team members also participated to 13 PhD and HDR committees and are very active in teaching courses in several Licence and Master modules. Notably, the team leader carried on several teaching responsibilities (co-director of the Master 2 of Endocrinology and Metabolism at the Faculty of Medicine of Paris-Sud, responsible of a teaching module in cellular and integrative physiology of the faculty of Sciences of Paris-Sud, in charge of two teaching units in endocrinology at the Master 1 and 2 levels).

Assessment of the strategy and the five-year plan

The team possesses all the necessary scientific expertise and technical know-how to conduct the proposed projects and to achieve a fruitful completion. Building upon previous achievements, projects will be divided into two main objectives. The first one, original and achievable, will aim at elucidating the molecular mechanisms involved in insulin and leptin resistance in the hypothalamus, the goal being to provide novel insights into the control of obesity, diabetes and food intake. The second objective, more ambitious but also more risky, will lie in identifying the profile of hypothalamic micro RNAs expression involved in metabolic programming, this in order to identify potentially novel targets for the treatments of food intake disorders. This correlative approach will be coupled to a more invasive approach consisting in silencing micro RNAs of interest using anti-mRNAs.

The specific experiments are in most cases clearly identified, reasonably well focused and pertinently targeted. The first objective is appealing and benefits from solid preliminary findings that should lead to success. In contrast, the second objective sounds like a huge undertaking given the international competition with very low throughput and no guarantee that the RNA profiling will lead to the identification of pertinent targets. Previous experimental studies in the field have favoured this screening approach but results have been mixed, the risk being to end up with a long list of potential targets, but still no clear means to prioritize them. One key step in the validation stage will be to select the most pertinent animal models with the proper high fat diet that will offer a high power of discrimination of the targets.



Conclusion

▪ Strengths and opportunities:

This team possesses a wide range of expertise both at the conceptual and methodological levels, which offers a solid ground for understanding the cellular and molecular mechanisms underlying food intake. The team has produced good quality research and its involvement in training and teaching is excellent. The potential to raise additional funding given the projects envisioned is present.

▪ Weaknesses and threats:

Some of the technical approaches used in the first research axis, especially those dealing with the recordings of food intake behaviours and metabolism could be more refined using automated procedures in order to strengthen reproducibility, generate more detailed dependent measures, and increase throughput. This could lead to potentially more attractive results and interpretations of the findings.

The second research axis may suffer from uncertainties regarding the identification of the targets and there is the risk that the findings turn out to be less exciting than expected. This makes it high risk but potentially high reward.

▪ Recommendations:

The team leader is dynamic and very knowledgeable of his field but efforts are still needed if the team wants to gain a higher international visibility and attractiveness. Priority should be given to develop a more integrative strategy when addressing specific questions of the project in order to generate publications in top-rated journals. This could be achieved via more intensive external collaborations with academic laboratories or with pharmaceutical companies, especially for the second axis, in order to share the workload and the expenses needed to complete the experiments. Internally, it will be important for the team leader to create the adequate synergistic atmosphere that will enable the different team members to express their full work force.



Team 14: Acoustic Communications

Name of team leader: Mr Thierry AUBIN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	6	6
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	12	12

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	4	
Theses defended	10	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	4

• Detailed assessments

Assessment of scientific quality and outputs:

The Acoustic Communications team has been very productive during the past 6 years publishing an impressive 67 original articles in peer-reviewed international journals, ranging from specialist acoustic journals to a few in higher impact journals like PNAS. However, it also has been a large team with 6 core members and 17 temporary members (post-docs and PhD-students).

In contrast to many groups that study acoustic communication in model species in a laboratory setting this team primarily has worked in the field, studying various aspects of acoustic communication of wild populations in very different habitats ranging from deep ocean to tropical rainforest. To follow this approach the team has established a number of international collaborations. In addition, it has developed a number of new and creative methods and tools, especially an open source signal processing tool that sets a new standard and is now used in many bioacoustics



groups around the world. It is characteristic of the team that in order to establish general rules of communication in vertebrates, for each question it has studied a number of species (and not just one) living in different habitats, which makes their conclusions very robust.

One series of field experiments, for instance, investigated how group identity is coded in songbird songs. Using advanced playback techniques it was documented that sequences of shared syllables code for group identity in three bird species living in very different habitats and thus may be a general rule of songbird communities. Another series of field experiments investigated the sensory basis for mother-pup recognition in a number of seal and sea lion species with different social structures causing different selection pressures on the recognition system, which explains the different use of sensory modalities.

Assessment of the team's academic reputation and appeal:

The visibility of the Acoustic Communications team is excellent and it is respected on the international scene. The Team Leader (TL) has an excellent track record and a high citation index. During the past 6 years he has co-authored 34 original articles in peer-reviewed international journals and 4 book chapters. There has been extensive national and international media coverage of his (and other team members') research. The group leader has been very active in the scientific community. For instance, he has been referee for project proposals to national and international granting bodies, he and another team member are academic editors of PLoS One, and he has served on a large number of scientific committees. Team members (31 times & team leader 20 times) have been invited as speakers at national or international meetings. They also have been invited to give 18 seminars in France and neighbouring countries and have made 92 contributions to national and international meetings. Finally, team members have co-organized one international bioacoustics conference and 15 symposia or workshops at other international conferences. During the 6-year period the team has been very successful in funding, being awarded from 15 different funding bodies reflecting the many different field studies (e.g. National Geographic Society, Emirates Center for Wildlife Propagation Foundation) and technical developments (e.g. AIRBUS Industries). The team has long-term collaborations with several scientists in North America, Brazil, Australia, and Europe in addition to collaborators in France. Its academic appeal is also reflected in a number of international PhD-students and postdocs.

Assessment of the team's interaction with the social, economic and cultural environment:

Most remarkably, team members have had 2 patents registered (for tracking whales and for scaring birds in airports) during the 6-year period, which reflects the team's focus on developing new technology.

Assessment of the team's organisation and life:

The team is very well structured with scientists at different levels of their scientific careers, and with a large number of activities efficiently organized worldwide.

Assessment of the team's involvement in training through research:

The team carries a very heavy teaching burden with 5 team members contributing a total of 578 hours per year in a large number of different university courses, mainly at the master's level. During the past 6-year period team members served on 26 PhD theses and 5 HDR committees. 9 PhD-students and 14 masters students supervised by group members successfully defended their theses during the same period and 5 students are presently working on their PhD-projects.

Assessment of the strategy and the five-year plan:

The proposed research is partly a continuation of the three themes from the past 6-year period but new and ambitious research directions will be added. The former theme of mother-pup recognition in pinnipeds, for instance, will be extended from studying one sensory modality of the recognition system at a time to mapping the integration of all three distance modalities in order to make inferences about multimodal communication in vertebrates. The feasibility, however, is difficult to judge.

As a new direction, the team plans to revisit the thoroughly studied subject of vocal learning in songbirds as the textbook statements are based mainly on standardized laboratory studies, which may have underestimated the influence of environmental impact during ontogeny. The reason for laboratory studies is that up to now it has been extremely difficult to study song learning under natural conditions. The team, however, will take advantage of



cutting-edge procedures and technology including automatic broadcasting and recording devices to study a common open-ended learner. The study is ambitious and may produce a more nuanced picture of vocal learning that may challenge present textbook notions. This study will be performed in parallel with IDEX on human language acquisition. A similar use of advanced technology including GPS transmitters and data loggers attached to birds is planned for another ambitious but feasible study, where long-term vocal interactions of a network of widely spaced birds will be studied in real time and may answer questions about communication network dynamics that have been impossible to answer so far.

Conclusion:

- **Strengths and opportunities:**

- the ability to develop cutting-edge methods and technology;
- multidisciplinary approach in project design through the use of diversified tools;
- publication in high-impact international journals;
- very good funding record;
- strong international collaboration.

- **Weaknesses and threats:**

Heavy loads of teaching and academic chores, especially on youngest team members.

- **Recommendations:**

The experts committee urges the team to continue the good work but to aim for a larger fraction of original articles in high-impact journals.

Team 15: Neurobiology of Executive Functions

Name of team leader: Ms Valérie DOYERE and Ms Nicole EL MASSIOUI

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	6	4

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	5	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

- Detailed assessments**

Assessment of scientific quality and outputs

The “Neurobiology of executive functions” team is involved in investigating the neural correlates of executive functions, although their main research topic is narrower, and mostly focuses on associative learning and retention mechanisms and on the role of emotion in regulating these processes. This research is currently conducted both on animal models (rodents) and in human beings, both in normal or pathological conditions (e.g. Parkinson and Huntington patients). Their work is organised along three lines of research:

- 1) the influence of the stimulus processing in associative learning;
- 2) the role of emotion in modulating these processes;
- 3) the neural basis of time perception.



The “Neurobiology of executive functions” group is headed by two researchers, who also happen to be the only two permanent members of that team. There are both CNRS researcher with little teaching commitment. The report mentions that one additional CNRS permanent researcher could join the team in the foreseeable future. Nowadays, four PhD students are doing a thesis under their supervision; there is no post-doc in the lab for the moment, although the team has attracted several post-docs over the last 6 years. No technician or engineer is linked to this research group.

The scientific production of the “Neurobiology of executive functions” team is very good given its small size. They published 26 papers over the last six years, and most of them were published in mid- to very high-impact Neuroscience journals, such as Journal of Neuroscience, Current Biology, Nature Neuroscience. Some of these high-impact factor papers resulted from a long-term international collaboration in the context of a “Laboratoire International associé” (LIA).

Assessment of the team's academic reputation and appeal

The attractiveness of the “Neurobiology of Executive Functions” team is very good, again with respect to the small size of this research team. Nowadays, the two PI supervise 4 PhD students, and over the last 5 years, they hosted two foreign visiting scientists and five post-docs. Post-doc supervision again led to publication in the context of international collaboration.

The international recognition of the “Neurobiology of Executive Functions” team is also very good as judged on the number on invitation to participate in international meetings as invited speaker and to give seminars. In addition, this team has managed to establish a very wide network of national and international collaborations, which has contributed to build its reputation. The two PIs of the “Neurobiology of Executive Functions” team have also contributed to the organisation of several conferences and meetings both in France and abroad.

As far as their funding is concerned, the team has attracted a large number of grants over the last six years, both from national and international funding agencies.

Assessment of the team's interaction with the social, economic and cultural environment

The two group leaders participated in several events in the media over the last few years and gave several public lectures on their research topic.

Assessment of the team's organisation and life

The team is a small group headed by the only two permanent members of the team.

Assessment of the team's involvement in training through research

As already mentioned, five PhD students are, or have been, trained in this lab over the last 6 years and the team has also attracted a substantial number of post-docs over that period of time.

Assessment of the strategy and the five-year plan

The proposals for the near future follow up on earlier works of this team on the neural correlates of associative learning and on the modulation, by the amygdala, of neural circuits involved in associative learning. In particular, they plan to pursue the following three lines of research:

- 1) neural mechanisms and structure underlying the temporal processing of stimuli in associative learning, focusing especially on the interactions between the amygdala and cortico-striatal loop;
- 2) the role of the striato-cerebellar circuit in associative instrumental learning, which will be investigated by disconnecting the striatum and frontal cortex from the cerebellum by means of thalamic lesions;
- 3) the role of the amygdala in regulating executive functions.

The originality of the approach relies on running in parallel animal and human models. This is reinforced by the use of a transgenic animal model in which it is possible to inactivate specific genes in particular brain structures.



Conclusion

▪ Strengths and opportunities:

- the research topic addressed by the team is relevant and highly topical;
- very good publication record, some of which being issued in high-impact Neuroscience journals;
- high attractiveness in terms of PhD students, post-docs and visiting scientists;
- extensive network of national and international collaborations;
- the variety of approaches followed by this team is quite wide (electrophysiology, pharmacology, behaviour in rats; Parkinson's disease and Huntington's disease patients, patients with cerebellar lesions);
- large number of funding sources.

▪ Weaknesses and threats:

- the small size of the team might be detrimental for its future development;
- some of the researches performed by this team strongly rely on national and international collaborations, and this might be risky if they should be discontinued;
- the large variety of approaches followed by this team might be seen as a disadvantage too, given the rather modest size of the group.

▪ Recommendations:

- select a label for the team that is more appropriate and more focused on the actual research topics;
- secure young scientist's recruitment, or merge with others team at Neuro-PSI, since the small size of the current team might be detrimental for its future development and might jeopardize its survival;
- ensure the autonomy of the team in terms of high-level publications;
- identify potential collaborations inside Neuro-PSI;
- ensure the autonomy of the team in terms of research since relying too strongly on other national and international teams may be perilous if these collaborations should be discontinued.

Team 16: Neural Code and Auditory Perception

Name of team leader: Mr Jean-Marc EDELINE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	2
N2: Permanent EPST or EPIC researchers and similar positions	2	4
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	3
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	6	10

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	2	5

- Detailed assessments**

Assessment of scientific quality and outputs:

During the past 6 years the Neural Code and Auditory Perception team has been in a transition phase with only 2 permanent members throughout the period, but with 2 members retiring, 2 new members being included, and 3 new members waiting to join by 2015. Activities and publications of retired members have not been available for evaluation.

Nevertheless, the team has been rather productive during the 6 years publishing in peer-reviewed international journals 26 original articles, 20 of which deal with different aspects of sound information processing in the auditory cortex of mammalian model animals, while 6 articles focus on aspects of bird song and its neural representation and processing. The articles are generally of high quality and have been published in mid- to high-impact neuroscience journals including J Neuroscience, J Neurophysiology, Neuroscience, Brain Research, and PLoS One. Together the



papers already have been cited more than 270 times (bird song papers alone about 40 times), which is very good considering the short period of time.

The auditory cortex theme is divided into three related subthemes. In one major theme the team members have investigated the role of intracortical inhibition on coding of natural sound stimuli and have contributed to reject earlier hypotheses and to suggest new roles of neuromodulators, the latter of which was summarized in a review paper in *Frontiers in Neuroscience* by the team leader. The other two subthemes have more applied appeal with one suggesting that age should be taken into consideration when predicting the severity of acoustic trauma, while the other investigated the cumulative effect of exposure to noise over extended periods of time.

In the songbird theme another subset of team members have investigated the representation of the bird's own song in the HVC nucleus. They showed that the previously demonstrated specificity for the bird's own song involved multiple neurones and depended on the proper sequence of individual syllables. This is compatible with distributed population coding.

Assessment of the team's academic reputation and appeal:

The team leader is visible in his field and has a fine scientific track record with a high citation index. Over the past 6 years he has contributed with 13 original papers in peer-reviewed international journals (1 as first and 6 as senior author), including *Journal of Neuroscience* and *PLoS One*. In addition, he has produced a review in a peer-reviewed open access journal and one book chapter (both as single author) and has been invited to 4 international workshops or conferences in USA, Italy and Germany and to 5 national meetings. He serves as a review editor of an open access journal and has served in 3 ad hoc committees. The team has received funding from seven national (and one international) granting bodies. During the presentation it was stated that the review in *Nature Reviews Neuroscience* was under revision, which constitutes a clear sign of growing awareness of the group's output.

Assessment of the team's interaction with the social, economic and cultural environment:

During the 6-year period the team has received no patents but established a strong collaboration and contract with the private company Neurelec. The team is involved in vulgarization activity.

Assessment of the team's organisation and life:

The team is organized in two-sub-groups led by the 2 permanent members and will soon join by 3 new members with complementary expertise.

Assessment of the team's involvement in training through research:

During the 6-year period the team has completed one PhD-thesis, one PhD-thesis will be defended in the near future, while a third PhD-student is still working on his project.

Assessment of the strategy and the five-year plan:

The proposed 5-year project is partly a logical continuation of existing research but also introduces new directions while maintaining the segregation in a mammalian auditory cortex theme and a birdsong theme.

The former theme is now laudably focused on applied aspects of cortical neuron responses to cochlear implant stimuli and to noise exposure of differently aged subjects, respectively. Two subprojects will test first how auditory neurons respond to the reduced sound signal information conveyed by cochlear implants. Secondly, in a daring project the team aims at recording cortical activation through chronic cochlear implants in awake behaving guinea pigs. Collaboration with a private research company and specialized manpower ensures the feasibility of the project, which may yield much important real-life information of clinical relevance. A third subproject will thoroughly test at the synaptic level how age influences the cortical resistance to daily noise exposure at legal intensities. This requires introduction of the powerful method of calcium imaging but again this seems feasible. Altogether the proposed mammalian auditory cortex themes are daring, focused, very interesting, and have important implications.

The project for the birdsong theme on neural representation of song sequences was not well developed in the report. A series of experiments using open ended and closed ended songbird learners will investigate how song sequences are represented in two different brain nuclei under different conditions, which may produce new insights



into their role in song control. As part of a local IDEX project, the sensitivity of birds to irregularities of songs will be tested, in analogy to human babies.

Conclusion:

- **Strengths and opportunities:**

The experts committee felt that the quality of the group's research was leading to deserved increasing recognition in the field.

- **Recommendations:**

The team should aim to publish their work in more visible journals. The integration of the new members into the group's research activities should be monitored attentively.

Team 17: Neurobiology of Decision Making

Name of team leader: Ms Sylvie GRANON

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions	2	3
N3: Other permanent staff (without research duties)		1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	4	6

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	3

• Detailed assessments

Assessment of scientific quality and outputs

The “Neurobiology of decision-making” team is interested in studying how motivations and emotions may influence and modify decision-making processes. This highly relevant and topical question is addressed in a mouse model and the main questions the team is currently studying are as follows:

- 1) the neurobiological and neurochemical bases of choices, focussing especially on neural correlates of inter-individual differences;
- 2) how environmental factors, such as the stress, may influence the brain circuits underlying decision-making focusing particularly on the prefrontal cortex;
- 3) the contribution of the cholinergic system to these functions.



The “Neurobiology of decision-making” group consists of four permanent scientists, including two CR1 at the CNRS and two lecturers at the Université Paris 11, having important teaching duties. The “Neurobiology of decision-making” team is rather novel since it was created in 2008. This team is composed of 3 permanent scientists (1 professor, 1 assistant professor and 1 CNRS researcher); according to the report, two more researchers should join the team in 2015. No technician or engineer is linked to this research group. Nowadays, only one PhD student is doing a thesis under the supervision of that team.

The scientific output of the “Neurobiology of decision-making” team is rather modest, although, as already said, they are currently working on a highly topical and relevant issue. Their more remarkable contribution concerns the role of beta2-nAChR in the prefrontal cortex in the decision making processes, which has led to two papers, one in the FASEB Journal, and the other one in Cerebral Cortex. This research is in direct line with the previous achievement of the group leader when she was a fellow in a renowned neuroscience laboratory working on the nicotinic receptor-based signalling at the Pasteur Institute. Overall, this group has published only a modest number of papers (30) over the last five years (2008-2013), and most of them were issued in mid-impact neuroscience journals. Though, it is worth noting that they have participated in the development of original behavioural analysis software to quantify mice social interactions; this study has been published in Nature Methods in 2012. Finally, over the last two years, the publication rate of this group was very low (5 papers). To be fair, it needs to be said that two permanent members of this team have very heavy teaching commitments and that the establishment of this team is rather recent.

Assessment of the team's academic reputation and appeal

The attractiveness of the “Neurobiology of decision-making” group appears rather modest too. Nowadays, there is only one PhD student in this team, and no post-doc. The report mentions they had 2 PhD students and 2 post-doc over the last 6 years.

The international recognition of the “Neurobiology of decision-making” team is good as judged on the number on invitation to participate in international meetings as invited speakers. Nonetheless, as stated in the report, most of their current collaborations are established with French labs.

As far as the team's funding is concerned, the situation is rather critical. All their recent funding resources arose from French agencies and, more ominously, the report states no grant beyond 2013, which may jeopardize the team's future and impede its development.

Assessment of the team's interaction with the social, economic and cultural environment

The group leader participated in a few events in the media over the last few years and gave one public lecture on her research subject.

Assessment of the team's organisation and life

The team is a recently established small group that will be soon joined by two additional CNRS researchers. This will need deep re-organization and focusing.

Assessment of the team's involvement in training through research

As already mentioned, only 3 PhD students are, or have been, trained in this lab over the last 6 years.

Assessment of the strategy and the five-year plan

Their proposals for the near future follow up on earlier works on neurochemical and cellular mechanisms of decision-making. The new proposal is constituted of three different axes. The first one is in line with the questions currently addressed by the group leader and colleagues on the circuit and neurochemical characterization of the prefrontal cortex in decision-making. The questions are clearly stated but the project is deeply dependent on two technical approaches that are not currently available in the team or institute, namely optogenetics and in vivo recordings, to be done in collaboration with a group in The Netherlands. There is a transfer of technology between the Netherlands group (Mr Francisco BATTAGLIA) and the team, since electrophysiological experiments are performed in Orsay by a co-directed PhD. The two other lines of research appear rather puzzling and not really in line with the main topics of the team; they seem to depend on the arrival of two additional permanent researchers in 2015. These



two lines do not appear as original and innovative and deep reformulation of projects and hence restructuration of the group is mandatory.

Conclusion

▪ Strengths and opportunities:

- highly relevant and topical research theme;
- interesting prospects of developing new experimental approaches;
- addition of two extra permanent members in the near future;
- perspectives of collaborations with other teams at Neuro-PSI.

▪ Weaknesses and threats:

- rather modest scientific output;
- low attractiveness in terms of PhD students and post-doc;
- highly unfocused scientific project for the next five-year period.

▪ Recommendations:

- secure funding for the next few years;
- the PI should focus her energy on strengthening her team; to become the deputy - director of the new “Cognition & Behavior” department for the next 5 years might not be beneficial for the team;
- the team should develop a more coherent scientific project for the near future;
- secure the recruitment of some PhD students and post-doc.

Team 18: Cellular and Molecular Mechanisms of Plasticity and Memory

Name of team leader: Mr Serge LAROCHE and Mr Cyrille VAILLEND

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions	3	4
N3: Other permanent staff (without research duties)		2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	8	8
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	13	16

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	6	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	4	5

• Detailed assessments

Assessment of scientific quality and outputs

This team, which is presently part of the CNPS in Orsay, is composed of 5 permanent researchers including the group leader, 1 post-doctoral fellow and 5 PhD students. Its central objective is to explore the neural bases of learning and memory functions and to unravel the cellular and molecular mechanisms underlying brain plasticity, memory processes and memory dysfunctions associated with Alzheimer's disease and certain forms of intellectual deficiencies, the ultimate goal being to identify potential therapeutic strategies at the genetic, pharmacological or behavioural levels. To tackle this extraordinary vast research agenda, the team has identified four different lines of research in rodents: namely the identification of cell signalling pathways with a particular emphasis on the role of the transcription factor zif268 in memory formation; the functional contribution of adult-born hippocampal neurons to memory processing; the identification of mechanisms underlying cognitive alterations in animal models of inherited



intellectual disabilities (Coffin-Lowry syndromes and Duchene muscular dystrophy); and the use of models of known risk factors for Alzheimer's disease to better understand the mechanisms that trigger it.

The demonstration that the activity-dependent gene *zif268* controls the selection, maturation and functional integration of new-born neurons in the adult learning brain stands among the major and most influential achievement of the team within the last 5 years. A collaborative work examining the long-term stability of hippocampal place cells in mutant mice has also identified the crucial contribution of *zif268* in the formation of stable neuronal representations of space. Overall, between 2008 and 2013, the track record of the team is of very good quality with 37 articles, including original research papers in excellent (2 PNAS including one in collaboration) or competitive specialized journals in the field (such as *Human Molecular Genetics*; *Brain Structure and Function*, *Cerebral Cortex*, *Neurobiology of Aging*), 5 topic reviews and 2 book chapters. However, the scientific production is rather heterogeneous with excellent publications for the first two lines of research listed above but a more modest output for the two remaining ones.

Assessment of the team's academic reputation and appeal

The high number and diversity of national/international collaborations and supervised PhDs reflect the excellent impact and attractiveness of the team. The team leader is creative and internationally recognized and all team members display an excellent record of invited conferences/seminars (total of 33) and communications in national and international conferences (total of 47). From 2008 to 2013, its members have been highly efficient in raising research funds (several ANR and international EU grants (FP7) as well as grants from different foundations supporting research), and attracting PhD (3) and post-doctoral students (6), some of which coming from abroad. One post-doc, 5 PhD and 2 Master students will be actively involved in the next team structure. The team has put in place a large number of effective national and international collaborations. Particularly noteworthy is its presence in EU consortiums composed of other renowned researchers in the field and it can be anticipated that such brainstorming will contribute to generating major advances in the field of Cognitive Neuroscience. The team leader was also involved in the organization of several conferences and meetings.

Assessment of the team's interaction with the social, economic and cultural environment

The team leader was particularly active in publishing in popular science magazines and in diffusing scientific knowledge to the medias and general public. Notably, he acted as a scientific adviser for a scientific exhibition on memory and participated to several debates on the neural bases of memory.

Assessment of the team's organisation and life

Regular meetings are organized within the team to monitor progress and coordinate the scientific research of PhD and post-doctoral students. Management and life of the team seem to be adequate to enable a smooth functioning.

Assessment of the team's involvement in training through research

Four PhD thesis were defended in the team throughout the 2008-2013 period and 4 others are underway. Two team members obtained their "Habilitation à Diriger des Recherches (HDR)". Team members also participated in 24 PhD and HDR committees and are actively involved in teaching courses in several Licence and Master modules. Altogether, the involvement of the team in training and teaching is quite impressive.

Assessment of the strategy and the five-year plan

In direct line with past achievements, the project focuses on brain mechanisms of normal and impaired (intellectual deficiencies and pathological aging) memory in rodents and addresses pertinent societal questions. It is scientifically coherent and original, and will be achieved using a wide range of multi-scale approaches (some new state-of-the-art) combining behavioural analyzes of cognitive functions in rodents, electrophysiology in vivo, optogenetic control of neuronal activity, cellular and molecular biochemistry as well as genetic investigations. Several of the many proposed experiments benefit from solid hypotheses and preliminary findings. There is no doubt on the short-term feasibility of some of the scientific projects in terms of researchers' expertise and leaderships, research facilities, collaborations and funding.



However, the overall five-year plan appears quite heterogeneous with a strong and exciting first axis that include new important conceptual developments and two others that exhibit a laudable willingness of translational goals but that are not very competitive with methods perhaps too conventional to face the international competition. The development of new molecular tools to rescue cognitive deficits associated with intellectual deficiencies is at high risk (but potentially high gain) because of their difficulties to be properly modelled in animals but could generate cutting-edge results. As usual in the field of Cognitive Neuroscience, some of the proposed experiments are very low throughput and will require additional funding to ensure completion in the best conditions.

Conclusion

▪ Strengths and opportunities:

This is a creative team, which has produced high quality research both internally and via its collaborative network and which is expected to continue to produce major advances in the field of learning and memory. The team leader is internationally recognized in this field of research and is also actively involved in the management of research and teaching duties. Some findings have been influential and advanced methodological tools have been used or are currently under development to achieve the next five-year plan, which attests of the excellent potential and dynamism of the team.

▪ Weaknesses and threats:

The research projects, while ambitious, appear quite diverse and involve many different aspects and experimental models. Maintaining the same efficiency within the different lines of research envisioned on the one hand, and resolving inevitable along the road pitfalls on the other hand, will be a tremendous task. The team leader can count on his excellent integrative vision of his project and field, and as a previous research unit director, he developed solid managerial qualities and skills. However, he will need to generate sufficient synergistic interactions between team members to achieve full success.

The team leader specified that he will retire in 2018. To anticipate this departure, one of the current team members was presented as the next team leader. To ensure a smooth transition towards the completion of the future projects, he will start acting as a co-leader. It will be one of his important duty to secure new funding resources in due course, but also to gain international recognition by publishing more papers in a senior position in top-rated journals.

▪ Recommendations:

The future research agenda has a broad scope with many lines of research and there is the danger that some of these lines will not benefit from sufficient conceptual and methodological advances. It will be important to find a good balance between the different proposed experiments. To ease this process, the team should consider prioritizing the topics in which it has been the most competitive so far, and if not abandoning, at least postponing some of them. Such a refocusing strategy could enable the team to reach the level of excellence it deserves by getting its findings published in a higher number of outstanding journals.

Team 19: Sensory Neuro-Ethology

Name of team leader: Mr Nicolas MATHEVON

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	6	7
N2: Permanent EPST or EPIC researchers and similar positions		
N3: Other permanent staff (without research duties)	1,5	1,5
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	3
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	10,5	11,5

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	4	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit	5	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	3	3

- Detailed assessments**

Assessment of scientific quality and outputs

The team Sensory Neuro-etholgy is studying acoustic communication in a wide variety of vertebrate species with a strong focus on communication in a complex noisy environment. The originality of the team relies on its phylogenetic approach associated with both field and laboratory studies. Most experiments are behavioural studies coupled with fine acoustic techniques but some studies also investigate the neural basis of behaviour. All tenured members are university employees as Associate (4) and Full Professors (2) having important teaching duties and academic responsibilities. They have received support from 3 technicians, 2 post-docs, also with teaching duties as “Attaché Temporaire d’Enseignement et de Recherche” (ATER), and 4 PhDs. The two professors are members of the “Institut Universitaire de France” (IUF) a selective status providing some research funds and a reduced teaching load. The team is housed in the Université Jean Monnet de Saint-Etienne, about 500 km south of Paris.



The quality of the scientific production of the team is excellent. Over the last 6 years, from 2008 to 2013, they published 46 papers in international journals, which correspond to an average of 7 to 8 papers per year. Most importantly, several papers appeared in high-ranked journals such as Nature Communication, Current Biology, Animal Cognition, and Journal of Acoustic Society of America (JASA). The team members played a major role in these studies. In general, it is of note that 75 % of the papers were exclusively produced by team members while 25 % resulted from internal and external collaborations. The team leader played a major role (first or last author) in about 50 % of the production reflecting his important impact on the team production, while the other half was co-authored by other team members. The team presents its work in the context of a phylogenetic comparative approach with data collected in very different species (e.g. fishes, birds, alligators, non-human primates, and human babies) but the different projects do not seem to be integrated in a general model. In conclusion, with a work force of less than 3 full-time FTE, the team still manages to produce interdisciplinary well-recognized research in their fields of interest.

Assessment of the team's academic reputation and appeal

The team leader has a fine track record and he as well as his team is becoming very visible in the fields of bioacoustics and neuroethology. During the past 6-year period he was first author on 2 original articles and co-authored another 33 original articles and a review paper, mainly as senior author. Many of these articles received extensive media coverage at publication. The group leader as well as the other full professor was among the 2 % of French university professors distinguished by membership of IUF. In addition, the other full professor was awarded the Young Researcher Prize 2011 and a PhD-student was awarded a Fulbright grant to study at UC Berkeley.

To perform the very diverse studies the team had 8 international and 6 national collaborators. The team co-organized the XXIII International BioAcoustic Congress 2011 and a Conference of the French Society for the Study of Animal Behaviour 2012. Team members were invited speakers at 4 international and 5 national conferences and gave 2 invited international and 3 national seminars. In addition, team members gave 40 oral presentations at national and international meetings. Finally, the team was very successful in funding, receiving grants from 10 different granting bodies during the past 6-year period. Through the past 6-year period team has consequently established itself on the international scene of bioacoustics.

Assessment of the team's interaction with the social, economic and cultural environment

Team members are very active in dissemination of their knowledge. They regularly give conferences opened to a broad audience and one member of the team is in charge of the diffusion of the scientific knowledge at the Université Jean Monnet de Saint-Etienne.

Assessment of the team's organisation and life

The team is a large group involved in research worldwide. Management of the team seems to be adequate to enable good organization of the projects.

Assessment of the team's involvement in training through research

Since all tenured members are Associate or Full Professors they are heavily involved in teaching and academics responsibilities. They are more specifically involved in the Master "Ecologie and Ethologie" at Université Jean Monnet de Saint Etienne. Six PhDs have been defended in the team during the 2008-2013 period and four are ongoing. Two members belong to the "Conseil National des Universités" (CNU), which means regular meetings in Paris important for the career evaluation of the French Associate and Full-Professors. In addition, one member is the Head of the "Biology Department" of Université Jean Monnet de Saint-Etienne.

Assessment of the strategy and the five-year plan

The proposed research of the Sensory Neuro-Ethology team is a continuation of the three existing multi-directional projects but also contains new goals within the general frame of acoustic communication studied in laboratory and field. The multi-directional projects are described in very general terms with no mention of methods, technology, logistics, or pilot-studies, which makes it difficult to judge the project's feasibility, especially those that will take place in the field in Africa and South America. However, the team successfully performed similar daring field-studies in the past. Study of acoustic communication networks in a variety of social mammals will continue, as



will that of acoustic adaptation to environments with dense vegetation. Study of juvenile crocodiles will be expanded to elucidate how olfactory cues modulate responses to conspecific calls.

A new goal concerns the adaptive value of the cries of human babies and is a continuation of a current project. The study aims at elucidating the kind of information encoded in the cries, the possible modulation of cries by the social environment, the cross-cultural reaction of caregivers, and brain imaging of caregivers responding to baby cries. The subject has received little attention in the literature and may have great potential. However, it will probably require the establishment of substantial collaboration not only with biologists but also anthropologists, psychologists, linguists, and neurologists - besides brain imaging facilities and the willing subjects. Another new goal is to elucidate various aspects of pair-bonding through acoustic communication of five different songbird species both at the physiological, the behavioural, and the population levels involving several collaborators. This project does not seem to involve new methods and seems to be feasible. A highly exciting new goal aims at getting to a new understanding of acoustic communication in wild living bonobos (in West Africa), with special emphasis on possible coding of individual identity and social position as well as on describing 'conversational rules' in a species living in fission-fusion groups with frequent change of group composition. The project involves complicated logistics and collaboration is foreseen but the project's feasibility is not possible to judge.

So, the scientific strategy of the Sensory Neuro-Ethology team is sound and holds promise of exciting results over the next 5-year period. However, the experts committee questions the fact that this team based at the Université Saint-Etienne remains a member of the Neuro-PSI project. Indeed, the whole philosophy of the Neuro-PSI project is to house all teams in the same building on the Saclay plateau in order to promote scientific interactions. The logic of having in the Neuro-PSI project a team based so far away seems to contradict the basic philosophy of the project. In addition, the team Sensory Neuro-Ethology has proven its ability to conduct high-quality research based on its own local resources (manpower, animal housing and grants), though in close collaboration with other teams of the Neuro-PSI project.

Conclusion

▪ Strengths and opportunities:

- publications in high-ranked international journals;
- multidisciplinary approach in a well-established national and international network;
- two professors are members of the Institut Universitaire de France (IUF);
- success in their grant applications.

▪ Weaknesses and threats:

- no full-time researchers;
- heavy teaching and academic responsibilities;
- geographical situation, 500 km from the laboratory.

▪ Recommendations:

Keep going in their successful original approaches



5 • Conduct of the visit

Visit dates:

Start: Monday, February 17th 2014 at 9.00 am

End: Wednesday, February 19th 2014 at 5.00 pm

Visit sites: Gif-sur-Yvette & Orsay

Institution: INAF

Address:

Conduct and programme of visit:

The 3-day visit took place from February 17th to 19th 2014. The overall organization of the visit was very satisfactory and the director and his collaborators should be complimented for their involvement. The time reserved for interviewing the director and department directors was appropriate and, thanks to the availability of the proposed director Mr Philippe VERNIER throughout the rest of the visit, all important aspects of the research unit's present and future organization were discussed in depth. The written information provided prior to the visit was adequate, and each department and team's oral presentation constituted a very useful complement. The discussions with the director alone and together with the three department directors, as well as the discussion with the funding bodies occurred in front of the entire experts committee. For the discussions involving the technical staff, the PhD students/postdocs and the staff Researchers, the experts committee splits into three separate groups. The unit presentation by the director and the three department's presentations by their corresponding leaders were open to all unit members and all team members did attend the presentation of their leader. Each team leader was given time of presentation followed by discussion with the entire experts committee in presence of all team members, who were all free to answer both scientific and organizational questions. The final report presented here is based on the reports that were sent in and was approved by all the experts of the experts committee.

February 17th (Orsay)

08.30-08.45 am	Arrival on-site (Orsay)
08.45-09.15 am	Experts committee discussion (closed door)
09.15-09.20 am	Presentation of AERES evaluation by the AERES Scientific Delegate (DS), Mr Laurent GROG / Presentation of the experts committee (President: Mr Serge SCHIFFMANN)
09.20-09.50 am	Unit presentation by Mr Philippe VERNIER

Department Cog-Behaviour

09.50-10.10 am	Department presentation (Mr Jean-Marc EDELINE)
10.10-10.40 am	Team 1 Mr Thierry AUBIN (questions)
10.40-11.10 am	Team 2 Mr Nicolas MATHEVON
11.30-12.00 pm	Team 3 Mr Jean-Marc EDELINE / Ms Catherine DEL NEGRO
12.00-12.30 pm	Team 4 Mr Serge LAROCHE / Mr Cyrille VAILLEND
12.30-01.30 pm	Lunch (on site) with lab members (d ^{pmt} Cog. Behav.)
01.30-02.00 pm	Team 5 Ms Sylvie GRANON
02.00-02.30 pm	Team 6 Ms Valérie DOYERE / Ms Nicole EL MASSIOUI



02.30-03.30 pm Parallel meetings: all students/postdocs, ITAs, permanent researchers (without team leaders and unit director)

04.15-06.30 pm Closed door meeting

February 18th (Gif-sur-Yvette)

Department Mol-Circuit

09.00-09.20 am Department presentation (Mr François ROUYER)

09.20-09.50 am Team 7 Mr Ronald MELKI (questions)

09.50-10.20 am Team 8 Mr Mohammed TAOUIS

10.20-10.50 am Team 9 Mr Martial RUAT

11.15-11.45 am Team 10 Mr Hervé DANIEL

11.45-12.10 pm Team 11 Mr Gilles FORTIN

12.10-01.00 pm Lunch (on site) with lab members (d^{pmt} Mol. Circ.)

01.00-01.30 pm Team 12 Mr Jean-René MARTIN

01.30-02.00 pm Team 13 Mr François ROUYER

02.30-04.00 pm Meeting with Funding Bodies (CNRS, Université Paris-Sud)

04.15-05.00 pm Interview with director(s)

05.00-06.45 pm Closed door meeting

February 19th (Gif-sur-Yvette)

Department Dev-Evol

08.55-09.15 am Department presentation (Ms Sylvie RÉTAUX)

09.15-09.45 am Team 14 Ms Laure BALLY-CUIF (questions)

09.45-10.15 am Team 15 Ms Sophie CREUZET

10.15-10.45 am Team 16 Mr Jean-Stéphane JOLY

11.00-11.30 am Team 17 Ms Muriel PERRON

11.30-12.00 pm Team 18 Ms Sylvie RÉTAUX

12.00-12.30 pm Team 19 Mr Philippe VERNIER

12.30-01.15 pm Lunch (on site) with lab members (d^{pmt} Dev. Evo.)

01.15-05.00 pm Closed door meeting, including lunch for expert committee members only

05.00 pm End of visit

Specific points to be mentioned:

The meeting with the head of the doctoral school didn't take place since the head of the doctoral school could not be present.



6 • Supervising bodies general comments

Le Président de l'Université Paris-Sud

à

Monsieur Pierre GLAUDES
Directeur de la section des unités de recherche
AERES
20, rue Vivienne
75002 Paris

Orsay, le 5 mai 2014

N/Réf. : 123/14/JB/LM/AL

Objet : Rapport d'évaluation d'unité de recherche
N° S2PUR150009373

Monsieur le Directeur,

Vous m'avez transmis le 10 avril dernier, le rapport d'évaluation de l'unité de recherche «- Institut des Neurosciences Paris Saclay» - INPS – N° S2PUR150009373, et je vous en remercie.

L'université se réjouit de l'appréciation portée par le Comité sur cette unité et prend bonne note de ses suggestions. Elle suivra avec beaucoup d'attention la fusion des deux unités qui la constituent et, lors de son installation dans le nouveau bâtiment de Neurosciences, la fusion avec l'unité UNIC.

Vous trouverez en annexe les éléments de réponse de Monsieur Philippe VERNIER, Directeur de l'unité de recherche.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de ma sincère considération.



Jacques BITTOUN
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Remarks and answers to the AERES report on Neuroscience Paris-Saclay Institute (Neuro-PSI)

Project Director : Philippe Vernier

Collectively, the board of directors and myself would like to express their gratitude to the AERES committee and its chairman for this detailed and very precise report. We thank the Committee for its positive and favourable comments on the creation of the new Research Unit. This is a clear recognition that the direction we have taken is the right one and this will certainly help us to gain the necessary recognition and support from our funding bodies and institutions.

The report represents a tremendous amount of work. It gives us an in-depth, sharp and very insightful analysis of the overall project, of its objectives, its organization with a special care taken toward the technical staff. In addition, it provides a fair assessment of the project of each of the research groups.

We also appreciate the precision and clarity of the suggestions made by the Committee, which will contribute to, and help us to meet the challenges of the Neuro-PSI project which reinforces the enthusiasm of all personnel of the future Institute to engage into this challenging and collective project. We generally acknowledge the constructive remarks and proposals made in the report by the Committee. They provide an accurate and realistic agenda for the Directory Board of Neuro-PSI. We would like to make the following comments:

- We are fully aware of the heterogeneity in the quality of part of the research projects in all Departments. Following suggestions from our Scientific Advisory Board, we had already reorganized the teams to strengthen the overall Unit and Departments. We will pay attention to the integration of new members in groups, with the aim of reinforcing the scientific coherence of the research projects. This issue will continue to be worked out with the help of our Scientific Advisory Board and funding Institutions.

- Transdisciplinarity and interfaces with mathematics, physics and engineering are certainly more present in many of the Neuro-PSI teams that it may have appeared in the written documents and oral presentations, which have all been brief.

- Developing neuro-ethology is one important aim for Neuro-PSI, with the objective of increasing interactions within and between Departments. Specifically, the three teams working on acoustic communication and auditory perception (Aubin, Edeline and Mathevon) constitute a continuum between neuro-ethology, signal processing, cognitive and computational neuroscience, and form a unique combination of knowledge and skills. Mathevon's team thus represents a major piece in this framework, with which exist strong interactions with other teams (co-funded projects, co-advised PhD thesis, co-authorships in international journals), and the geographical distance between the groups has never been a difficulty.

- As suggested by the Committee, the recruitment of young and talented new groups will be the priority, as soon as the new Building will be close enough to be ready,

and this will be done with the help of our Scientific Advisory Board. This will be accompanied by a clear policy of space allocation to new teams within the new Building.

- Regarding the anxiety of our technical and administrative staff at the time of the visit of the Committee, the situation has significantly improved, since we have pursued providing clear and direct information to our personnel. A General Assembly of NeuroPSI has been organized with the direction of CNRS and of the Faculty of Science of the University Paris-South, and an open process of Human Resources allocation has been set up, simultaneously with two other large-scale projects in Biology within the Paris-Saclay area.

-Finally, all the advices and suggestions made by the Committee for the students and post-docs -especially foreigners-, for a better integration of professors and assistant-professors with heavy teaching duties, for scientific animation, solidarity funds, the somewhat rigid organization of the Department...etc, will be seriously taken into account by the Directory Board of Neuro-PSI. As a matter of fact, the structure of the proposed Unit is really new, and the challenge is now to make the new ensemble much stronger and efficient.



Philippe Vernier