IBENS - Institut de biologie de l'école Normale Supérieure

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Institut de Biologie de l'Ecole Normale Supérieure

IBENS

Under the supervision of the following institutions and research bodies:

Ecole Normale Supérieure

Institut national de la santé et de la recherche médicale

Centre National de la Recherche Scientifique

January 2013

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

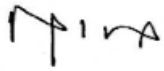
Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head



Pierre Glaudes

The president of AERES "signs[...], the evaluation reports, [...]countersigned for each evaluation department by the relevant head of department (Article 9, paragraph 3, of french decree n°2006-1334 dated 3 november 2006, revised).

Grading

Once the visits for the 2012-2013 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).
This score (A+, A, B, C) concerned each of the six criteria defined by the AERES.
NN (not-scored) attached to a criteria indicate that this one was not applicable to the particular case of this research unit or this team.

Criterion 1 - C1 : Scientific outputs and quality ;
Criterion 2 - C2 : Academic reputation and appeal ;
Criterion 3 - C3 : Interactions with the social, economic and cultural environment ;
Criterion 4 - C4 : Organisation and life of the institution (or of the team) ;
Criterion 5 - C5 : Involvement in training through research ;
Criterion 6 - C6 : Strategy and five-year plan.

With respect to this score, the research unit concerned by this report (and, when necessary, its in-house teams) received the following grades:

- Grading table of the unit: Institut de Biologie de l'Ecole Normale Supérieure - IBENS

C1	C2	C3	C4	C5	C6
A+	A+	A+	A+	A+	A+

- Grading table of the team: Cell Biology of Transcription

C1	C2	C3	C4	C5	C6
A	A	NN	NN	A+	A

- Grading table of the team: Functional Imaging of Transcription

C1	C2	C3	C4	C5	C6
A	A+	NN	NN	A	A

- Grading table of the team: Eukaryotic Chromosome Replication

C1	C2	C3	C4	C5	C6
A	A	NN	NN	A	A

- Grading table of the team: Expression of Eukaryotic messenger RNAs

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A+	A+

- Grading table of the team: Molecular Mechanisms and Epigenetic Regulation of Genome Rearrangements in Ciliates

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A+	A+

- Grading table of the team: Genome Organisation and Dynamics

C1	C2	C3	C4	C5	C6
A	A+	NN	NN	A+	A

- Grading table of the team: Computational Systems Biology

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A+	A

- Grading table of the team: Genomics Responses to Environmental Signals in Photosynthetic Organisms

C1	C2	C3	C4	C5	C6
A+	A+	A+	NN	A+	A+

- Grading table of the team: Arabidopsis Epigenetics and Epigenomics

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A+	A+

- Grading table of the team: Small RNA-directed Control of the Arabidopsis Innate Immune Response

C1	C2	C3	C4	C5	C6
NN	A+	NN	NN	A	A+

- Grading table of the team: Evolution of Caenorhabditis

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A+	A+

- Grading table of the team: Development and Evolution of Neural Circuits

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A	A+

- Grading table of the team: Development of the Nervous System

C1	C2	C3	C4	C5	C6
A	A+	NN	NN	A	A+

- Grading table of the team: Wiring the Forebrain During Embryonic Development

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A+	A+

- Grading table of the team: Mitosis and Vertebrate Neurogenesis

C1	C2	C3	C4	C5	C6
A	A	NN	NN	A	A

- Grading table of the team: From Development to Behaviour

C1	C2	C3	C4	C5	C6
A	A	NN	NN	A	A

- Grading table of the team: Cilia Biology and Neurogenesis

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A	A+

- Grading table of the team: Cerebellum Group

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A+	A+

- Grading table of the team: Coding Sensory Information in the Rat Cortex

C1	C2	C3	C4	C5	C6
A	A	A+	NN	A+	A

- Grading table of the team: Inhibitory Transmission

C1	C2	C3	C4	C5	C6
A+	A+	A+	NN	A+	A

- Grading table of the team: Computational Biology and Applied Mathematics

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	A+	A

- Grading table of the team: Structure and Function of Glutamate Receptors

C1	C2	C3	C4	C5	C6
A+	A+	A+	NN	A	A+

- Grading table of the team: Zebrafish Neuroethology

C1	C2	C3	C4	C5	C6
NN	A+	NN	NN	A	A

- Grading table of the team: Cellular Biology of the Synapse

C1	C2	C3	C4	C5	C6
A+	A+	A+	NN	A+	A+

Evaluation report

Unit name:	Institut de Biologie de l'Ecole Normale Supérieure
Unit acronym:	IBENS
Label requested:	
Present no.:	
Name of Director (2012-2013):	Mr. Antoine TRILLER
Name of Project Leader (2014-2018):	Mr. Antoine TRILLER

Expert committee members

Chair:

Chair: Mr. Hinrich GRONEMEYER (Institut de Génétique et de Biologie Moléculaire et Cellulaire, Strasbourg)

Co-chair: Ms. Colette DEHAY (Stem Cell and Brain Research Institute, Lyon)

Experts:

Mr. Eva S. ANTON (University of North Carolina School of Medicine, Chapel Hill, USA)

Mr. Richard M. AMASINO (University of Wisconsin, Madison, USA)

Mr. Rafal CIOSK (Friedrich Miescher Institute, Basel, Switzerland)

Mr. Laurent FAGNI (Institute of Functional Genomics, Montpellier)

Mr. Mark FARRANT (University College London, London, United Kingdom)

Mr. Vincent GELI (Center of Research in Cancerology of Marseille, Marseille)

Mr. Leon LAGNADO (MRC Laboratory of Molecular Biology, Cambridge, United Kingdom)

Mr. Bernard DE MASSY (Institut de Génétique Humaine, Montpellier)

Mr. André S. RIBIERO (Tampere University of Technology, Tampere, Finland)

Mr. Colin SEMPLE (MRC Human Genetics Unit, Edinburgh, United Kingdom)

Ms. Michèle STUDER (Institute of Biology Valrose, Nice)

Mr. Elmar WAHLE (Martin Luther University, Halle-Wittenberg, Germany)

Mr. Lucas WALTZER (University of Toulouse III, (UPS), Toulouse)

Mr. David WILKINSON (MRC National Institute for Medical Research, London, United Kingdom)

Ms. Rosa COSSART (Institut de Neurobiologie de la Méditerranée, Luminy) representative of INSERM CSS

Mr. Jochen LANG (University of Bordeaux 1, Bordeaux) Representative of CoNRS

Mr. Michael DUBOW (Université Paris-Sud, Orsay) Representative of CNU

Scientific delegate representing the AERES:

Mr. Patrick BLADER

Representative(s) of the unit's supervising institutions and bodies:

INSERM

Mr. Etienne HIRSCH

INSB/CNRS

Mr. Laurent KODJABACHIAN

ENS

Mr. Yves LASZLO

1 • Introduction

History and geographical location of the unit

The "Institute of Biology of the Ecole Normale Supérieure" (IBENS), created in 2010 at the ENS, resulted from the fusion of four ENS (Ecole Normale Supérieure)-CNRS units and two ENS-INSERM units to produce a unique UMR (Unité Mixte de Recherche) ENS-CNRS-INSERM. The IBENS is made up of 285 research staff, forming 24 teams. IBENS teams are grouped in 4 sections: Functional Genomics, Environmental and Evolutionary Genomics, Developmental Biology, and Neuroscience.

The IBENS is affiliated to the ENS, the CNRS and INSERM.

The IBENS objectives are to make scientific progress in the mechanistic understanding of biological processes at multiple levels (biomolecule, cell, organisms). These objectives are supported by a scientific policy that entails independent research groups that constitute scientific units, transparent and collegial governance and shared resources. The location of the IBENS facilitates collaborations with the departments of physics, chemistry, mathematics, and computing science at the ENS and other research institutions.

Scientists at the IBENS have access to a number of common services and facilities, including rodent and amphibian animal houses, a zebrafish aquarium, confocal and electron microscopy, bioinformatics, protein production and genomics.

Only the so-called 'constitutive teams' have been evaluated during the visit; a number of 'associated teams' exist but their specific role and integration in the research at the IBENS was not assessed.

Management team:

The founding and present director of the IBENS is a prominent and highly regarded scientist in the field of synapse biology and synaptic receptor dynamics. He has received several prestigious honors and is co-founder of a foundation that promotes the cross-fertilization between biology, physics and chemistry and co-founder of the Ecole de l'INSERM, part of an MD-PhD program. He also directs the multidisciplinary LabEx 'Memolife' which associates teams of the IBENS, the Biology Center of the College de France and the ESPCI and which aims at implementing a multi-scale analysis of the memory processes. He is also partner of European 'Blue Brain' flagship project.

The day-to-day governance and management of the IBENS relies *de facto* on 3 main bodies :

- *The directorial committee/Comité de direction (CoDir)*, comprising the director, 2 executive directors, the administrative coordinator and the 4 section coordinators. The CoDir meets every two weeks. It deals with scientific and organizational strategy and manages most of the decisions relating to the day-to-day running of the institute. Team and platform leaders are occasionally invited to discuss specific issues.

- *The executive committee (CoEx)* assists the Director and implements the decisions of the CoDir and team council. It is composed of the director, the two executive directors, the administrative coordinator and the related administrative personnel. The CoEx prepares budget applications, manages recurrent funding and institutional grants, recruitment of nonscientific staff, administrative and scientific follow-up of engineers, technicians and administrative staff from INSERM, CNRS and ENS. It coordinates building works, prepares most institutional grant applications and takes care of internal and external scientific communication.

- *The team council/Conseil des équipes (CodEq)*, composed of all the teams and service leaders, is a strategic committee with decision-making power.

Governance and organization of the IBENS are specified in the 'Règlement intérieur', which needs updating to reflect the reality and include bodies like the CoEx.

In addition to the above governing bodies there are:

- *The Laboratory Council/Conseil de l'Institut*, which replaces the team council once a year and gives advice on internal matters. The representation of postdocs and students in Laboratory Council and *CodEq* needs clarification.

- *The "Comité des ITA"*, comprising the director, the elected ITA members, the section and platform coordinators and the administrative director/coordinator, meets 3 to 4 times a year.

- *The "Comité Hygiène et Sécurité"* meets every 2 months.

A Scientific Advisory Board (SAB) is composed of 12 high-profile scientists (6 French, 5 foreign European, 1 US scientists) and representatives of ENS, CNRS and INSERM advises the IBENS. It met for the first time in October 3-4, 2011 and provided a detailed written recommendation concerning various subjects, including aspects of governance. IBENS sees the primary role of the SAB as advising on recruitment of new team leaders and evaluating the quality and management of research.

AERES nomenclature: SVE

Unit workforce:

Unit workforce	**Number as at 30/06/2012**	**Number as at 01/01/2014**	2014-2018 **Number of project producers**
N1: Permanent professors and similar positions	11	13	11
N2: Permanent researchers from Institutions and similar positions	46	46	45
N3: Other permanent staff (without research duties)	24.75	25.75	23.75
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	3	2	2
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	63	50	50
N6: Other contractual staff (without research duties)	10	8	5
TOTAL N1 to N6	157.75	1 44.75	136.75

Percentage of producers	***87.80 %***

Unit workforce	**Number as at 30/06/2012**	**Number as at 01/01/2014**
Doctoral students	58	
Theses defended	66	
Postdoctoral students having spent at least 12 months in the unit	68	
Number of Research Supervisor Qualifications (HDR) taken	12	
Qualified research supervisors (with an HDR) or similar positions	35	41

2 • Assessment of the unit

Strengths and opportunities:

Over the past few years the IBENS has solidified its position as a world-class highly competitive research institute. Among its Principal Investigators (PIs) there are many leaders in their respective field of research, revealed, for example, by the various advanced and starting ERC grants and the Labex Memolife. The presence of excellent junior PIs predicts an exciting future. The overall scientific level of this institute is impressive.

The IBENS was created and is directed by an outstanding scientist with a strong and charismatic personality. The director should be congratulated, as should all of the IBENS PIs, scientists and ITA, for the past achievements. The evaluation committee encourages the IBENS to not only maintain this level but also to increase excellence and ambition even further, and recommends that the responsible institutions support the IBENS on this journey.

The IBENS is a highly visible and attractive research location. This is apparent from the outstanding level of overall scientific production, the level of international collaborators, the partnering in international consortia with highly ambitious goals (e.g., Blue Brain) and major ecological dimensions (e.g. Tara Ocean), and not least from the recruitment of highly talented junior and senior scientists (7 during the 2009-2011 period). The committee would like to congratulate the IBENS for its recruitment program.

While the institute offers excellent common services and facilities, including cutting edge technological platforms, there have been enormous technological advances in particular in so-called "OMICS" technologies and the associated bioinformatics and - as for all similar institutes - future investment in this area with significant ambition will have to be considered in a continuous manner.

The institute has a significant critical mass and multiple synergies that are very efficiently exploited by the teams. Indeed the committee was impressed by the multidisciplinary research which was generated through local interactions with the departments of physics, chemistry, mathematics, and computing science at the ENS. In addition, important interactions exist with other research institutions in the Paris area and beyond. The recruitment of excellent students from the ENS is certainly a non-negligible asset of the IBENS.

The financial situation of the IBENS is very good. The PIs can be very content with the current overheads which are rather low compared to other institutions. This situation could be used to generate resources to further improve the scientific infrastructure.

Weaknesses and threats:

Vision. Due to its origins, the IBENS scientists develop very heterogeneous sets of research projects. Indeed, it is the philosophy of this institute to attract the very best scientists and associate them to the thematic fields that are studied in the four sections. This philosophy has worked well and the IBENS has attracted highly talented junior and senior scientists. However, the flip side of the coin is an increasing diversity and need for additional space (e.g., team & section, plant growth), resources and infrastructure (e.g., bioinformatics). It is therefore rather surprising that a long-term vision for the development of the IBENS has not yet been formulated.

Foreign scientists. Institutes of world-class level like the IBENS generally attract talent worldwide. The low number of foreign scientists – especially of young scientists - is therefore surprising.

International consortia. The IBENS teams have the scientific quality and recognition to not only participate in European and international consortia but they should develop the ambition to lead such activities.

Governance & administration. There is rather limited autonomy of the sections and no deputy director has been elected, which does not support the preparing of future leaders with governance expertise. There are worries about the contractual long-term stability of administrative staff, which is required for continuous administrative support, also at the level of the sections.

Communication. There is sub-optimal communication at various levels within the governance structure. Partricularly, communication from the main governing bodies that meet frequently (CoDir, CoEx) but also from the CodEq (towards tenured scientists, post-docs, PhD students and ITA) needs to be improved significantly.

Renovation. Despite past efforts the general structure and apprearance of some parts of the IBENS building are disappointing and incompatible with the scientific reputation of this institute. While the committee did not have the opportunity to extensively visit the site, the rooms in which the oral presentations took place need serious renovation and the working conditions described for the housing of Xenopus in the -2 sub-basement appear unacceptable.

Recommendations:

Vision. While the current scientific 'philosophy' of the IBENS has been no doubt very successful, diversity has to be carefully balanced with the resources (people, space, finances, technological infrastructure, etc.) that can be attributed to the PIs/sections. The leaders within the institute, in close interaction with the PIs, should develop a long-term vision of where the IBENS is going to invest in human capital and resources in the future in order to not only preserve the current level of excellence but reach out for even higher standards than those attained today, taking into account the increasing technological level and the rapid change of the technology landscape. In this respect yearly retreats of the PIs at suitable location outside of the institute may be an opportunity to shape a largely accepted vision for the future.

Ambition. Given the high scientific level and leadership of several PIs more efforts could be made not only to be partners in but also to establish/lead international consortia. This may also help to recruit international talent.

Technologies. Scientists and platform leaders overseeing the technological development ("OMICS", Mass Spectrometry, microscopy, etc.) should form a technology assessment team that meets regularly to evaluate technology developments, which are of importance to the IBENS, and to recommend timely integration of these on site. Some modern technologies, such as Chromatin Interaction Analysis by Paired-End Tag Sequencing (ChIA-PET), are not yet established at the IBENS, and a reflection is necessary if IBENS wants to integrate such technology in house or in collaboration with outside specialists. The same may be done for the organization of the bioinformatics service. The IBENS has excellent bioinformatics groups and other groups will increasingly need bioinformatics support. A common effort of the institute (i.e., space and personnel) to not only coordinate existing bioinformatics resources but to build up a competent service should be discussed.

Governance & organization. As was pointed out by the SAB in October 2011, there is a need for a collective organization. There have been clear improvements, such as a retreat of all PIs, and the apparent functionality of CoDir and CoEx. However, communication of the decisions and the corresponding rationales to the personnel of the IBENS must definitely be improved.

The IBENS should reflect on whether it wants to maintain its current organization in four non-autonomous sections. The committee realized that strong synergies exist between the sections of Development and Neurosciences on the one hand and between the Functional Genomics and Environmental and Evolutionary Genomics on the other hand. One possible model would be to join the two sections in these pairs and increase their autonomy to create 'real' departments with attributed space, administrative support and finances. The two leaders of these departments may for example act as director and deputy director of the institute.

The governance structure of the IBENS should facilitate the development of future leaders with sufficient governance expertise as heads of sections/departments.

The retirement of the Director of the IBENS at the end of the upcoming review period underlines the need of developing a recruitment policy to favor turnover while maintaining the scientific identity and policy of the IBENS. This process should be initiated so as to best prepare the 2019-2023 period.

Communication. Communication must be improved at several levels. Members of CoDir and CoEx should communicate the decisions and the corresponding arguments to the PIs and platform leaders of their sections. A clear bidirectional path of information (to the PIs) and proposal (from the PIs) should be established with these main decision-making bodies. The direction should ensure that the mandatory meetings of the Laboratory Council/Conseil de l'Institut, as well as those of the Comité des ITA take place. PIs and platform leaders are responsible for communication towards their group/platform members. Intranet facilities should be efficiently used for communication, for example of the present report on Past Research and Projects at the IBENS. Team leader seminars may be established to discuss strategies and prepare for synergies.

Space & Renovation. There is a need to find space for the plant biologist to house plants. Apparently this space is in principle available on site but the administrative procedure is taking too long. The Directions of the IBENS and ENS should act rapidly to support the excellent plant science at the institute.

Despite past efforts renovation is clearly necessary. The appearance of the main seminar room is incompatible with the excellent level of science at this institute and there are serious worries about the working conditions in the Xenopus breeding station.

3 • Detailed assessments

Assessment of scientific quality and outputs

The scientific production of the IBENS is outstanding at the international level. IBENS scientists have published at high frequency in prestigious journals, received prizes and honors and obtained highly competitive grants. During the past 5 years, the IBENS published 560 peer-reviewed studies in international journals, including a large fraction in top-tier journals. Of these 560 peer-reviewed papers, 365 were published with an IBENS group leader as last author. 119 studies are published in prestigious journals such as Nature (10) or other Nature series journals (24), Science (6), Cell (5), Neuron (14), PNAS (25), EMBO J (13), PLoS Genetics (8), Developmental Cell (4), or Current Biology (12). In addition, IBENS scientists have generated 11 patents and obtained 2 licenses.

Since 2007 a total of 66 IBENS PhD students have defended their theses.

Assessment of the unit's academic reputation and appeal

The life science at the ENS, represented largely by the IBENS, has an excellent academic reputation as is revealed, among other indicators, by its ranking at the 46th position for the period of 2010 to 2011 by « The Times Higher Education Supplement »; evaluated were teaching, research, knowledge transfer and international outlook. In addition, numerous prizes for its PIs and prestigious grants demonstrate the scientific excellence of the IBENS.

Of note, 6 ERC grants (4 junior, 2 advanced) have been awarded to IBENS scientists. Moreover, IBENS members have obtained several competitive European or French grants, including HSFP Research grants (3), ATIP/Avenir grants (6) or "Ville de Paris" start-up grants (3). Several IBENS members have received prestigious honors, such as memberships of the French Academy of Sciences (2) or the EMBO (5), EMBO Council memberships (1), CNRS "Médaille d'Argent" (2), "CNRS Médaille de Bronze" (2) or the FENS EJN Young Investigator Award (1).

IBENS members have been invited to more than 450 national and international conferences.

The research at IBENS is highly competitive. It has recently been awarded extensive funds from the "Investissements d'Avenir" program and coordinates MemoLife, a « Laboratoire d'Excellence (Labex)". MemoLife is composed of IBENS research teams, the CIRB ("Centre Interdisciplinaire de Recherche en Biology") of the College de France and the 2 teams of the "Ecole Supérieure de Physique-Chimie Industrielle".

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

There is a significant impact of work done at the IBENS on the economic and in particular on the ecological sector, which is rarely seen at other institutions.

The IBENS organizes seminars for the general public and contributes to social programs. For instance, the "Conférences de la rue d'Ulm" given by internationally renowned scientists are open to a broad audience. The IBENS contributes actively to outreach programs, including the "Fête de la Science" and organizes several open days.

The IBENS has developed strong partnerships with other prestigious research Institutes such as College de France, ESCPI through the Labex MemoLife.

During the last 5 years, several IBENS PIs have been actively involved in technology transfer activities, as is apparent from patents filed (11) and licenses (2) obtained.

The IBENS has established partnership with industry and several contracts have been signed (e.g., the partnership between IBENS and Nikon, which has been reported in the press (Les Echos 07/10/2010). In the Neuroscience section innovative technologies based on "acousto-optic deflectors" have been developed and are commercially exploited by a French start-up company (Kaluti system).

The committee was particularly impressed by the contribution of the IBENS to the Tara Oceans Expedition. This project, co-coordinated by a PI of the IBENS is a major effort to understand the impact of climate change on the ecosystems. Tara Expeditions is a non-profit association based in France that provides samples and data to the scientific community worldwide. One of their main objectives is to increase environmental awareness among the general public, and particularly young people. The Tara Oceans Expedition is highly visible in the media with numerous presentations on public television worldwide, notably in France (FR3 Thalassa, FR2 Téléjournal, TF1 Téléjournal), Spain, Italy, Greece, India, Chile, USA (Fox News, ABC News, NPR), and UK (BBC Breakfast, Newsround, Sky News, BBC World, ITN, BBC Radio2, Radio4, and World Service) and articles in newspapers and magazines describing the links between ocean life and climate, including Le Monde, Libération, Figaro, the Guardian, The Independent, The Daily Express, The Times of India, Sciences et Avenir, Geo, National Geographic, and Métro. Moreover the Tara Oceans experts have contributed to, and are acknowledged in 'Planet Ocean,' a film produced by Yann Arthus Bertrand and Michael Pitiot. The expedition and the results obtained can be followed in real time on the Tara homepage and its FaceBook site; in addition the co-coordinator from the IBENS has given a large number of seminars in France, the US and other European countries about the project.

Assessment of the unit's organization and life:

The IBENS scientific policy relies on the existence and cooperation of independent research groups, grouped into 4 sections, which have a mainly operational function. The research teams that have been evaluated are the so-called "constitutive teams" of IBENS. "Associated teams", which maintain links with their laboratories of origin correspond to teams working in units with additional affiliations were not presented and have not been evaluated here. Their status and implication in the scientific life and representation in managing bodies should be clarified.

Each team is led by a single PI (with one possible exception), who is fully responsible for the science, personnel and finances of the team. All teams have access to the common platforms and facilities. The organization of the IBENS in sections provides a certain identity, but that does not pose a barrier to establish links and collaborations between sections. An elected scientific coordinator manages each section; the succession of two coordinators has already been defined. Sections provide a practical level of interaction, ease discussions on scientific strategy within a given field and on the organization of internal and external seminars. The section representatives discuss the action of the CoDir and the CodEq, thereby contributing to the decision-making process. Governance and organization of the IBENS are specified in the 'Règlement intérieur'. However, the committee recognizes that this needs updating to reflect the reality and include bodies like the CoEx. CoDir and CoEx are the main decision-making body of the institute.

During the visit the committee got the impression that three aspects need improvement: (i) communication provided by the governance bodies, (ii) representation of staff scientists, post-docs and PhD students on these bodies, in particular the CodEq, and (iii) increased administrative support at the section level. In addition the direction should ensure that the yearly meetings of the Laboratory Council/Conseil de l'Institut, the meetings of the Comité des ITA (3 or 4-times a year) and the bimonthly meetings of the Comité Hygiène et Securité take place. Communication should support compliance by providing information and the rationale behind decisions taken by the CoDir and CoEx to PIs, and PIs should inform team members about issues/decisions/proposals discussed at the CodEq. Intranet facilities may be used to provide access to documents of general interest (Règlement intérieur), such as the AERES report on past research and projects and minutes of the decision-making bodies. The committee endorses the wish of the scientific research staff for more information about administrative issues, budget allocation and technical staff recruitment. The administrative support to the four sections appears rather limited. The committee received very favorable feedback about the first retreat of all IBENS personnel that was held in May 2012 and noted the commitment of the direction to organize such a retreat every 2 years. The Committee understood that there is a significant interest in (at least) yearly section meetings; regular team leader presentations should be considered as a means of communicating team achievements and strategies in a coherent context.

In financial aspects the IBENS is in a rather favorable situation, which is not the least due to the efficient recruitment of grants. The annual budget from ENS, CNRS and INSERM (which represents 22% of the total budget) is split into two parts. (i) The "management budget" (10% of the total budget) covers expenses for administration, communication, building and maintenance work. (ii) The remainder is distributed to the teams according to their size. A tax on the surface area occupied by each team (70€/m^2) and a small percentage of funds from the team grants (excluding fellowships) are applied. No grant money is diverted to the management budget. Running costs of common services and facilities are billed to users. Investment in new equipment is usually funded by specific grant applications.

The IBENS has a Scientific Advisory Board of 12 high-profile international scientists. At the introductory meeting in October 2011 the SAB performed a global analysis of the IBENS and provided a number of very useful recommendations. The most important function of the SAB was specified in the director's response to the SAB report as to 'guarantee a high standard in the recruitment of new group leaders'.

Common platforms and facilities are key structures of the IBENS organization, available to all teams. A technology assessment group should be formed to ensure service performance and development, and the implantation of novel technologies at the institute. All IBENS platforms are open to external scientists (two are IBiSA-accredited). Strategic investments have been made in the past few years to establish state of the art platforms in:

- *High-throughput sequencing (HTS).* An Illumina HiSeq sequencer has been purchased together with 4 local scientific institutes (Collège de France, Université Pierre et Marie Curie, IBPC, ESPCI ParisTech and Institut Curie). The IBENS genomic platform supports teams on Next Generation Sequencing (NGS) applications ranging from *de novo* sequencing of genomes and transcriptome analyses by RNA-Seq or small RNA-Seq for small non-coding RNAs, to ChIP-Seq for epigenomics studies by genome-wide profiling of DNA-binding proteins, histone modifications or nucleosome positioning, and chromatin architecture studies. In view of the increasing complexity and coordinate bioinformatics/IT demand of NGS-based technologies and the rapid development of novel sequencing technologies and applications, an important and urgent point of reflection for the future will be which technologies and expertise to set up/maintain at the institute itself or in collaboration with outside specialists.

- *Bioinformatics*. The committee emphasizes that maintaining a competitive stand in the various (epi)genomics-chromatin architecture applications of HTS requires a strong investment in bioinformatics. The IBENS provides, and has recently recruited strong expert knowledge in bioinformatics services. Care has to be taken that the bioinformatics service provided to the teams is sufficiently staffed without deviating the bioinformatics development teams from their research/development tasks. The IBENS has the finances and the expert base to maintain the important balance and mutual relationship between bioinformatics development and high-level bioinformatics service to the teams.

- *Imaging & optogenetics*. Optogenetics offers the opportunity to probe and monitor molecular processes and cell-types of interest in arbitrarily large numbers of user-defined locations. This approach is revolutionizing biological sciences, in particular in the field of neuroscience where optical manipulation and readout are gradually replacing electrical stimulations and recordings. Important grants from the Région Ile-de France (NERF) and Fondation pour la Recherche Médicale (FRM), under the coordination of two IBENS PIs, have made it possible to implement a facility for viral transgenesis at L2 security level. This facility will include injection setups, animal facility and Imaging equipment. Both multiphoton imaging and photo activation, and single photon fiber-optic relayed *in vivo* optogenetics will be implemented. Plans exist to develop methods to generate dynamic spatiotemporal patterns of illumination and capabilities for super-resolution imaging and single-molecule photochemistry.

- *Proteomics*. The protein production facility at the IBENS manages a collection of equipment related to protein overexpression, cell lysis, purification and analysis. As part of an informal network involving neighboring institutes of the Montagne Sainte Geneviève, the teams interested in protein production and analysis (IBPC, Curie, ESPCI, College de France) can access other equipment like fermentors, fluorimeters, mass-spectrometers, X-ray sources and peptide synthesizers.

- *Genotyping*. The committee understood that there is a general wish to establish a central facility for animal genotyping as exists in other institutes.

The PhD students and postdocs actively participate in the organization of the IBENS life. The SPIBENS (association of Ph.D. students and post-doctoral scientists at IBENS) is financially supported by IBENS. SPIBENS organizes various initiatives. The administrative team and the SPIBENS International Committee have established an 'International Welcome Booklet' for foreign students and postdocs, following a suggestion of the SAB. IBENS has also established a 'Welcome House' to assist new staff (Ph.D. students, postdoctoral research assistants, new researchers and engineers/technicians) in administrative procedures. The committee greatly appreciates that SPIBENS is taking initiatives to establish a partnership with the BNP Paribas to provide easier services to international students and postdocs for opening of bank accounts. But the committee has learnt also that there is still a need to improve administrative help to foreign students/postdocs. SPIBENS participated to the organization of a two days international conference (May 14-16, 2012) with Institut Curie and College de France. 200 students and post-docs were registered for the conference, including 22 SPIBENS members and a strong international participation. SPIBENS also helped organizing a Lunchtime Conference Program, at which students and post-docs could present their data to L3 students and organizes monthly Happy Hours.

The IBENS offers an active scientific lecture program:

"IBENS Conferences" are a forum where internationally renowned scientists speak. Four prestigious conferences are planned per year. *"IBENS seminars"* are organized by each section. They take place twice a week and are given by PIs or the equivalent. Each team will be able to benefit in this framework from two invitations per year. *"SPIBENS seminars"* are organized by students and postdocs; this initiative should be supported by senior PIs to ensure its success.

Assessment of the unit's involvement in training through research

Following the general policy of the ENS to link research and high-level teaching to generate an environment for innovation, the IBENS has extensive experience in teaching both at undergraduate and graduate levels. The 46th rank for 2010 to 2011 in the Times Higher Education World Ranking for Life Sciences, which judges universities across their core missions – teaching, research, knowledge transfer and international outlook – underscores the excellent international standing of the IBENS.

In line with the long-standing tradition at the ENS, training at IBENS is firmly rooted in research, and largely based on individual tutoring. A significant number of IBENS scientists (circa 50) are involved in undergraduate training by giving lectures and mentoring students.

The IBENS promotes early integration of students in laboratories. The IBENS as a whole is strongly involved in teaching at the Bachelor and Master degree levels, in addition to its more traditional role in advanced training. A core of about 20 permanent university teaching staff members (Professeurs and Maîtres de Conférences) doing their research at IBENS is engaged in undergraduate training, complemented by an equivalent number of scientific staff from the IBENS. In addition, about 50 IBENS scientists give lectures and tutor students.

The IBENS promotes multidisciplinary training. At the Bachelor and Master 1 levels in biology, various courses are included in the core curriculum to expose students to other scientific disciplines (mathematics, physics, and chemistry, all taught by experts from the field). Conversely, IBENS members organize introductory courses in biology for students reading mathematics, physics, chemistry, earth sciences, and cognitive science. In addition, students at the ENS are required to validate additional courses to obtain the "Diplôme de l'ENS" (DENS), and biology students are strongly encouraged to take additional courses in physics, chemistry, environment, geosciences, computer sciences, and cognitive sciences.

In collaboration with the UPMC the IBENS has initiated a new program in Systems Biology. This new Master program is devoted to Cell Systems Biology and welcomes French and foreign students that are motivated to pursue interdisciplinary studies of living systems, have a strong background in biology and/or other constituent disciplines of Systems Biology (mathematics, computer sciences, engineering, physics and chemistry).

The IBENS is also involved in interdisciplinary training of medical students. A small number of highly selected medical (or pharmaceutical) students are recruited at the beginning of their third year of studies to receive, in addition to their medical training outside the ENS, a strong training in fundamental biology, often with additional courses in mathematics, physics, or chemistry. The "Ecole de l'Inserm", which was cofounded by the IBENS director in 2006 and provides a specific scientific training to MDs and is part of the MD-PhD program, appears as a logical extension of this interdisciplinary MD training but no specific information was provided. The Ecole de l'Inserm selects each year 20 students from all over France. Finally, members of the IBENS participate in state of the art courses organized by prestigious partners, notably at the Pasteur and Curie Institutes.

The IBENS is highly involved in doctoral training: its 57 PhD students benefit from an active intellectual life, with weekly seminars and journal clubs in each section, and section seminars to meet and discuss with leading international experts (about two-thirds coming from abroad). The IBENS also organizes advanced courses (a few days to two weeks) open to PhD students (and/or post-doctoral fellows) from other institutions, in particular to those enrolled in the partner doctoral schools ('Brain, Cognition and Behaviour', 'Interdisciplinary for Living Systems', 'Diversity of Living Organisms' and 'Complexity in Living Organisms').

The IBENS has also organized advanced practical courses aimed at scientists coming from academic institutions and the industry, in particular for high technology imaging or high-throughput transcriptomics studies.

Assessment of the five-year plan and strategy

The scientific program of the IBENS for the coming 5 years consists mainly of (i) consolidation of the current status, (ii) investment in high throughput technologies and (iii) boosting of projects at the interface with physics, chemistry and applied mathematics. The IBENS plans to extend its educational activities through the MemoLife project, which is anticipated to form an integrated top-level center for interdisciplinary training open to international exchanges.

The IBENS future strategy includes establishment of two new platforms: (i) the Plantalgue and the Bioinformatics Platform. The Plantalgue platform will reinforce the infrastructure of the evolutionary genomics section, thereby increasing its visibility and attractivity; (ii) the Bioinformatics platform will be set up in collaboration with the genomics, computing and imaging platforms, in order to meet the bioinformatics needs of the MemoLife Labex groups at IBENS, College de France and ESPCI.

Twenty-four research teams are involved in the coming five-year project. The departure of two teams (one each from the Developmental Biology and Neuroscience sections) in 2013 will open new prospects for recruiting new teams and competitive calls have been launched. Emerging fields and systemic approaches are prioritized in these calls and care will be taken to preserve the balance between the sections.

The IBENS is a young and exceptionally successful Institute. The roots of the institute and the philosophy of recruiting the best have imprinted a high diversity of research themes. The management has provided the teams, loosely grouped into four sections, with efficient technological support in the different research domains. The outstanding scientific achievements prove that this policy has worked remarkably well.

The Committee feels that at this stage of the IBENS expansion, an important issue will be to envision how to manage growth in the long-term. This may require a common reflection to shape a vision for the IBENS of the future, taking into account the growing need for companion technologies and support services, particularly with respect to costly technologies that change very rapidly. An example is the plethora of technologies based on high throughput sequencing – ranging from transcriptomics and (epi)genomics to chromatin architecture – that require implicitly efficient bioinformatics services and tool development to the benefit of a great number of teams.

This reflection may include the consideration of reshaping the organizational structure of the Institute to optimally support the scientific and technological vision in the long term. Regarding the future beyond the next period, the IBENS should decide whether the present organization is optimal to sustain long-term growth of the four axes or whether it might be appropriate to move towards a more departmental structure with autonomy of, for example, two departments and the corresponding governmental adjustments.

4 • Team-by-team analysis

Team 01: Cell Biology of Transcription

Name of team leader: Mr. Olivier BENSAUDE

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	2	2	2
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	1
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	4	4	4

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The team has been working on the regulation of RNA pol II-dependent gene transcription for many years and focuses its works on the role of non-coding RNAs.

Following their important discovery of the HEXIM/7SK ribonucleoprotein complex as a negative regulator of the elongation factor P-TEFb (CDK9/Cycin T), they identified and recently mapped the interface between HEXIM1 and Cyclin T1 (submitted). In collaboration, they studied the interaction between components of the 7SK snRNP (NAR 2008) and they participated in the phylogenetic identification and analysis of 7SK RNA (Mol. Biol. Evol 2009).

In parallel, they started to analyse the role of other non-coding RNA such as U1 that they identified as associated with the RNA pol II. They showed that, in contrast to other splicing snRNAs, the U1 snRNA was recruited to transcription unit independently of splicing (JCS 2010). Furthermore, they found that phosphorylation of Ser-2 on RNA pol II CTD participates in the recruitment of some RNA processing factors (but not U1) to facilitate co-transcriptional RNA maturation (splicing and 3'-end cleavage) (NAR 2012).

The study of ncRNA in gene regulation is a hot topic that has become very competitive. The team has made significant contributions to the field and performs elegant mechanistic studies based both on classical biochemical and innovative imaging approaches. The publication record shows a regular production in good journals. Over the 2007-2012 period, 13 publications have been accepted, including 4 reviews. Concerning research papers, the majority stems from collaborative works (Retrovirology 2007, NAR 2008, Cell Cycle 2009, MB Evol 2009, PloS One 2010, MCB 2011), and members the team are principal authors on 3 publications (MCB 2007, JCS 2010 and NAR 2012). Given the size and composition of the team, this is a very good production.

Assessment of the team's academic reputation and appeal

The group leader has a long-standing and excellent scientific reputation. He is regularly invited to international conferences and courses (4 invitations in 2010-2012; including 1 FASEB meeting). He is president of the "Cell Stress Society International" and member of the editorial committee of "Transcription". The publications of the team are well cited.

As a leader in the field of P-TEFb and 7SK and thanks to its technical expertise, the team is strongly engaged in several fruitful international collaborations. It also has strong links with a second team at IBENS which originated from the same team.

Research is well funded with continuous support from French agencies and charities (ARC 2009, Ligue 2010; partner in an ANR 2012).

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

Not applicable

Assessment of the team's organisation and life:

This small group comprises currently 3 permanent staff (2 senior scientists and one engineer), 2 PhD students and 1 post-doc. The team regularly attracts students (M2 & PhD) and post-doctoral fellows. It was recently reinforced by the arrival of a senior research scientist, whose strong background in structural biology of RNA complexes will be very beneficial.

The PI has important management duties. In 2009, he took the head of the UMR8541 that participated in the foundation of the IBENS. Since 2010, he is coordinator of the IBENS Functional Genomic section and member of the IBENS Direction Committee.

The PI will retire in the middle of the next contract and it is anticipated that the team will then be closed.

Assessment of the team's involvement in training through research

During the 2007-2012 period, 5 PhD students defended their theses (2007; 2009; 2010; 2012; 2012). In addition, the PI actively participates in teaching at the ENS (L3 and Master levels). He is responsible for one L3 module for students in chemistry. Moreover, he is involved in the coordination of two international exchanges program (ENS / Northwestern University –Chicago; and ENS / East China Normal University).

Assessment of the five-year plan and strategy

The team leader will reach retirement in the course of the next contract period and the project is refocused on the structural and functional analysis of 7SK and P-TEFb. It is comforting that the working forces and support for the project have already been secured with a two-year contract for a technician and the arrival of a PhD student as well as a post-doc in 2012.

Taking advantage of the competences of the senior scientist that recently joined the team and initiated this project, they will use a combination of biophysical methods (crystallography, NMR…) to define the structure of the core 7SK snRNP. An ambitious photoactivatable amino acids replacement strategy is proposed but the group should also consider to use cross-linkers for natural amino acids that may yield results more rapidly. In parallel, the group will investigate the dynamics of interaction between 7SK snRNP and P-TEFb in living cells. In collaboration with other teams at the ENS and in Lille, they will aim to investigate *in vivo* the dynamics of P-TEFb complexes.

The project is well focused and perfectly matches the expertise of the team and its collaborators. The methods are appropriate and will complement each other well. This project will provide a better mechanistic understanding of the mode of action of 7SK and P-TEFb in the regulation of transcription.

Conclusion:

- Strengths and opportunities:

The team has strong expertise in biochemistry, structural biology and imaging. It uses an interesting paradigm to address in details the function of a ncRNA in transcriptional regulation. The project tackles an important question, it is focused and uses original techniques. The group has a solid reputation. Appropriate collaborations have been established.

- Weaknesses and threats:

An issue could be the relatively small size of the team. However, this is mitigated by the numerous collaborations. The ambition of the project is limited due to the forecasted retirement of the group leader.

- Recommendations:

The team has been undertaking good research for many years in a highly competitive field and deserves support.

Team 02: Functional Imaging of Transcription

Name of team leader: Mr. Xavier DARZACQ

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	2	2	2
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	6	2	2
N6: Other contractual staff (without research duties)	2		
TOTAL N1 to N6	12	6	6

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	3	
Theses defended	2	
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	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The scientific quality and output of this group are at a good level. The studies that were published in high impact factor journals were so far, however, led by another internationally highly reputed team. Nevertheless the experience gained via this interactions will allow this group to be able to reach these same levels. The committee believes that the work developed is at an initial stage, where most efforts are on the development of experimental techniques, rather than extracting new knowledge from them. This is expected, and required, at a initial stage and should lead to good results.

Assessment of the team's academic reputation and appeal

This team is still at a stage of developing its reputation. Nevertheless, particularly due to the maintenance of strong ties to a leading team in the field, it is developing fast. The group has already established collaborations both within France and abroad. The fact that experimental techniques are being developed should aid in the establishment of novel links to groups interested in using these technologies and contribute to a rapid increase in reputation.

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

Not applicable

Assessment of the team's organisation and life:

The team is rather large, with 3 senior scientists, including the PI, 5 post-doctoral fellows, 3 PhD students, 4 engineers and 1 MSc student. These are divided into subgroups, working on independent but related topics. This team studies several topics, each of which is addressed by one of the subgroups; the studies are adequately organized and there is close contact. The ambition towards high impact publications should be encouraged. There is potential for growth but in the significant number of senior scientists the emphasis should be on the recruitment of junior team members.

Assessment of the team's involvement in training through research

Only the PI and only one of the present members of the team are authors in the list of publications provided. Thus, it is important that the PI ensures scientific output of the team members.

Assessment of the five-year plan and strategy

The team plans to continue studies along four major directions, all of them heavily technology development-oriented and related to the 'mechanics of gene expression'. One comprises the development of novel techniques of vizualization of gene expression. Another addresses the question of how spatial organization in the nucleous affects gene expression. The third is the study of gene expression regulation. The fourth is the study of how cells react to forces. Each of these aims will be pursued by a subteam, which appear well balanced and organized.

Conclusion:

- Strengths and opportunities:

This team consists of several senior scientists with previous experience in their area of research. There has been extensive collaboration with one of the highly renowned groups in the field. The research on the regulation of gene expression at the single molecule level in live cells has great potential. The team members are well integrated and experienced and it is expected that the amount and quality of publications will increase rapidly.

- Weaknesses and threats:

The present composition of the group is such that there are more senior than junior researchers.

- Recommendations:

When developing novel experimental techniques, there should be an emphasis on dissemination and applicability. In particular, the team should make efforts to demonstrate wide applicability and show how this can be achieved by simple means. In short, applicability and usability should be taken into account.

In some research projects, the final goals are not clear from a biological point of view. A clear vision should be established about the final goals for developing novel experimental techniques.

The team should increase the ambition towards high level publications that originate from the team's own efforts and increase its international visibility.

Given the number of senior researchers this group has the potential to recruit new MSc and PhD students.

Team 03: Eukaryotic Chromosome Replication

Name of team leader: Mr. Olivier HYRIEN

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2	2
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	4	4	4

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	0	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

Aim of the team is to understand DNA replication origin location and firing time, and how cells respond to problems in replication fork progression.

One important achievement of the group was to highlight the organisation of replication at the Megabase scale with a temporal order of origin firing, leading to a replication fork polarity and nucleotide composition skew due to mutations. This work resulted from successful collaboration with bioinfomaticians. An important investment was made to model the experimental data on replication timing and substitution rates, to show the replication mutational asymmetry and its correlation with replication timing domains. This work led to publications in Gen Res (2010), Chr. Res (2010), MBE (2011), PLoS Comp Biol (2011), NAR (2012), and PloS Comp Biol (2012).

The role of Topoisomerase II (TopoII) in DNA replication: The Topo II inhibitor ICRF-193 slows down S phase, but this effect is seen when added in G1, and this treatment blocks origin cluster activation by an unknown process (a publication is in revision).

The group has expertise with DNA combing and is thus involved in collaborations, such as the one on the role of c-Myc on DNA replication. C-Myc appears to increase density of early origins (paper submitted, collaborating group last and first author).

The group has developed a project on the effect of psoralen crosslinks on DNA replication and the effect of deficiency of DNA polymerase η, showing increased proportion of stalled forks; this work is also done in collaboration.

Overall the strength of the group comes from its ability to experimentally analyse and model large-scale replication domains or other features of DNA replication using an interdisciplinary approach. The coherence and strength of the group for the other projects is less convincing. The Team has published important papers highlighting the organisation of replication at the megabase scale with a temporal order of origin firing. Other interesting papers stem from the interaction with DNA replication groups in Paris and New York. Overall, the scientific production is satisfactory without being excellent.

Assessment of the team's academic reputation and appeal

This group is well recognized in studying replication and modeling experimental data on replication timing. However, this group lacks of international recognition and diffusion.

The team has 12 publications (2008-2012) and 3 technical papers; the PI has signed 5 publications of those as last or first author. These 5 papers appeared in PLoS one (3x), Chr. Res., and PloS comput Biol. Invitations to international and international meetings are limited.

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

Not applicable

Assessment of the team's organisation and life:

This team has a modest size (6 people) and appears to be well managed.

Assessment of the team's involvement in training through research

The group leader has organized an interesting interdisciplinary meeting to bring biological and physical approaches together, on a regular basis every two years from 2000 to 2009.

Assessment of the five-year plan and strategy

The future work comprises the validation of one feature of the current model of N domains: the cascade of replication firing. This would require the mapping of origins at high resolution, with the problem of population versus single cell analysis. The plans are:

Test methods developed and used by others to map origins. This seems of limited interest unless a major investment is put into these approaches. Even if differences between techniques are confirmed, it is uncertain whether the proposed strategy will allow understanding why.

Determine polarity from Okazaki sequencing. Experimental data and modelling.

High throughput DNA combing using quantitative DNA staining and mapping fibers by introducing dyes at endonuclease sites: potentially allowing the mapping of any DNA molecule! Interesting, ambitious, challenging.

Reprogramming DNA replication and chromatin structure during tumorigenesis, stem cell differentiation, senescence, oncogene induced senescence, overexpressing HMG, reprogramming. A huge project, impossible to evaluate without further information about schedule and investment in personnel and budget. Hardly compatible with the current size of the group.

Chromosome structure and origin firing, understand the role of TopoII in the control of S phase in Xenopus and human cells. Assays will involve expression of TopoII (wild type, mutant) and its effect on DNA replication and chromatin binding of MCM. These are rather indirect assays, unlikely able to pinpoint the mode of action of TopoII, which is certainly a difficult question to address. Whether plasmid DNA will help is not clear, since this DNA, although organized in chromatin, is not part of chromosomes. Similarly, deciphering the effect of HMG overexpression can be interesting however no experiment is proposed to identify how this could work.

Taken together the group develops new important methods to analyze and model large scale replication domains. The project is too focussed on developing methodological aspects at the expense of the biological questions. The ambitious goal to develop a method to map genome wide DNA replication was noted but the feasibility of this approach is difficult to evaluate at this point and was met with scepticism. The project concerning the role of Topo II in DNA replication project is not convincing in all aspects.

Conclusion:

- Strengths and opportunities:

The group has excellent expertise in DNA replication and origin mapping, and manages the difficult technique of DNA combing. One strength is the interdisciplinary approach with attempts to model DNA replication patterns.

- Weaknesses and threats:

The size of the group is such that it should not disperse its efforts in too many directions. Understanding the structural role of Topo II is interesting but the approaches are not convincing. The team should pay attention to securing funds for the projects.

- Recommendations:

The group should keep a better focus. The attempts to develop new technologies should be balanced with hypothesis-driven projects.

Team 04: Expression of Eukaryotic messenger RNAs

Name of team leader: Mr. Hervé LE HIR

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	2	2	2
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)	1	1	1
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	3	2
N6: Other contractual staff (without research duties)	1	1	
TOTAL N1 to N6	8	8	6

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	0	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team leader joined the IBENS in 2009. The PI's most recognized achievement is the discovery of the exon junction complex (EJC) when he was a postdoc. The EJC has been the focus of his work ever since. His contributions have established him as a leader in this field of research, which serves as a paradigm for mechanisms of RNP assembly and remodeling and for the understanding of how nuclear mRNA processing affects mRNA fate in the cytoplasm.

One important aspect has been the PI's involvement in structural studies of the EJC, most importantly the crystal structure of the core EJC and more recently the structures of proteins or protein complexes associated with the core complex. For example, together with collaborators, the team explored the structural basis for the interaction between a composite protein surface formed by EJC core proteins and an NMD factor, Upf3. They also explained how the interaction between two NMD factors, Upf1 and Upf2, modifies the RNA binding properties and catalytic activity of Upf1. While the team leader is not a structural biologist himself, his skill and diligence in reconstituting the protein complexes has been a major factor in the success of these studies. The team also used the purified proteins for functional studies, for example to elucidate the mechanism by which the EJC remains stably associated with its RNA ligand. A recent important discovery concerns the role of the protein CWC22 both in preventing non-specific, splicing-independent binding of the EJC and in allowing its deposition in the context of splicing. In a more cell-biological context, the team discovered that not all exon-exon junctions are decorated with an EJC, and there also seems to be binding outside the canonical position just upstream of a splice junction.

The topics tackled by the team are important and cover essentially the entire range of functions of the EJC.

The publication record of the lab is outstanding, with a large number of papers in leading journals like Molecular Cell and Nature Structural and Molecular Biology. At least one paper in the latter journal with the PI as the corresponding author was published after the group's report had been submitted.

Assessment of the team's academic reputation and appeal

The team's reputation is excellent. Their work is published in very good journals and frequently cited. The team leader has an outstanding list of collaborators. He is a member of research networks and is frequently invited to meetings and for individual seminars. He is very well known and respected in the RNA community.

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

Not applicable

Assessment of the team's organisation and life:

Judging both from the oral presentation during the site visit and from the publication output, the team seems to be very well organized. There is a precise vision of what the group wants to achieve. Group members are gaining recognition through their high quality papers. The fact that the team leader will be the new head of the Functional Genomics section at IBENS speaks to his qualities as an organizer and a team leader.

The group is also well integrated at IBENS, as it has established collaborations both within IBENS and elsewhere at the ENS.

Assessment of the team's involvement in training through research

The team currently has one graduate student and several postdocs. Even though the group only started in 2009, most of these group members are already authors on prominent papers. Judged by this success, the training they receive is excellent.

Assessment of the five-year plan and strategy

The projects to be dealt with in the future are a logical continuation of the group's current work. Much remains to be learned about the function of the EJC at the molecular and cellular level, so exciting research is to be expected.

One goal is to continue the structural and mechanistic work on the EJC, including single molecule studies of the helicases within or associated with the EJC. Connections of the EJC with NMD, splicing, and translation will be investigated. Another proposed line of research is to examine the connection between the EJC and transcription and chromatin modifications. Finally, the team leader proposes to expand the transcriptome-wide analysis of EJC deposition to other cells/tissues. The goal here is to examine the regulatory potential of the EJC, e. g. in differentiation.

The projects are very focussed in the sense that they are all related to the EJC, but they cover almost the whole spectrum of EJC-related questions that one can think of. There is also a good mixture of 'safe' projects that are likely to succeed very soon and more long term, exploratory endeavors that may lead to new directions. The group is making good use of collaborations to tackle problems that they cannot handle on their own.

Conclusion:

- Strengths and opportunities:

Very good record and equally good prospects. The research program is logical and appealing. The future directions are straightforward and promising.

- Weaknesses and threats:

No apparent weaknesses. Results of the exploratory projects will be important to determine future directions of the group.

- Recommendations:

This is a team worthy of supporting with high priority.

Team 05: Molecular Mechanisms and Epigenetic Regulation of Genome Rearrangements in Ciliates

Name of team leader: Mr. Eric MEYER

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	1
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	1
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	4	4	4

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
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	1	
Qualified research supervisors (with an HDR) or similar positions	1	1

Assessment of scientific quality and outputs

The team has a very good publication records with 12 publications and 1 chapter in a CSH laboratory manual in the period from 2008 to 2012; among those the PI is last author on one Nature, one TIGs, and 2 NAR publications. In addition the team contributed to two Genes and Development and two PLOS Genet papers.

The originality of this team has been on the discovery of new mechanistic paradigms as a result of the development of precise and well-planned research projects. One of these discoveries published in 2008 (Nature) established a link between mRNA splicing and translational control, the other in 2008 (Genes and Development) and 2009 (NAR) was the discovery of the role of small RNAs in genome rearrangements of Paramecia. Indeed the team succeeded to elaborate a model for the molecular mechanism underlying these rearrangements. This is a major breakthrough in the field and is the result of the collaboration with a previous PhD student in PI's lab.

Assessment of the team's academic reputation and appeal

The team leader has very strong experience and is highly recognized in the field, and has been able to communicate his expertise to junior scientists who have now established their own laboratories and remarkably to keep good relationships with these groups allowing them to collaborate on various projects.

The team leader has a major international reputation and was co-organizer of a FASEB conference in 2011, and invited to the Keystone meeting "Gene silencing by small RNAs" in 2012.

The group has been highly successful in the national competition for funding with ANR grants and obtained a new ANR grant for four years starting in 2012. This grant includes funding to recruit postdocs.

The current project, which involves NGS sequencing, is funded by France Genomic.

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

Not applicable

Assessment of the team's organisation and life:

The team is well-organized, structured, with postdocs, engineer and students.

Assessment of the team's involvement in training through research

The group leader is involved in teaching and training students. A previous PhD student has successfully established her own lab.

Assessment of the five-year plan and strategy

The future projects are highly convincing, based on original and challenging questions, taking advantage of the expertise and tools developed by the team. One of the challenges is to test various predictions from the hypothesis of the model of scRNA scanning for genome rearrangements. Another one is to test the hypothesis for a role of this scanning pathway in speciation. The team has developed powerful genetic tools to answer these questions, and will develop genomic approaches to analyse the components involved in the control of genome rearrangements.

Future projects:

1) Sequencing the micronuclear genome: Clearly an essential step, everything should be done to succeed; in addition to identifying all sites of rearrangements and locations of IES, this project aims to answer whether they are genes or pseudogenes specific to the micronucleus.

2) Mechanisms of scRNA and siRNA pathways: In particular, the project aims to analyse the timing of mac RNA elimination, to evaluate modification of RNAs and sequestration of mac RNA?

   Search for new functions (screen based on mating type function) and analyse effects by whole genome sequencing of Mac to detect IES specific functions. Also, genes isolated from the siRNA screen will be tested for effects on scRNA pathway.

   Altogether, these molecular and genetic approaches provide a very strong and convincing strategy to address these questions.

3) Evolution: Effect of heterozygosity on rearrangements. Strategy: analyse by deep sequencing F1 (mating type heterozygotes) and also interspecific hybrids. This should allow to examine the generality of the previous finding on the mtB locus and to test the impact of sequence divergence.

   This aim addresses the important question of genetic incompatibilities, with very exciting implications on speciation.

4) Evolution of mating type determination. What is the question besides exploring the various strategies used? Given the interest and investment required for other projects, is it reasonable to explore this additional aspect? A more detail experimental plan would have been appreciated to evaluate this point further.

Conclusion:

- Strengths and opportunities:

The group is one of the leaders in the field of genome rearrangements in Paramecium. The epigenetic regulation is fascinating and integrates quite well in the global progress about small RNA functions. The group has discovered an important role for small RNAs thus opening new avenues of research. The group has expertise in most tools for the experiments proposed. When needed the group can collaborate with other experts in the field thanks to their good interactions, which is obvious from previous collaborative publications.

- Weaknesses and threats:

None

- Recommendations:

Maintain international contacts, invest more in participation to international meetings and enhance visibility, which should be straightforward given the production of the group.

Team 06: Genome Organisation and Dynamics

Name of team leader: Mr. Hugues ROEST CROLLIUS

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	2	1
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3		
N6: Other contractual staff (without research duties)	1		
TOTAL N1 to N6	6	3	2

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

This team, part of the Functional Genomics section, was established in 2004. The major goal of their research has been to use bioinformatics approaches to reconstruct ancestral genomes, due to the challenge of being unable to obtain fossil records of very ancient DNA. They developed a method called AGORA, as well as the simulator called MAGSIMUS, whose goals are to understand and explain the processes that can occur in eukaryotic genomes. This has led them to study the role and consequences of gene rearrangements, as well as uncover ancestral coding sequences and cis-regulatory sequences. They have also developed a database called GENOMICUS for comparative genome analysis. The group has produced seven publications since 2008, with two of these published in Nature Genetics and Science, though their participation in these last two is in the context of a large group of authors. Additional publications are in PLoS Genet, Genome Biol and Bioinformatics but in view of the size and quality of the team the output could be increased even though the difficulty in developing robust new programs in bioinformatics is recognized by the committee. The group should also be congratulated for depositing two patent applications in the past couple of years.

Assessment of the team's academic reputation and appeal

There's no question that the PI is a well-funded and strongly considered scientist. The PI has a grant from the European Union and two from the ANR, and has been invited to give talks at national and international meetings. The team has clearly taken on a challenging subject and brought it to fruition.

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

The PI has submitted two patent applications as well as two software registrations with the French software protection agency.

Assessment of the team's organisation and life

It is difficult to understand the actual day-to-day functioning of the group, as most of its members are either graduate students or Postdocs. The recruitment of a second engineer this past year should help to provide the day-to-day care and stability that a modern research group requires.

Assessment of the team's involvement in training through research

There is no information here as to the number of people who have been trained over the past several years, but this is a relatively young team and it can be suspected that it is only now that the people who have worked here will begin taking on permanent positions. Nonetheless, the team currently has two Ph.D. students and four postdoctoral fellows and thus appears to be a very good site for bioinformatics training.

Assessment of the five-year plan and strategy

The PI states "in the last few years, our group has pursued many interests in the field of genome and molecular evolution." It is possible that they have pursued too many interests. They present two main programs for the future, one called the Ancestrome and the other called the Regulome. There is no doubt that understanding the dynamics underlying the evolution of eukaryotic genomes will have important information and implications for our basic understanding of life on earth as well as the genesis of certain diseases such as cancer. Thus, the team leader is working in an important area. It will be very important for the group to make major contributions by publication in high-impact international journals. They certainly have developed the necessary tools to make major contributions and the committee is highly optimistic about their future.

Conclusion:

- Strengths and opportunities:

Tool development for binformatics analyses, such as algorithms to reconstruct ancestral genomes, tools for comparative genome analyses.

- Weaknesses and threats:

Diversification, too many projects. Limited scientific output.

- Recommendations:

The team should define a competitive niche for original tool development in the future (ancestral genomes, regulomes, others?) and pursue projects (in collaboration) which require major bioinformatics support to gain visibility and publish at higher frequency in important journals.

Team 07: Computational Systems Biology

Name of team leader: Mr. Denis THIEFFRY

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	2	1
N2: Permanent EPST or EPIC researchers and similar positions			
N3: Other permanent staff (without research duties)			
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	2	1
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	2	4	2

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The past five years have seen an impressive volume of original research from this group, in spite of the fact that this period was interrupted by their move to IBENS in February 2010 and subsequent problems with renovations to lab space. Their productivity appears to have been unaffected. Whether one views their publications over the previous five years or since moving to IBENS their publication record is very good, containing a steady accumulation of solid computational/methodological papers in the best genre-specific journals (PLoS Comp Biol, Nature Protoc, Bioinformatics), as well as applied studies using the novel methods developed to test clear hypotheses and gain new biological insights (including high impact publications). Both their past and future work are organised into distinct but complementary areas. The group's work to establish qualitative dynamical modeling methods, and the development of associated software, has been original and important work, as illustrated by the range of applications. Their recent work developing software for the analysis of ChIP-seq data may also have a broad impact given the explosion of epigenomic studies. Other highlights include an important (Develomental Cell) study of the role of a microRNA in the control of neurogenesis using logical modeling techniques. This team is an internationally competitive group in biological network inference.

Assessment of the team's academic reputation and appeal

The group's collaborations range from local projects with other IBENS groups, to broader European projects and participation in large international consortia. The PI is clearly taking leadership roles in these projects. He participates in community leadership activities such as conference/symposia/workshop organisation and editorial work, and also serves on funding body committees. The group also has a consistent history of staff exchange with other reputable institutes in Europe, and they have recently recruited an experienced researcher to lead the ChIP-seq analysis work.

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

Not applicable.

Assessment of the team's organisation and life:

The group appears well organised, developing flexible software tools to address significant problems in modern, high throughput biological data analysis. They have proved equally effective in arranging collaborative studies to put these tools into practice. It seems there have been issues with resource and lab space provision since the group moved to IBENS, but it is anticipated that these will be resolved soon. The group appears to lack a website, other than the minimal information on their IBENS page, which makes it difficult to judge the group's everyday organisation and practices.

Assessment of the team's involvement in training through research

The PI has a good track record in student teaching and supervision, serving as supervisor or assessor to many students, before and after his move to IBENS. He has also been involved in organising international schools and workshops in regulatory network modeling, epigenomics and the societal impacts of science.

Assessment of the five-year plan and strategy

The future plans continue the themes established in the group's previous work. They will continue to elaborate their existing software tools for logical network modeling and ChIP-seq data analysis, consistent with their established expertise and experience. Novel and timely areas, within their established themes, such as modeling post transcriptional regulatory phenomena are also to be introduced. They will continue to apply these tools in a wide variety of collaborations with experimental groups, building upon past collaborative projects and initiating new ones. There can be little doubt that the proposed work is important and feasible, however the emphasis on collaborations seems to come at the expense of novel algorithm development.

Conclusion:

- Strengths and opportunities:

The strong research track record of this group, combined with their plans to build on established expertise and collaborations are likely to result in high impact and productive science.

- Weaknesses and threats:

There appears to be a need to strengthen the staffing in this group at the postdoctoral level, once they have occupied their new lab space. The committee finds no significant weaknesses/threats in their scientific track record. Their future plans are certainly feasible but arguably lack novelty from the computational point of view.

- Recommendations:

The committee noted that the team appears to emphasize collaborative projects at the expense of developing new tools/algorithms and recommends they guard against this.

Team 08: Genomics Responses to Environmental Signals in Photosynthetic Organisms

Name of team leader: Mr. Chris BOWLER

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions		1	
N2: Permanent EPST or EPIC researchers and similar positions	2	2	2
N3: Other permanent staff (without research duties)	2	2	2
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	5	5	5
N6: Other contractual staff (without research duties)	1		
TOTAL N1 to N6	10	10	9

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	4	
Theses defended	10	
Postdoctoral students having spent at least 12 months in the unit	12	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	3

• Detailed assessments

Assessment of scientific quality and outputs

The team's efforts have been in two areas. One is the molecular regulation of the plant developmental switch that occurs upon exposure to light—a process known as photomorphogenesis. The second is the biochemistry of why diatoms are highly successful marine organisms. In both areas the team has been productive, and has done original research that has led to new levels of understanding.

The photomorphogenesis research is focused on mechanisms of chromatin-level gene regulation as this rapid developmental switch unfolds. One project involves heterochromatin analysis at the global level—an ambitious and important area to understand. Another project is the role of a specific complex (CUL4-DET1) in both light-regulated gene expression and UV DNA damage repair. The study of DET1 interfaces with a 3rd project on global histone H2B monoubiquitination (H2Bub) changes during photomorphogenesis. Together these studies appear to open a new area of the study of photomorphogenesis at the level of chromatin dynamics and the link to DNA repair.

The diatom research has resulted in two paradigm-shifting discoveries. One is that reducing power (electrons) can shuttle from the chloroplast to the mitochondria and photosynthesis and respiration may be obligatory interdependent. This discovery has important implications for the evolution of photosynthetic pathways and for understanding carbon flow in oceans. The second is that diatoms contain a urea cycle quite similar to that of mammals (ornithine-based, etc.) but this cycle has a unique role in diatoms in carbon and nitrogen metabolism that is, in part at least, related to the generation of their silica-based cell wall. The team is beginning to explore chromatin dynamics in diatoms as well.

The team has a strong publication record including high-profile papers in *PLoS Genetics. EMBO J,* and *Nature.*

Since 2010 the team has recruited major national and international funding with 3/5 grants attributed in 2012.

Assessment of the team's academic reputation and appeal

The team's strong academic reputation is reflected in the strong publication record and the numerous presentations in a range of countries and venues given by the team leader. The diatom project is a broad and highly visible collaboration and the Team leader is one of the scientific coordinators of the Tara Ocean Expedition. Another indicator is the involvement the team leader in the EMBO Council.

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

As noted above, the team's projects are creating new scientific directions and their work on diatoms has been paradigm shifting. The team leader is involved in scientific governance and large project coordination. The team is responsible for two important scientific databases: the diatom digital gene expression database and the Phaeodactylum epigenome browser.

Assessment of the team's organisation and life:

No specific comment

Assessment of the team's involvement in training through research

The students and postdocs are publishing good papers, and answered questions thoroughly during the review. They seem to be very well trained and good researchers.

Assessment of the five-year plan and strategy

The five-year plan involves two areas with two interesting projects that appear to be coherent and coordinated. One is the chromatin dynamics of rapid changes in gene expression following light exposure. Plant photomorphogenesis provides an ideal system for dissecting the chromatin changes that accompany rapid changes in gene expression in a multicellular because all the cells can be instantly exposed to induction. The other area is diatom studies and one gets the sense that diatom research will become the primary focus of the Team leader. The diatom work is in several areas including some quite novel findings about a pathway of electron flow from chloroplast to mitochondria and its role in carbon assimilation and the role of the urea cycle in diatoms. The other projects are early-stage broad investigations into genetic variation (DNA sequence vs epigenetic) and the genomics of diatom biodiversity. Understanding plant photomorphogenesis may provide for important advances in agriculture (growing plants at higher densities) and diatoms are important players in planetary carbon and mineral cycles. These are very important projects, and this team is doing cutting-edge research in them.

Conclusion:

- Strengths and opportunities:

Paradigm-shifting discoveries in diatom biology.

Global ecological dimension of ocean diatom research originating from this team.

Highly mediatic Tara Oceam Expedition.

- Weaknesses and threats:

Diversification

- Recommendations:

Focus on diatom research; reflect about reorganizing group, e.g. by spinning off of plant research project.

Team 09: Arabidopsis Epigenetics and Epigenomics

Name of team leader: Mr. Vincent COLOT

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	2	1	1
N2: Permanent EPST or EPIC researchers and similar positions	3	2	2
N3: Other permanent staff (without research duties)	1	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	2	
TOTAL N1 to N6	9	7	4

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	4	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	2	

• Detailed assessments

Assessment of scientific quality and outputs

2008-present: 24 publications and 2 methods articles.

11 publications first or last authors (in Genomics, Dev Cell (review), PLoS genet, TIG, Embo J(review), Science, Heredity, Embo J, PNAS, Genome Biol, Bioinformatics).

The team has taken a very strong lead in the field of epigenetics in *A. thaliana*. A major achievement was the characterization of 4 distinct types of chromatin states in their plant model Arabidopsis (EMBO J paper in 2011). A major breakthrough was the development of a tool to study transgenerational epigenetics by generating epigenetically modified recombinant inbred lines, taking advantage of a loss of DNA methylation. This led the team to identify the role of RNAi in establishment of these epigenetic marks (Science 2009).

Assessment of the team's academic reputation and appeal

The group leader has an excellent record of international communication and visibility as shown by: Elected EMBO member, member of AERES committees, president of SFG, member of ITMO, organizer of 8 international conferences, invited to Gordon Research (2012), to CSHL (2012), ESF-EMBO meeting (2011), Keystone (2010) and others in UK, Japan, Netherland.

Current funding: ANR BIOAdapt until 2016 and "ANR blanc" until 2014 (co PI)

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

Not applicable

Assessment of the team's organisation and life:

The team is well structured and composed of 1 assistant prof, 1 researcher, 1 postdoc, 2 PhD, 3 engineers. Importantly the team has managed to develop bioinformatics expertise with the recruitment of engineer to develop the analysis of the various genome wide epigenetic projects.

Assessment of the team's involvement in training through research

Excellent teaching contribution and members of many thesis committees.

Assessment of the five-year plan and strategy

The specific points addressed will be:

1) Epigenetics and development: the root apical meristem and the role of PRC2
2) Epigenomics in *Brassicae* (*A. alpina*), a comparative study. This is a challenging and exploratory project.
3) Use of EpiRL to find QTLs, flowering time and length, map the QTLs (around 900 total in the genome)
4) Stress induced epigenetic variation: stability, variability.
5) Impact of the loss of DNA methylation on genome stability. Preliminary data show the activity of some transposable elements, it will be very exciting to understand this reactivation process.
6) Effect on meiotic recombination. So far the loss of DNA methylation did not reveal spectacular changes, but an unexpected down regulation of pericentromeric regions, one expect that finer analysis could be very interesting.

These projects involve various approaches aimed at understanding the consequences of epigenetic modification and their heritability. The questions are well presented, convincing and the team will take advantage of the tool of epigenetically modified lines they have developed, which opens the way to several collaborations. Some projects will involve bioinformatics analysis for which the group has now good expertise.

Conclusion:

- Strengths and opportunities:

Excellent and highly recognized expertise and contribution in the field.

Innovation of new approaches and development of new tools for exploring epigenetic in plants.

Strong expertise in genetics, molecular biology and bioinformatics with potential for many collaborations.

- Weaknesses and threats:

No weakness.

- Recommendations:

The global analysis of the epigenome should lead to the identification of specific questions and hypothesis-driven projects.

Team 10: Small RNA-directed Control of the Arabidopsis Innate Immune Response

Name of team leader: Mr. Lionel NAVARRO

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	1
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
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	5	5
N6: Other contractual staff (without research duties)	2	4	2
TOTAL N1 to N6	9	11	9

Doctoral students	Doctoral students	Doctoral students
Doctoral students	1	
Theses defended	0	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	0	0

• Detailed assessments

Assessment of scientific quality and outputs

This is a new Team that was created in 2010. The Team studies the plant's innate immune response—the process by which plants sense the presence of pathogens by recognizing pathogen-specific molecules known as Microbe-Associated Molecular Patterns (MAMPs). Recognition triggers changes in gene expression designed to "fight" the pathogen and these changes in gene expression can involve microRNAs (miRNAs). One novel area of study is a newly discovered system by which bacteria suppress miRNA-mediated regulation in plants; the team is working out the molecular details and biological relevance of this system.

In the area of pathogen/host interactions, plant/pathogen interactions have often been at the cutting edge of advances in multicellular eukaryotic systems. An example of this is that the Team is applying their knowledge of plant/pathogen interactions to a study of animal dysentery caused by *Shigella flexneri*—an important area of research as dysentery results in over 1 million deaths each year. Preliminary data indicate that parallels to the plant/pathogen system exist; *Shigella* appears to transfer "effectors" to animal cells that suppress the induction of a specific miRNA.

This is a very promising start for a relatively new Team. So far a PNAS paper has been published, and as new members of the Team have the time to get established more high profile papers are likely.

Current funding is provided by several start-up grants, the Fondation Schlumberger and the ANR.

Assessment of the team's academic reputation and appeal

As noted above, this is a relatively new Team, but the Team leader has given several talks at conferences and seminars in Europe and one at an international meeting in Japan since joining IBENS.

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

Not applicable

Assessment of the team's organisation and life:

The team's projects, although spanning plants to humans, are focused on bacterial host interactions and the role of pathogen-injected "effectors," and thus the projects are well coordinated. There is an additional project to evaluate whether there are any epigenetic effects in the plant genome following exposure to a pathogen "ellicitor"; this is a logical collaboration with the team headed by V. Colot.

Assessment of the team's involvement in training through research

The students and postdocs are engaged in an exciting area of research and thus appear to have strong training opportunity.

Assessment of the five-year plan and strategy

As noted above, this team has a promising research plan with interesting preliminary results to pursue. Overall the team's research effort appears to be going in an interesting and important direction.

Conclusion:

- Strengths and opportunities:

Promising young team with high potential and extensive grant support.

- Weaknesses and threats:

The large size of the team could be a significant challenge to a young PI.

- Recommendations:

Consolidate the team.

Team 11: Evolution of Caenorhabditis

Name of team leader: Ms. Marie-Anne FELIX

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	1
N2: Permanent EPST or EPIC researchers and similar positions			
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	6	4
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	6	8	6

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team focuses on quantitative traits underlying evolution, using *C. elegans* and related species as models. Additionally, they study *Caenorhabditis* ecology, with emphasis on the interactions with natural pathogens. In contrast to developmental genetics, for which this model organism is very well known, the questions raised by the PI are fairly unique. The PI had the vision to use the potential of this organism for "evo-devo" studies, and consequently pushes the envelope, with remarkable success, to study developmental traits across environments and evolution.

Among the recent achievements is the quantitative demonstration that evolutionary differences in organ development can be explained by changes in the strength of the underlying signaling pathways and that phenotypic variation can be selected through the favorable effect of the underlying genetic alteration on a different trait. Moreover, the PI and colleagues described various *Caenorhabditis* pathogens such as microsporidia or RNA viruses. Remarkably, the virulence of the latter has been shown to depend on the natural variation in the robustness of somatic RNAi. These are major achievements addressing key questions at the interface between evolutionary and developmental biology, which have been widely recognized and appreciated. Consistently, the publication output has been very high, and the above findings were published in top journals (Developmental Cell, PLoS Biology, Current Biology).

Assessment of the team's academic reputation and appeal

The PI is a recognized leader in the field, which, in addition to the self-evident publication output, is reflected by numerous prizes, etc. The PI is recognized in the community as the person to contact regarding issues related to *C. elegans* ecology and natural variation. For example, during the last international *C. elegans* meeting, the PI organized a very popular and trend-setting workshop on the evolution, ecology, and genomics of *Caenorhabditis*. Consequently, the PI has a wide collaboration network. The PI has been recognized by a recent EMBO membership, the Award of the Bettencourt-Schueller Foundation and the CNRS Silver Medal.

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

Not applicable.

Assessment of the team's organisation and life:

It is excellent.

Assessment of the team's involvement in training through research

The PI trained a number of students (both undergraduate and graduate) and postdocs. The committee appreciates that at least two former lab members now have their own labs.

Assessment of the five-year plan and strategy

The future plans have a strong foundation in the past research. Addressing dosage requirements for key components of signaling pathways underlying vulval development, in more or less distantly related species, and taking advantage of forward and reverse genetic tools is a logical continuation of the past work. The second theme, the co-evolution of host-pathogen interactions, is more ambitious but perhaps offers more opportunities for breakthrough discoveries. The putative connection between sensitivity to a viral infection and the nematode RIG-I-like protein, as well as exploring the possible connection with epigenetics in the host-pathogen arms race, sound particularly exciting.

Conclusion:

- Strengths and opportunities:

The PI has an excellent record of cutting-edge research and is widely respected in her field. The research program is extremely compelling for both its intellectual richness and scientific excellence. The future directions are logical and promising.

- Weaknesses and threats:

None detected.

- Recommendations:

The arrival of this PI has been a major gain for the IBENS, particularly strengthening the environmental and evolutionary genomics section. The institute is advised to continue providing an attractive environment for this team by further supporting this section. This is particulary important considering the imminent departure of the only other C. *elegans* lab.

Team 12 : Development and Evolution of Neural Circuits

Name of team leader: Mr. Jean-François BRUNET

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	2	2
N6: Other contractual staff (without research duties)	1	1	1
TOTAL N1 to N6	7	6	5

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team has carried out pioneering studies of the transcription factor, Phox2b, which has key roles in formation of the visceral nervous system. During the last 5 years, the PI has published 18 papers, either as last author or co-last author with a long standing senior colleague from the group or in collaborations, most of them in high quality journals, such as 3 PNAS, PLoS Biology, Current Biology. The programme will continue to focus on the visceral nervous system, using Phox2b as an entry point to study the functions of specific visceral neurons, how they arise during development, and evolution of the nervous system. The team has successfully characterized several related functions of Phox2b, such as the etiopathology of the human disease CCHS, a deadly respiratory dysfunction caused by mutations of the PHOX2B gene in humans; mouse Phox2b gene mutants that delete specific visceral neurons (RTN/pFRG) are found to phenocopy some but, interestingly, not all aspects of this disease. The team has also analysed the transcriptional code of Phox2b-expressing medullary interneurons, how sensory neurons guide the migration of motor neuron axons and cell bodies during the formation of visceral circuits of the head, and its late role in neuronal differentiation. They also uncovered that Phox2b is required in the switch from somatic to visceral sensory neuron phenotype. In studies of homologous functions of Phox2b in other species, such as hemichordates and protostomes, evidence has been obtained for a more ancient centralised nervous system than previously thought. These are innovative studies that make significant conceptual advances and are indicative of a continued high productivity and international impact of this team.

Assessment of the team's academic reputation and appeal

The PI is known and respected worldwide for his excellent work. The team collaborates with different labs at the national and international levels that are more oriented to functional physiology. The appropriate combination of genetics and physiology has lead to an impressive number of excellent publications with high impact. The PI also has been invited to many international conferences.

The topic is important and highly relevant to theme of the unit. The PI has established excellent local and international collaborations with an array of experts in the field. These collaborations are very productive and useful for assessing his data in more clinical-related issues, such the understanding of the human CCHS pathology.

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

Not applicable

Assesment of the team's organisation and life & Assessment of the team's involvement in training through research

The group is quite small for the number of excellent publications. This implies that projects are well thought out with clear and focused lines of investigations and that management and teaching abilities are very good. Some of the senior post-docs have left and have obtained permanent positions in France. The PI now needs to increase his group in order to have a critical mass for his future projects. In the future he should also try to obtain tenured positions in order to have more permanent scientists in his lab.

Assessment of the five-year plan and strategy

The future projects are in line with the previous strategy of research and focuses on unravelling novel roles for Phox2b in the visceral nervous system. Since they previously found that ablation of the RTN is not sufficient to recapitulate the human disease, they envisage to use intersectional transgenic strategies to search for additional Phox2b+ respiratory neurons and analyse the transcriptome of dB2 neurons. This is undoubtedly an excellent genetic strategy to identify novel molecular players required in the differentiation of the desired nuclei and, more generally, to unravel further aspects of the physiology and pathology of breathing. The genetic and molecular strategy proposed by the PI is perfectly adequate to his goals. As suggested by the PI, uncovering the role of these neurons and their connectivity pattern might be also achieved using optogenetics, an approach that is well established at IBENS. Very interesting, but also laborious and challenging, is the approach of using rabies viruses to elucidate the connectivity of interneurons in the ventrolateral hindbrain. The novel approach of killing cells by using a mutated form of the sodium channel ASIC2a is very promising. The potential role of neuron-neuron interactions is very interesting and innovative, and promises to be an informative area to explore. With regard to the transcriptomics screens, the strategy will depend upon what is found. Nevertheless, a good perspective of the possibilities is described, and this work is clearly very important as a basis for the future functional studies.

Conclusion:

The PI has clear-cut and focused ideas on how to pursue the projects and use a series of state-of-the-art genetic and molecular technologies. These will be crucial for unravelling new mechanisms in the connectivity and physiology of visceral motor neurons. The proposal is well written, clear and ambitious while remaining realistic taking into account their previous achievements

- Strengths and opportunities:

The application of mouse genetics together with cutting edge physiological and molecular approaches is very impressive. The molecular approaches will, most likely, result in the identification of novel genes and transgenic lines that will be useful to the scientific community. The opportunities have been well identified by the group.

- Weaknesses and threats:

The aims are ambitious and involve major efforts. It is difficult to predict how successful the transcriptomics and subsequent functional studies will be, but these are definitely important to undertake.

- Recommendations:

The PI may consider increasing the size of the team to achieve all goals.

Team 13 : Development of the Nervous System

Name of team leader: Mr. Patrick CHARNAY

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions		1	1
N2: Permanent EPST or EPIC researchers and similar positions	4	3	3
N3: Other permanent staff (without research duties)	2,5	2,5	1,5
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3		
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	9,5	6,5	5,5

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	3	
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 PI is an international leader in developmental neurobiology who discovered roles of the transcription factor Krox20 in hindbrain segmentation and in development of myelinating Schwann cells in the peripheral nervous system (PNS). His current studies focus on two topics: how Krox20 expression is regulated in the hindbrain, and roles of Krox20 at the interface of the central and peripheral nervous system.

With regard to segmental gene regulation, detailed in vivo dissection of regulatory elements of Krox20 has revealed positive and negative inputs on the segmental expression of Krox20. They also found novel repressors (the Nlz factors) of the Krox20 auto-regulatory loop, which are activated by class 1 Hox genes, allowing them to design informative mathematical modelling of the transcriptional circuitry of Krox20 expression. In related work, the lab found that FGF signalling sets the boundaries of the Krox20 expression domains in a concentration-independent manner, suggesting new ideas about how FGF acts in spatial gene regulation.

In the PNS studies, the group showed that Krox20 acts to segregate Schwann cells and central glia. This is a very interesting finding, also relevant to human disease and future therapeutic applications. Other studies showed that Schwann cells specified by Krox20 are part of the nociceptive sensory neurons in the dorsal root ganglia. These cells, which can also be identified by a novel marker (Prss56), have great potential in regenerative medicine, as they seem to act as neural stem cells not only in the adult subcutaneous nerves, but also in the two adult neural stem niches. These are exciting findings that suggest novel concepts, constitute a major advance toward the development of regenerative therapies, and also raise new questions about the underlying mechanisms.

The group has made excellent progress in the past few years and has been highly productive in terms of publications: a total of 38 articles from the group plus a number of papers in collaboration, including Development (3 papers), PNAS (1), Developmental Biology (3), Mechanisms of Development (3), and J. Neuroscience (2).

Assessment of the team's academic reputation and appeal

The PI is known worldwide for his excellent work, has received many prestigious awards and is also an EMBO member. He attracts many talented young people and the majority of his previous post-docs and PhD students now have positions in research. He is also part of several expert committees in France and abroad and his research is regularly funded by ANR and other agencies.

The topics being studied are highly relevant to the theme of the Unit and important in the context of the field. Furthermore, the PI collaborates with many local, national and international high-profile scientists. He is the current Coordinator of the Developmental Biology Section of IBENS and has recruited in recent years high profile young scientists that are doing very well at the Institute.

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

Not applicable

Assessment of the team's organisation and life

The team is composed of 3 senior scientists (2 DR2 and 1 CR1), 3 post-docs, 2 PhD students, 2 IE (one is half-time) and one technician. Thus, the critical mass and the experience of his collaborators are good enough to ensure proper advancement of the proposed projects. Two major collaborators are senior scientists who have worked for years in his lab and are instrumental for the success of the projects and for the training of PhD students and young post-docs. There should be a reflection about the career development of the senior scientists.

Assessment of the team's involvement in training through research

The team has trained several PhD students and post-docs that have now their independent positions. In the last 3 years, 5 PhD students obtained their degree and are co-authors of at least one publication. At present the team could accept more PhD students since the number of tasks proposed in the proposal is very high and the number of senior scientists and post-docs is high enough for allowing proper training and supervision.

Assessment of the five-year plan and strategy

The proposed future studies continue the same two lines of research. Studies of Krox20 gene regulation in the hindbrain will address, through a series of in vitro and in vivo studies, how Nlz acts in repression and how FGF signalling sets the position of the r3/4 boundary. The group aims to use state-of-the-art approaches, such as Cre-lox mouse genetics, FISH analysis on hindbrain sections, Chromosome Capture, ES differentiation towards an r3 fate and studies on epigenetic chromatin modifications including ChIP experiments. This will unravel the basis of functional cis interactions between distant enhancers that have been uncovered. These and other studies will be used for further modelling of Krox20 regulation that underlies hindbrain segmentation. They are all logical extensions of the previous work that may give new insights of wider significance for gene regulation.

The other line of work will follow up the discovery that Prss56-traced cells are part of the adult neural stem cell niches. The group will investigate their properties in the CNS and their regeneration potential in the PNS by using a combination of in vitro assays and in vivo transplantation approaches. The group aims to characterize the morphology, molecular profile, self-renewal and multipotency of Prss56-traced cells in the SVZ. Finally, they aim to characterize their clonal potential by generating a novel long-term fate mapping Prss56 mouse allele that could be used in various animal models with CNS and/or PNS lesions. These are exciting experiments that are very likely to give important new insights into the biology of adult neural stem cells. In light of the great potential of this new line of work, the group is no longer working on roles of Krox20 in CNS/PNS segregation, but this is being continued by a collaborator. The committee agrees with this refocusing.

Conclusion:

This is an excellent and exciting programme that is likely to give important insights into mechanisms of spatial gene regulation and into stem cell biology. In addition, the research has many aspects dealing with regenerative therapies that are nicely explained in the proposal.

- Strengths and opportunities:

Important strengths of the programme are that it focuses on key questions using incisive approaches. The opportunities have been well identified by the group.

- Weaknesses and threats:

No significant weaknesses were identified, but it is not always clear how the work will be subdivided amongst the group members. The aims are numerous and involve many different approaches.

- Recommendations:

To recruit more young scientists, such as PhD students and post-docs. There should be a clear scientific program and career perspective developed for the senior scientists in the group.

Team 14 : Wiring the Forebrain During Embryonic Development

Name of team leader: Ms. Sonia GAREL

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	3	3
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	5	5	5

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	3	
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 research program is focused on deciphering the intercellular interactions guiding the placement and wiring of neurons in the developing forebrain. Further, they aim to understand how these neural circuits, once established, are maintained and remodelled during postnatal life. This work has led to the discovery of how a selective subset of migrating neurons establish a guidance system to facilitate the appropriate growth and organization of thalamocortical and corticothalamic axons in the developing brain. In the last 2 years the team has dissected the molecular mechanisms and pathways guiding these migrating cells to their proper location. The group found that the repellent guidance molecule Slit2 is required in orienting the migration of these cells in mammalian and non-mammalian species, although in slightly different manners. Moreover, through a collaboration they found that so-called corridor cells impact on the topography of thalamocortical projections and that this precise organization is controlled by two matching gradients of Slit1 and Netrin1 guidance cues. Recently, the team also found that the signaling system controlled by Sema3E/PlexinD1 is involved in regulating the timely progression of corticothalamic axons towards their reciprocal thalamic nuclei ensuring also proper encounter with thalamocortical axons. This innovative and very competitive work has been published in high-ranking Journals, such as in Neuron (2) and Current Biology (1). These studies have provided conceptually novel insights into neuronal wiring in the brain and lead to a better idea on how the major reciprocal connections between cortex and thalamus in the mammalian brain are precisely controlled in time and space.

Assessment of the team's academic reputation and appeal

The PI is an outstanding young scientist well known for work on neuronal wiring in the developing brain and discoveries are at the forefront of the developmental neuroscience field. The team leader has been extremely successful and productive in the last few years by publishing in high impact journals and being invited in important national and international meetings. The PI is well recognized internationally as proven by multiple invitations to important conferences in the field. Prestigious grants have been obtained, such as an HFSP research grant, the Avenir French starting grant and recently she has been nominated as an EMBO Young Investigator.

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

Not applicable

Assessment of the team's organisation and life

This recently established team is composed of 3 post-docs, 3 PhD students and 1 technician. This is a very balanced group in which post-docs and students can work together on similar projects, as presented in the activity report. The size of the group is also appropriate for having an interesting mass and for proper management. In the next future, the PI should try to obtain more tenured positions, so that the load of salary costs can be decreased from her grants.

Assessment of the team's involvement in training through research

The PI is currently training 3 PhD students and has also been involved in teaching duties, such as giving occasional classes to Master students and she is also responsible of a course of undergraduate students.

Assessment of the five-year plan and strategy

The PI proposes several inter-related new directions. The future studies of the team continue in the same direction, but also challenge new interesting avenues. Overall, the main novelty of the research is the focus on functional studies in post-natal and adult brains. First, they will continue to characterize the development of corridor neurons and identify how axons interact with them to establish the correct projection pathways. The team has fate mapped corridor cells and aims to kill them genetically using conditional ablation in vivo.They will use behavioral approaches to directly test the function of their derivatives (amygdala nuclei) and to investigate the functional consequences of an abnormal cortical barrel field map in somatosensory cortex.

An excellent combination of mouse genetic tools and innovative cell biological tools such as microfluidic devices will be utilized to investigate how distinct axons interpret multiple guidance cues.

Second, earlier work on embryonic neuronal migration has lead to the identification of a second phase of migration of Cajal-Retzius cells in early post-natal brain that was not characterized before. The PI has identified a mouse mutant (Ebf3 null) that will be used to explore the significance of this second phase of migration for neuronal allocation and circuit formation/maintenance in cerebral cortex.

Lastly, the characterization of microglia in the developing brain suggests potentially important roles for these non-neural cells in neuronal migration and axon guidance. Using mouse models with impaired microglial generation (Pu.1 mutants, Csfr1 pathway inhibition), the plan is to decipher these roles and characterize the underlying signalling pathways. The microglial developing neuron interplay is an unexplored aspect of brain development and is worth putting extra efforts. The studies on the interactions between the immune cells and neural cells in the developing brain are likely to lead to novel insights into neuronal developmental mechanisms and has high clinical relevance due to the role of microglia in prenatal inflammation. There are many examples showing that factors and cells cooperate in similar ways in neuronal and immune cells, and the interplay between these two disciplines can be very attractive for discovering new therapies in neurological diseases.

Conclusion:

The PI leads an excellent research group focused on furthering our understanding of the mechanisms underlying neuronal wiring in the brain. The success of the research resides partly in properly forming young students and post-docs, in focusing on precise key biological questions using incisive approaches and in collaborating with the right national and international teams. The future research program is outstanding and there is no doubt that the PI has the right capacities and the proper critical mass to do well in the next five years.

- Strengths and opportunities:

The application of mouse genetic tools in tandem with cutting edge cell biological methods and in depth brain development analysis is impressive.

- Weaknesses and threats:

Some of the genetic approaches to manipulate corridor neurons or intermediate targets (in aim 1) may also affect other aspects of cortical development that may impact cortical wiring indirectly. Consideration of how to deal with these possibilities will be useful. Furthermore, the type of behavioural tasks the team plans to use is not clear. The PI will need to find an appropriate collaborator to implement this approach.

Considering the importance of Cajal- Retzius cells for the emergence of cortical circuits, the studies on the characterization of second phase of migration of Cajal- Retzius cells (in aim 2) might benefit from exploring the importance of this phase for overall circuit development/activity using electrophysiological methods.

Aim3 may benefit from inclusion of live imaging studies to explore the nature of axon or migrating neuron-microglial interactions in the developing brain.

- Recommendations:

No specific recommendations.

Team 15 : Mitosis and Vertebrate Neurogenesis

Name of team leader: Mr. Xavier MORIN

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
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.)	2	3	2
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	3	5	3

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	1	
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 studies a very important topic in developmental neurobiology: the regulation of cell division plane that is believed to determine proliferation vs differentiation decisions of neural progenitor cells. This topic is being studied mainly using the chick model, and continues the studies initiated at the Developmental Biology Institute in Marseille prior to arriving at the IBENS. These build upon the discovery that LGN, a G-protein signalling regulator, regulates spindle orientation. When this is defective there is a mispositioning of proliferating cells rather than a change in fate; this reflects a major controversy in the field regarding the relationships between plane of cell division and fate. To help clarify this controversy they are characterizing in detail how spindle rotates to its final orientation and have gone on to identify additional regulators (NuMA) of spindle movement, described in an excellent J Cell Biol publication in 2011. To systematically address the causal relationship between spindle orientation and cell fate determination and avoid complications resulting from using multiple different tools and models, the PI has developed a Cre inducible dominant negative LGN mouse model. However, the exploitation of this model to study roles in fate determination has not (yet) been successful for technical reasons. Recognizing the limitations of the chick model to image and characterize the regulators of spindle orientation, the group is developing a micropattern/ optogenetics-based on in vitro cell culture model suitable for RNAi screens. Finally, in collaborative work the group is making use of the Brainbow technique for imaging and lineage tracing in the chick. This team has made a promising start, with several publications, one in a top journal (J Cell Biology), as well as several reviews in top journals (e.g., Dev Cell). While not all of the projects have been successful so far, the efforts made to develop new approaches that may overcome previous limitations are appreciated. The team has established very productive collaborations with leading experts, in particular on the imaging studies.

Assessment of the team's academic reputation and appeal

This junior group is developing an excellent reputation through its high impact publications in a competitive field.

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

Not applicable

Assessment of the team's organisation and life & Assessment of the team's involvement in training through research

The PI has been team leader since 2009, with a present team of 2 postdocs, a student and one technician. The team leader is active in graduate teaching and other aspects of student training.

Assessment of the five-year plan and strategy

In future studies, aimed at ultimately understanding how neural progenitors modulate their symmetric vs. asymmetric divisions in vertebrates, the team will analyse in more detail the dynamics of LGN complex and the potential role of actomyosin during neuroepithelial proliferation, use an in vitro system of oriented cell division to screen for LGN complex assembly and downstream effectors, and attempt to use optogenetic manipulations to explore molecular mechanisms underlying spindle orientation. In addition, experiments will be pursued (using manipulation of Inscuteable, LGN, and Par3) to clarify contradictory findings on the role of cell division plane in fate determination, including whether these reflect differences between mouse and chick. These studies are important to gain insights into complex relationship between cell fate determinants, regulators of spindle orientation, and cell polarity pathways during progenitor differentiation. These are logical extensions of the previous work that seek to address key questions regarding the mechanisms and role of regulating cell division plane with innovative technologies. As discussed in the conclusions below, there are some strategic issues that need to be carefully considered.

Conclusion:

This junior team has made an excellent start.

- Strengths and opportunities:

A significant strength is the combination of functional manipulations and imaging, and the efforts to develop new approaches in recognition of the limits of the chick model.

The various micro pattern/ optogenetics/ Brainbow technique based assays being developed are technologically cutting edge and may bring unexpected new insights to this field. This is undoubtedly a worthwhile effort for the field and for the lab.

- Weaknesses and threats:

Given the importance of the topic, this is - not surprisingly - a highly competitive area. It is encouraging that this group has already made important contributions, but the next phase of the work will be crucial, and it is very important to consider the strategies carefully. In particular, it is essential to critically assess whether the in vitro model does faithfully reflect key aspects of the in vivo situation such that the screens will find relevant regulators. Although the screens are likely to yield important new molecular insights and are elegant and rigorous in their design, a balanced effort and contingency plan needs to be in place to safeguard against potential failures of this high risk-high reward strategy.

While the PI's decision not to pursue inducible DN-LGN mouse model in light of other more promising leads is a rational one, efforts may be undertaken to try and get some output from the investment. For example, this model could be tested (in utero or in vitro) with viral Cre vectors, including those that express short acting Cre, instead of the time-consuming crosses with Cre lines.

- Recommendations:

It is encouraging that efforts are being made to use the mouse model which is more amenable for advanced genetic manipulation than chick.

The assay and technology development efforts are excellent and should be continued with necessary safeguards.

Efforts to increase senior authored research publications in high profile journals will help solidify the PI's position in the neurogenesis field.

Team 16 : From Development to Behaviour

Name of team leader: Mr. Frédéric ROSA

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	5	5	5
N3: Other permanent staff (without research duties)	2	2	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	1	1
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	9	8	7

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	4	
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	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The group consistently produces high quality work which is published in journals with high impact factors (Current Biology, Development, PNAS). Their studies adress three diverse topics: mechanisms of collective cell migration in the prechordal plate; development of taste buds and related work on feeding behaviour; and the role of specific RNA binding proteins in muscle development. This diversity is due to the first two topics being the focus of two lab members who are developing towards more independence. A number of interesting findings have been obtained on all three topics. Particularly notable is the recent demonstration that Fgf signaling plays a role in controlling the formation of taste buds, and the work on collective cell migration which has implicated E-Cadherin, Dsh/PCP and Rac1. Interestingly, it has been shown that these components act in a distinct manner from that found for other cell populations that undergo collective cell migration. The quantity of output is acceptable but could be improved in view of the number of tenured scientists.

Assessment of the team's academic reputation and appeal

The team is well regarded internationally, and this is reflected in the publications, grants and collaborations.

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

Not applicable

Assesment of the team's organisation and life

The organization of the team is rather unusual, since as mentioned above it covers three diverse and unlinked topics. The first two topics are driven by tenured staff researchers approaching independence, while the PI is focused on the last topic. Each of the topics have some synergy with other groups at IBENS working on development or sensory physiology in zebrafish. This is an interesting mix, although the variety of projects may decrease the effort that can be focussed on each topic. The team should make an effort to clarify the scientific strategies and the team structure in keeping with the career planning of the tenured scientists.

Assessment of the team's involvement in training through research

The team is actively involved in training, currently housing 4 PhD students and a Masters student. It is also notable that the leader provides members of the team with the support and encouragement to develop their own projects. Training is clearly provided with thought and care.

Assessment of the five-year plan and strategy

The future plans continue along the three main lines of enquiry that have been pursued over the last few years. These plans are cogent and interesting, and the group is likely to continue to produce original work on all three topics. The project investigating taste sensation at the functional level appears particularly novel.

Conclusion:

This is a productive group that studies important and interesting topics in developmental biology.

- Strengths and opportunities:

The group uses sophisticated tools and approaches to analyse gene function and cell behaviour in the amenable zebrafish model.

- Weaknesses and threats:

It isn't clear how the overall plans might relate to the proposed growth to independence of the younger tenure members of the team, in particular whether they will remain permanent members of the group. Due to the diversity of topics, there is a risk that less effort is being made on each of the studies.

- Recommendations:

Short term: To carefully plan the amount of efforts dedicated to each project and to maintain the synergy with other IBENS groups. Long term: Reorganize and focus considering the career planning of the tenured scientist.

Team 17 : Cilia Biology and Neurogenesis

Name of team leader: Mr. Nathalie SPASSKY

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	2	2	2
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2	2
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	5	5	5

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	1	
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 research program aims at understanding how the primary cilium function as a sensor that integrates external information to regulate neural stems cells during brain development and adult neurogenesis.

Key findings reported in recent publications include: defects in human cerebellar formation resulting from cilia dysfunction in Joubert (JS) and Meckel Syndrome (MS) patients, hypermorphic ciliogenesis in Huntington disease affecting brain homeostasis, identification of ependymal cilia as a link between hydrodynamic forces and planar cell polarity pathway during CNS development, and characterization of a ciliary membrane domain (ciliary pocket) critical for membrane trafficking in cilia. These are compelling, novel observations that have changed the way we think about the roles of cilia during development and adulthood, and importantly the involvement of cilia in human diseases, since they helped identify cilia-specific pathways impaired in neurodevelopmental and neurodegenerative disorders.

The PI has published several landmark papers in high profile journals (PNAS, Nature Cell Biology). These papers represent significant conceptual and technical advances.

The team leader has established several local and international collaborations with experts in the field. These collaborations are very productive and have lead to innovative technique development and fundamental observations in ciliary biology.

Assessment of the team's academic reputation and appeal

The team leader is a recognized leader in the field of cilia biology and developmental neuroscience.

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

Not applicable

Assessment of the team's involvement in training through research

The team leader has been a group leader since 2010. The PI currently lists 1 staff scientist, 1 engineer, 2 post-doctoral fellows and 2 PhD students. The scientist and engineer have been with the lab since 2012. Other lab members have been on board for the past 2 to 3 years. The post-docs do not yet have first or second author publications. The current size of the group is appropriate for the work being done now, but as future studies expand (especially on ependymal cell development) addition of post-docs/graduate students may be considered.

Assessment of the five-year plan and strategy

The proposed future research will systematically characterize cilia dynamics and behaviour during neural progenitor proliferation and differentiation and test the effects of cilia ablation/elongation on progenitor cell proliferation and neural stem cell division during corticogenesis. Their approach of labelling either cilia or centrioles with GFP-expressing constructs will be very useful for gaining insights into the biogenesis and dynamics of primary cilia during cortical development in normal and mutant conditions. Furthermore, they will explore the emerging importance of ependymal cells in neural stem cell niche by evaluating the importance of cilia in the specification and differentiation of these cells in the cerebral cortex. With the help of their ependymal cell culture assay and RNA sequencing, they aim to identify, and then functionally test, novel genes involved in specifying NSC towards an ependymal fate. This is an important step since very little is known about how multi-ciliated ependymal cell differentiation is regulated.

Ependymal cilia and their activity are clearly important for proper adult neurogenesis and as such these studies are timely and likely to yield high impact observations. Several excellent mouse genetic tools, collaborations with experts at IBENS and elsewhere, cilia imaging and interesting biophysics approaches are in hand to ensure the success of these studies. However, as noted below, some potential pitfalls need to be considered carefully.

Conclusion:

This is an outstanding research group making vital contributions to our understanding of the importance of cilia signalling for development and in neurological disorders.

- Strengths and opportunities:

A significant strength is the combined application of genetic tools and imaging methods to decipher the importance of primary cilia in brain development and dysfunction.

The use of advanced imaging and modelling to selectively study cilia dynamics and functions are elegant approaches to dissect the mechanisms relevant to cilia signalling.

- Weaknesses and threats:

It will be important to explore or attend to the cilia specific versus extra-ciliary functions of some of the molecular models that will be utilized to study how primary cilia regulate neural stem cells. For example, Ift88 has known non-ciliary functions and some effort should be made to distinguish such functions in the proposed studies on cilia and neural progenitor development. Moreover, it will be important to pinpoint whether the abnormalities the team has found in cilia-dependent mutants and/or overexpressed/knock down cells are due to defects of primary non-motile cilia (and thus dependent on Shh- or other signalling pathways) or of motile cilia involved mainly in regulating the flow of key molecules contributing to the NSC biology.

- Recommendations:

Effort should be made to clearly distinguish ciliary versus non- ciliary signalling that may underly changes in neural stem cell behaviour being analysed in the proposed studies.

The group has established a number of valuable and productive translational collaborations. The future scientific program should continue to build on these efforts.

In light of the importance of the work, additional effort to present at high profile international meetings such Gordon conferences or CSHL meetings is worth considering.

Team 18 : Cerebellum Group

Name of team leader: Mr. Boris BARBOUR

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	2	1
N2: Permanent EPST or EPIC researchers and similar positions	4	4	3
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	5		
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	11	7	5

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	4	
Theses defended	2	
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	3	4

• Detailed assessments

Assessment of scientific quality and outputs

The group's research is clearly focused on the understanding of cerebellar function at multiple levels of investigation, from molecules to behaviour. The research is rooted in the classical study of synapses and networks (in vitro an in vivo) but is of broad scope, novel and imaginative. For example, the group has pioneered the in vivo use of tetrodes to record neuronal ensembles in the cerebellar cortex. The group has a reputation for its innovative research.

Substantial progress has been made over the period 2008-12 and several of the studies published in this period have been groundbreaking – such as those characterising spillover of glutamate from climbing fibres (CFs), Purkinje cell (PC) synchrony, Golgi cell coupling, and high-frequency transmission at PF-PC synapses. Some of the avenues of research described are very much 'in progress' and not yet fully realised. Of these, the use of QD sensors for calcium microdomains and the use of a bacterial glutamate binding protein for the identification of glutamate spillover involve the development of novel methodologies that promise significant advances. Paradigm shifts in understanding of cerebellar function are likely with the identification of mechanisms underlying Purkinje cell resonance and ephaptic coupling at the cerebellar pinceau (specialised contacts between basket cells and PCs). Particularly intriguing are the in vivo approaches that have identified various oscillations in mossy fibres and Purkinje cells and described the functional organization of cerebello-cortical loops.

Since 2008, team members have co-signed 23 articles out of which 6 were as lead authors (Neuron, 2008; PNAS, 2009; 2 Neuroscience, 2009, J. Neurosci 2011, comment in Neuron, 2013). A review in Neuroscience is a "Highly Cited Paper" (last 10 years) according to the ISI Web of Knowledge.

Assessment of the team's academic reputation and appeal

The team has a well-established reputation in the field of cerebellar research both at synaptic and network levels of analysis. The team's excellent reputation and appeal is also indicated by the fact that it was able to attract highly qualified research scientists. Group members have been invited to organise and/or participate in various teaching courses on electrophysiology and imaging, for example, in Argentina (satellite to the Argentinian neuroscience conference), England (Plymouth MBL Microelectrode Techniques course) and France (ENP Spring School).

The group leader is member of the editorial board of two high quality journals (The Journal of Neurophysiology and Nature Scientific Reports).

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

The group has contributed to breakthrough technical innovations that include the development of nanodomain calcium sensors and use of a bacterial protein as a glutamate buffer.

Assessment of the team's organisation and life

The group is multidisciplinary in nature but is organised with a clear and logical scientific objective. Established collaborations with groups within and outside the IBENS attest to a broad and collaborative outlook.

The group leader is the head of the IBENS Neuroscience Section, which indicates a strong commitment in the life and organisation of the Institute.

Assessment of the team's involvement in training through research

The group leader is heavily involved in the organisation and teaching of courses in Masters programs and in the ENP Spring School.

The team is currently training 4 PhD students and 5 post-docs.

Assessment of the five-year plan and strategy

The five-year plan of the Cerebellum Group is a logical and credible extension of the ongoing work and is aimed at linking synaptic function and network dynamics – the primary focus is on 'plasticity'.

While parts of the in vitro work might appear relatively 'safe', being deceptively simple in concept, in reality they are quite demanding. The proposed work involves not only electrophysiology, but also quantitative immunolabelling (variations in synaptic weights and markers) or in vivo transfection and protein chemistry (NMDAR and NO signaling at the PF-PC synapse). In addition, testing the role of climbing fibre spillover in controlling PF-PC plasticity requires validation of the glutamate binding protein. Although challenging, together these approaches promise significant advance in the understanding of the induction and role of cerebellar synaptic plasticity.

Particularly intriguing and ambitious are the proposed in vivo studies aimed at characterising cerebello-cortical loops in normal and pathological conditions. These will combine cortical stimulation with cerebellar recording and imaging as well as optogenetic stimulation of Purkinje cells and other sites within cerebello-thalamic-cortical pathways. Integration of emerging optogenetic techniques that are already being exploited in cerebellar research is a logical move. The only comment here would be that, as presented, there is no explicit plan to integrate in vitro recordings within the in vivo projects – if appropriate these might bring an added weight/dimension to any study.

Overall, the proposed plan is challenging, original and consistent, and has an appropriate level of risk. It appears feasible. It is predominantly aimed at 'fundamental' research, but the plan to assess therapeutic potential of intervention in cerebello-cortical loops in models of Parkinson's is to be welcomed. Several aspects of the proposed studies are rather open-ended but we feel that the group is sufficiently dynamic to take advantage of different opportunities that may evolve during the research.

Conclusion:

This is an excellent multidisciplinary group with a good balance of tenured scientists, postdoctoral fellows and PhD students. Past research and future research plans are highly focused and contribute to the international recognition of the group regarding the operation and function of the cerebellar network.

- Strengths and opportunities:

The group's strength lays in its experience, its rigorous, quantitative approach and its situation within within a powerful multidisciplinary research environment at IBENS.

- Weaknesses and threats:

There are no obvious weaknesses, and the only threat is strong competition form other groups addressing similar topics with similar tools.

- Recommendations:

This team is successful and should maintain or improve its ambition. The investigation of cerebellar dynamics in vivo and their link to in vitro synaptic physiology is very important.

Team 19 : Coding Sensory Information in the Rat Cortex

Name of team leader: Mr. Laurent BOURDIEU

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	2	3	3
N3: Other permanent staff (without research duties)	0,25	0,25	0,25
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	1
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	3,25	4,25	4,25

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
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	0	
Qualified research supervisors (with an HDR) or similar positions	1	3

• Detailed assessments

Assessment of scientific quality and outputs

This is a relatively small team, which is working on in vivo imaging of multineuronal activity and the associated technology of multiphoton microscopy. The scientific theme of the team – coding mechanisms in the cortex – is an important one. The scientific output has been relatively sparse over the last 4 years, with just one or two publications in good quality Neuroscience journals but no publication in journals with impact factors at or above 10. The 2011 paper in Journal of Neuroscience investigating the representation of whisker stimulation in the rat barrel cortex is very good, demonstrating a protracted development of the functional map associated with direction selectivity in the barrel cortex. The development of a device for probing the whisker-to-barrel system with natural-like stimuli is also an excellent innovation, and in collaboration they have uncovered an intriguing spatial segregation of neurons detecting correlated defection of all whiskers and neurons detecting local deflections of individual whiskers.

In general, the team's has focused on improving the technologies associated with multiphoton imaging, and this work has been published in specialist journals, although some of these (such as Optic Express) are highly regarded. The use of adaptive optics to correct for the effects of scatter so as to image deeper in nervous tissue holds great promise for solving the dispersion problem and is a general strategy being explored by a number of groups around the world.

Assessment of the team's academic reputation and appeal

The group has a good national reputation (the group leader is frequently invited to give talks in France). International reputation is less strong. During the reporting period, the group leader was invited twice abroad (India and Argentina). At the moment, the reputation of the team mostly relates to its development of novel optical tools. For 2008-2012, the team has been involved in several national collaborations (most of them concerning technical aspects of their research activity). This is demonstrated by their participation in several French grants, including 3 ANR grants. The funding track record of the group is therefore very good. The team is successful in attracting talented scientists. Tthis team does not yet have a pronounced international reputation, but that it has the potential to get there.

The group leader is a member of the scientific committee of the "Brain-machine interface" research program from FRM, IRME and ICM., and is involved in the development of optical tools for Neuroscience.

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

The PI has established a collaboration with a non-academic partner.

Assessment of the team's organisation and life

The team does not appear to have the worforce to make important advances on both the scientific and technological fronts. The arrival of new personnel strengthens the technology side, as judged from recent work of the person in question. It will be important for the group to develop collaborations that attempt to make use of the technological work in answering specific scientific questions. They have fruitful collaborations, and the application of the Deep-OCM microscope to study myelination in the mouse cortex appears to provide good opportunities to further this.

Assessment of the team's involvement in training through research

The team currently includes two PhD students, and four have completed their PhD over the last 5 years. The group has three Masters students. The teaching load of the group leader is quite impressive (30 hours/year in the ENS L3 program). He is in fact an associate Professor at the ENS.

Assessment of the five-year plan and strategy

The 5 year plan is ambitious because it covers three broad areas: coding in the somato-sensory cortex, the processes of demyelination and remyelination and optical developments such as improvements in deep-tissue imaging in awake animals. The projects are a continuation of the previous research activities of the group, but they will need to be careful not to disperse their efforts. The intent to develop all aspects of the proposed project within excellent national collaborations will hopefully provide the critical mass to make each project productive. In general, it would have been good to see within the plan more direct connections between the scientific questions and technological developments beyond a common basis in multiphoton microscopy. The idea of developing a "double endoscope" system to image two distinct cortical areas is original and potentially of great use, and may be an innovation that would put the group on the international map if it were applied to a good question. Developing the use of AODs is a competitive field in which several groups around the world are developing similar technologies.

Conclusion:

- Strengths and opportunities:

The team has several important strengths, including good funding, excellent technological expertise and productive collaborations within France. They also have interesting observations on the coding of whisker stimuli in the barrel cortex which should provide the basis of scientific work.

- Weaknesses and threats:

Publication record of the team and it's international visibility should be improved.

- Recommendations:

The PI should give careful thought as to how much of the team's efforts should be focused on pursuing scientific questions with existing technologies as opposed to developing new technology. One strategy may be to focus on technological developments for Neuroscience and pursue collaborative projects with groups that are international leaders and have a good track record of publication. Another strategy may be to incorporate into the team post-docs or students who are primarily motivated by the scientific questions and who will focus on these while taking advantage of the technical expertise within the lab. Increase team visibility.

Team 20 : Inhibitory Transmission

Name of team leader: Mr. Stéphanne DIEUDONNE

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	4	4	4
N3: Other permanent staff (without research duties)			
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	1
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	5	5	5

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	3	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	2	3

• Detailed assessments

Assessment of scientific quality and outputs

This group was created in 2006 and studies synaptic physiology and in particular inhibitory function at multiple scales of investigation, from vesicular loading to dendritic integration and network function, mostly in three different structures (hippocampus, cerebellum and thalamus - the cerebellum being the most commonly studied structure in the group). Recent research activity has been directed towards network level analysis, which required the development of appropriate experimental tools and approaches, including the development and implementation of cutting-edge imaging devices.

During the past five years, the team has made several original and important findings concerning the regulation and dynamics of inhibitory (GABAergic and glycinergic) transmission in different brain areas, as well as the functional organization of cerebellar (but also thalamic) inhibitory circuits. Among these important results: they have uncovered a role for glutamine transporters in fueling GABA supply at hippocampal GABAergic synapses in cultures; using fast optical interrogation of cerebellar networks, they have revealed a novel feedback excitatory connection onto Golgi cells and dissected the relative weight of feedback vs. feedforward excitatory circuits onto these cells; shown that mGluR2 expression segregates between two types of UBCs regarding GABAergic vs. glycinergic contribution to inhibitory transmission; discovered an intriguing pontine glycinergic input to the thalamus with a potential function in regulating sleep-wake cycles. The development of an AOD-based RAMP microscope for ultrafast imaging is also an important part of the recent activity of this team.

The number, quality and impact of publications, communications and other outputs by the group is very good. The team has produced 3 reviews and 10 original publications between 2008-2012 including publications in Neuron (1) and J. Neurosci (2) as lead authors. Thus the primary research studies are published in excellent/very good journals.

Assessment of the team's academic reputation and appeal

The team was able to attract highly qualified research scientists and students and recruited recently a senior tenured scientist.

The team leader has a well established reputation in the field of cerebellum research and in the development of optical approaches for interrogation of brain circuits. Research from this team has identified new principles of organization and operation of inhibitory circuits. These are of importance given the major role on inhibitory transmission in controlling and shaping neuronal network dynamics.

The team is involved in several international and national collaborative projects (see below) and has an excellent track record of grant acquisition.

The PI is regularly invited to give lectures at prestigious international meetings as well as in prominent Universities. The PI is indeed an international reference for his contribution in developing new optical approaches for brain imaging; the PI is also recognized in the field of cerebellum research (one invitation to Gordon Research Conference in 2011).

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

The team leader has a strong record in the development and dissemination of fast optical imaging techniques. For that, he set-up a joint production with a non-academic partner, for the design of a RAMP microscope that allows for fast multiphoton imaging of physiological activity signals in vivo.

A patent was obtained concerning the "acousto-optic control software and digital multiphoton interface".

Assessment of the team's organisation and life

While only one PI was presented as team leader, de facto two PIs are co-leading the group, as indicated on the IBENS website. The team has a broad reservoir of expertise from 4 tenured scientists. The two junior tenured scientists have integrated the group recently (2011), which could explain the apparent imbalance between the number of tenured PIs and that of students (2) and postdocs (1). The group has no technical support.

One of the PIs is very actively involved in the life of the Institute since he is heading the user committee of the IBENS imaging facility (decisions on future investment, platform management, grant coordination for the platform), being very successful in raising grants to fund the platform.

The group has established several collaborations on different aspects of their research with international leading experts, as well as with IBENS teams. The distribution of the various research projects between PIs of the team should have been more clearly specified and supported by a rationale for chosing the dual team leader model.

Assessment of the team's involvement in training through research

The prinicpal team leader is involved in various teaching programs, through the participation to international summer schools (ex: Frontiers in Neurophotonics, EMBO courses), as well as the lecturing in the master program of the ENS and UPMC. Since 2008, the group had 3 post-doctoral fellows (currently one in the group) and 4 PhD students, 2 of them defended their PhD.

Assessment of the five-year plan and strategy

For the next five years, the team has presented a strong proposal focusing on the examination of the impact of the temporal dynamics of excitatory and inhibitory conductances in shaping neuronal information transfer function. These projects represent a further step in their endeavour to dissect the regulation and network integration of inhibitory circuits. Out of the 5 proposed projects, the first 2 are the logical follow-up of the group's previous results. They all build up on the group's established expertise. These projects will all implement several cutting-edge technologies in their experimental protocols but with some risk (like patterned optogenetic stimulations). All the necessary equipment to pursue this research program is available and sufficient funding was raised. The research plan includes:

1. Follow up of previous work on the role of neuronal transporters for vesicle loading at inhibitory synapses; aims at studying the molecular mechanisms by which the cytosolic concentration of GABA regulates the balance between resting and recycling vesicles as well as how activity regulates the trafficking of transporters in that process. Use of electrophysiological approaches combined with novel fluorescent probes to visualize receptor trafficking. Although coherent, this section of the plan is quite extensive, covering four different areas (VIAAT function and GABA supply, activity dependent regulation of SNAT-1, role of luminal Cl^- and H^+ on vesicular GABA release, irreversible transport in GlyT2).

2. Continue the exploration of cerebellar networks with a focus on Golgi cells and the examination of activity dependent gating of plasticity at excitatory synapses onto Purkinje cells. Examine the dynamics of the slow excitatory and inhibitory conductances onto granule cells using a variety of tools combined with electrophysiology.

3. Examine glycinergic networks in the deep cerebellar nuclei.

4. Test whether NR3-containing receptors, activated by glycine and glutamate, constitute a major component of slow synaptic integration in some structures of the forebrain (medial habenula, thalamus).

Investigation of the functional role of ponto-thalamic inhibitory projections is no longer included in the research plan.

Conclusion:

This is a strong team with a good output, good scientific environment, excellent equipment and good funding. This team is productive, publishing regularly in very good journals. This work has international impact in the field of imaging and organization of cerebellar networks (PI expertise).

- Strengths and opportunities:

Unique combination of elegant electrophysiological analysis and novel optical tools to address important questions at the circuit level.

Leadership in the development of imaging techniques, one of the recognized strengths of the IBENS Neuroscience group .

This team benefits from the excellent infrastructure and expertise at IBENS.

Many excellent collaborations.

International recognition of the PI.

Excellent level of funding and good equipment.

- Weaknesses and threats:

Lack of visibility of the second PI and dual team leadership.

The study of different brain areas at various different scales may be too much for a relatively small group.

- Recommendations:

It will be important to maintain the same quality of scientific research, technological development, productivity and funding. The team should try focusing on scientific questions to increase visibility and reinforce the coherence of the team and the visibility of both the PIs. Clarification of dual team leadership and attribution of responsibilities would be useful.

Team 21 : Computational Biology and Applied Mathematics

Name of team leader: Mr. David HOLCMAN

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)			
N4: Other professors (PREM, ECC, etc.)	1	1	1
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	1
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	3	3	3

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	5	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The objectives of the team during the past five years were to integrate biological processes using biophysical modeling, mathematical analyses and computer simulations. These studies focused on the modeling of cellular trafficking, including the trafficking of neuronal receptors, and early step of viral infection. The team developed the so-called Narrow escape and Dire strait theories to calculate the mean first passage time of a Brownian motion to a small absorbing window. The theory was applied to simulate calcium dynamics in dendritic spines and input ions in ion channels. It has been used to estimate the residence time of receptors at synapses to predict the modulation by direct molecular interaction of a transcription factor to find its target. Specific studies that took into account the geometry of dendritic spines provided major advances in quantifying how dendritic spines regulate 2D and 3D diffusion. The team developed a stochastic approach to estimate the number of receptors at the post-synaptic density (collaboration with a second IBENS team). The team also provided the first model of phototransduction in the retina (collaborations with several research groups outside France), boundary between morphogenetic regions in the brain and neurite outgrowth (collaborations with groups in Paris outside the IBENS). The team published 73 articles in specialized journals with high impact in the field.

To summarize, the team provided original concepts and theories that significantly contributed to better understand cellular trafficking of neurotransmitter receptors and viral particles. These contributions are complementary to experimental research, which explains the numerous collaborations and large panel of biological systems that have been investigated. In conclusion, the team is internationally recognized, and its scientific quality and production are excellent.

Assessment of the team's academic reputation and appeal

The team leader is very well recognized in the field of computational science. He obtained numerous and prestigious national and international awards, including an ERC-starting grant, HFSP and Chaire d'Excellence. The PI received the 2012 Bessel prize, has been invited to most prestigious national and international research centers and congresses in the field and organized 4 international meetings in France and abroad. The team leader developed a number of collaborations with very high quality laboratories. This testifies of an excellent influence and attractiveness of the team.

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

The team leader is well recognized for his expertise in modeling biological processes. He has been interviewed by the the CNRS Journal and the TV.

Assessment of the team's organisation and life

The team is composed of 12 members: 3 full time researchers, 9 students and 1 posdoct. No conflict appears to exist within the team. The team leader obtained more than sufficient financial support from an ERC and HFSP grants.

Assessment of the team's involvement in training through research

Although there is a considerable number of students and post-docs in the team (10 in 5 years), they seem well supervised and integrated in the research work. The team is offering them high quality research training and seminars. The team leader is involved in teaching at the Master 2 level and trains summer students. As a whole, the research training and teaching activities are very good.

Assessment of the five-year plan and strategy

The project is in the continuity with the past activity and will develop along 2 lines. The first objective is to derive a mathematical theory of diffusion in confined cellular domains. The second objective aims at modeling synaptic transmission, plasticity and chemical reaction in dendritic spines. This will be achieved through several collaborations with biologists at the IBENS and outside. There are very interesting aspects in this project that can provide novel insights in neuroscience, such as integration of a model of pre-synaptic terminal, glia-neuron interactions, heterogeneity of synaptic glutamate (AMPA) receptors and influence of spine geometry on these receptors trafficking.

This is an ambitious project. It implies a large number of sub-projects, as it is not unusual in modeling groups. They address either biological questions or try to lay foundation to novel methods. The program appear feasible given the past performance of the team. The objectives are likely to maintain the international reputation of the team.

Conclusion:

- Strengths and opportunities:

The team is of excellent quality. Its objectives match with those of neurobiologists at the IBENS. It provided major theoretical and practical contribution to important problems in cell biology in general and neurobiology in particular. The projects to be addressed in the coming years go along the same lines and will continue to address major questions close to experimental data. Its contribution to computational science is of high standard and this makes the team attractive.

- Weaknesses and threats:

The team lacks interaction with the commercial sector.

- Recommendations:

The team leader should put an effort on developing links to the commercial sector with the aim of materialising some of their developments.

Team 22 : Structure and Function of Glutamate Receptors

Name of team leader: Mr. Pierre PAOLETTI

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	2	2	2
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2	2
N6: Other contractual staff (without research duties)	1	1	1
TOTAL N1 to N6	6	6	6

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
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	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team was created in 2007. Its objectives have been to decipher the architecture, operation, pharmacology and patho-physiological roles of the ionotropic glutamate NMDA receptor subtype. To this aim, the team used multidisciplinary approaches, from 3D molecular modeling to generation of a genetically modified mouse model of pain. Their major findings are the discovery of unique architecture of the N-terminal domain of the GluN2A subunit of NMDA receptors. The team also found a novel NMDA receptor positive allosteric modulator of the GluN2B subunit. The Zn2+ ion is a negative modulator NMDA receptors. The team characterized a knock-in mouse expressing a Zn2+ insensitive NMDA receptor that displays enhanced allodynia, thus providing a novel animal model of chronic pain. In collaboration with a second IBENS team, they discovered the first auxiliary subunit (MOLO-1) of the nicotinic acetylcholine receptor, which controls the conductance and trafficking of the receptor in C. elegans. These findings are of primary importance in the field of neuroscience.

The team published a great number articles in very high impact journals, including Nature, Neuron, EMBO J. and Nat Neurosci Rev. Two Nat. Neurosci. papers resulted from collaboration. This level of publication is excellent and reaches the highest international standards.

To summarize, the team provided original and very important concepts regarding the glutamate NMDA receptor structure and function. They provided a novel animal model of pain, as well as novel ligand of the receptor. Altogether these findings open new avenues for future basic research and development of pharmacological tools of these receptors. In conclusion, the team is of excellent scientific quality and internationally competitive.

Assessment of the team's academic reputation and appeal

The team leader is very well known in the field of neuroscience. He obtained the prestigious FENS Young Investigator award in 2010. He has been invited in numerous most prestigious international meetings in neuroscience, including at a special FENS lecture in 2010. He developed a number of collaborations with very high quality laboratories in France and abroad. This testifies of an excellent influence and attractiveness of the team in the field.

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

The team leader is internationally recognized for his expertise in the structure, pharmacology and patho-physiology of NMDA receptors. He participates to important national programs at ENS, including the Labex Memolife. The team leader has been and is member of several scientific Committees, including those of CNRS and INSERM, and is a consultant for Genentech (USA). This activity is excellent.

Assessment of the team's organisation and life

The governance of the team is very good. No conflict appears to exist within the team. In the past years the PI obtained sufficient financial support from national and international institutions, as well as industry.

Assessment of the team's involvement in training through research

Students and post-docts of the team are well integrated. They are well trained by the members of the team. They benefit of all equipment and expertise of the researchers. They are well guided as the team is offering high quality seminars and participation to international meetings. The team leader is also highly involved in teaching, supervision and organization of Master 2 courses. As a whole, the research training and teaching activities are excellent.

Assessment of the five-year plan and strategy

The project is in the continuity of the past activity. The team will maintain its activity in structural aspects of the NMDA receptors, but will expand its research by studying patho-physiological roles of the receptors in native conditions such as brain slices and living animals.

The project will develop along 3 lines. First objective will be to understand the dynamics of conformational changes and concerted rearrangement of the different subunits of NMDA receptors. This will be achieved thanks to multidisciplinary approaches that will combine physical, computational and biological tools. Second, they will develop subunit-specific ligands capable of fine-tuning NMDA receptor functions. This may foster research and development of novel generation of NMDA receptor ligands, which has failed in the clinic in the past. Third, the team aims at understanding the physiological and pathological relevance of the modulatory sites of NMDA receptors, focusing on the Zn^{2+} and glycine sites. They will combine in vitro and in vivo studies, namely using their recently generated Zn^{2+}-insensitive knock-in mouse model, and by developing original genetically encoded biosensors to monitor environmental synaptic changes in real-time. These objectives should provide new insights in the physiological roles of NMDA receptors at the synapse and new targets for the treatment of several neurological and psychiatric disorders that result from functional alteration of these receptors. This is an ambitious and excellent project in a highly competitive field, but shows feasibility as the team clearly intends to use state of the art methods. The important objectives of the project are likely to maintain the leading international position of the team. These should be attractive for future students and post-docts, they should further improve visibility of the team towards academic institutions and industry, and help the team to implement its staff.

Conclusion:

- Strengths and opportunities:

The team is of excellent quality. It has proved its ability to accomplish very innovative and high standard research. The project is excellent.

- Weaknesses and threats:

Given the diversity and number of aims, the project may be too ambitious for such a small team. The PI should reflect about how to link molecular data and in vivo results.

- Recommendations:

In view of the performance of the team the committee recommends the PI to apply to more competitive international calls.

Team 23 : Zebrafish Neuroethology

Name of team leader: Mr. German SUMBRE

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	2	2
N6: Other contractual staff (without research duties)	1		
TOTAL N1 to N6	6	4	4

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	3	
Theses defended	0	
Postdoctoral students having spent at least 12 months in the unit	3	
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

This new group was created recently (2009) by a young team leader with an excellent past track record as a postdoctoral fellow and has exceptional financial support (Avenir, ERC young Investigator, Marie Curie IRG, Ville de Paris, etc). This group has been operational for only 2 years over the reporting period and it is therefore too early to evaluate the scientific quality and output of the team at this point in time. Nonetheless, the initial signs are positive and the presentation of the ongoing projects was very well received by the committee. The team leader's publications before arriving at IBENS are strongly related to the proposed project and are of very high quality (1 Cell, 1 Nature, 1 Neuron). The PI was a principal contributor (1st author) in the Nature paper.

The main goal of the lab is to understand the network basis of motor behaviors and simple cognitive tasks using transgenic zebrafish larvae expressing GCaMP calcium reporters. This is an excellent experimental model because it allows one to image activity over large populations of neurons in an intact behaving vertebrate. The experimental outputs of the lab are already quite impressive since a transgenic GCaMP3 zebrafish line was developed together with a virtual reality set-up (allowing virtual navigation in imaging conditions), a chamber for precise and local sensory stimulation, as well as analytical tools to automatically detect imaged neurons and corresponding calcium transients. With these tools, the team is in a position to start investigating the functional structure of sensory perception and spatial navigation in the vertebrate brain. The group has already obtained interesting preliminary data concerning, for example, the patterns of neuronal activation induced by visual illusions. Altogether, the PI has made an excellent start to establishing his own independent research program.

Assessment of the team's academic reputation and appeal

The impact of the work of the team leader is revealed by the high number of invited talks (including most recently to small international meetings), as well as by the rapid recruitment of post-docs and students. The team leader is likely to continue building his international reputation.

The team leader has a strong record in the development and dissemination of cutting-edge experimental approaches to analyze large scale neuronal network dynamics in the intact behaving zebrafish.

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

Not applicable

Assessment of the team's organisation and life

This team comprises 4 postdocs, 3 Ph.D students and 2 engineers. It is highly multidisciplinary as it gathers people with different scientific backgrounds including mathematics, physics, engineering, neurobiology, molecular biology and behaviour. A group of this size and diversity will be a managerial challenge for a new PI and the committee cautions against continued further growth in the immediate future. Directing the work of the 3 graduate students within a new lab is a significant responsibility and burden for a young PI.

One graduate student has started a PhD more than 3 years ago but is without any publication so far.

Assessment of the team's involvement in training through research

The PI is teaching two courses at the ENS (Functional imaging in Neuroscience and Neurobiology to mathematicians) as well as at the University Paris Diderot (Optogenetics). Since 2009, the PI has been able to attract graduate students (3) and postdoctoral fellows (4).

Assessment of the five-year plan and strategy

The project capitalizes on the technical ability of this team to monitor large portions of the brain simultaneously in a non-anesthetized behaving vertebrate within a simple nervous system. Importantly, this model is accessible to genetic manipulation.

Briefly, the project presented in the written report is organized along three main objectives: (1) study the maturation of spontaneous neuronal dynamics during the early development of the larva; (2) determine the functional network structure of internal decisions in the healthy and "autistic" larva; (3) investigate the mechanisms underlying the generation of rhythmic network dynamics with a potential role in supporting time perception. The originality of this project lies in the experimental model and techniques it will utilize. It addresses fundamental questions, some of which have already been deeply investigated in the rodent brain, but with an important and exciting advantage: the ability to monitor neural activity simultaneously in the sensory pathways, integration/decision centers and motor pathways. The ability to map the flow of signals through the nervous system while the zebrafish makes simple decisions in response to sensory stimuli is exciting and potentially extremely powerful. It would have been useful if the description of future work had provided more detail and explicitly described the added value of this type of approach in relation to the state of the art. Questions at the basis of the project are quite broad. It is an exploratory project sometimes lacking a main focus and a leading hypothesis. The multiplication of questions may be difficult to tackle for a single young PI.

Conclusion:

The publication record of the group is still in progress, but the PI's international recognition and exceptional talent at raising grants indicate a very promising team. The project is challenging and original and based on excellent technical expertise. The team size and projects are quite broad and may be quite overwhelming for a single PI.

- Strengths and opportunities:

Complementary multidisciplinary expertise.

Excellent experimental model.

Excellent funding.

This team is located in an excellent environment and the projects are challenging but feasible.

- Weaknesses and threats:

A relatively large number of post-docs and students with different projects to be managed by a single young PI who is still at an early stage in establishing his independent research program.

- Recommendations:

The committee looks forward to seeing the results of the teams exciting research project, and recommends that the PI aims now at consolidation in which projects are properly established before further growth of team size. Mentoring by more experienced PIs within IBENS may be helpful.

Team 24 : Cellular Biology of the Synapse

Name of team leader: Mr. Antoine TRILLER

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	1
N2: Permanent EPST or EPIC researchers and similar positions	5	5	5
N3: Other permanent staff (without research duties)	4	4	3
N4: Other professors (PREM, ECC, etc.)	1		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	5	3	3
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	16	13	12

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	6	
Theses defended	8	
Postdoctoral students having spent at least 12 months in the unit	6	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The team covers 3 areas of research around a common theme - the regulation of synaptic function. These areas are : (1) dynamics of glycine receptors ; (2) ultrastructural analyses of presynaptic molecules (SNAREs) and vesicles and (3) patho-physiological roles of the interactions between glia and neurons in synaptic functions.

(1): The team has uncovered mechanisms underlying the homeostatic regulation of synaptic glycine receptor number by lateral diffusion and the roles of kinases, integrins and the scaffolding protein gephyrin. They have extended these studies of molecular dynamics to presynaptic events controlling neurotransmitter release and discovered that changes in syntaxin 1A mobility are related to formation of SNARE complexes underlying exocytosis. These quantitative approaches to cell physiology are now being extended to pathological mechanisms related to Alzheimer's disease: the deleterious effect of Aß oligomers results from aggregation of the metabotropic glutamate receptor mGlu5. Collaboration with physicists has allowed the team to develop innovative tools, such as quantum dots, to track single molecules in neurons. The PI has developed important new concepts regarding synaptic stability and plasticity.

(2): The team has made use of the latest EM methods involving high-pressure freezing and electron tomography to observe the organization of vesicles and filaments in and around the active zone, providing evidence that priming and docking involve common molecules.

(3): The team studied the interactions between glia and neurons, with focus on microglia – the macrophages of the brain. They have demonstrated the role of NO synthase in neuronal cell death mediated by microglial activation, and the impact of inflammation in mothers on the development of synaptic function in newborn mice. The cellular basis by which microglia impact synaptic function are beginning to be unravelled by the demonstration that stimulated microglia cause an acute increase in spontaneous synaptic events.

This research group continues to be an international leader in the field of synaptic dynamics. The quality and originality of the experimental studies is complemented by innovative theoretical frameworks and the development of new techniques for studying molecular dynamics at the synapse. This team provided a major breakthrough in cellular neuroscience by the role of lateral diffusion of neurotransmitter receptors in synaptic plasticity.

Publication record is outstanding in quantity and quality and has been on an upward trajectory over the last 6 years (J Neuroscience (3), Embo J, Nature Neuroscience, Neuron (2)).

The team leader has been awarded several prestigious national and international prizes and grants, including an advanced ERC grant and partnership in the "Blue Brain" European flagship project.

Assessment of the team's academic reputation and appeal

The PI is a international leader in the field of cellular neurosciences. He is regularly invited to speak at the most important international conferences, as well as the best universities and research centers. He has recruited 6 postdocs and 6 students during the last reporting period, which testifies to the attractiveness of his group to young scientists.

The team leader is internationally recognized for his expertise in single molecule tracking techniques, molecular mechanisms that control receptor trafficking and synaptic plasticity. He has also created several important national programs at ENS, including the IBENS and labex Memolife.

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

The PI is member of the French Academy of Sciences, several international SAB committees and of the EMBO Council. Thus, the team leader is an outstanding researcher who is very active in promoting and organizing neuroscience both within and outside France. These organizational activities are praiseworthy and have a very positive impact on Neuroscience in Europe.

Assessment of the team's organisation and life

The governance of the team is excellent. The team leader has obtained high levels of financial support, mainly through national calls. He has gathered scientists with diverse and complementary skills to develop various projects. The committee recommends to the team leader also to seek funding through international calls, being ideally placed to obtain these type of grants.

Assessment of the team's involvement in training through research

The team offers excellent training opportunities for students and post-docs, who benefit fully from the scientific activity. They are guided well and acquired high standard professional experience in the past. The team is offering high quality seminars and international meeting participations and provides excellent strategy for the recruitment of postdocs and students. It also offers best choices to new PhDs to find high quality laboratories for their postdoctoral experience. The PI created a specific MD-science program.

Assessment of the five-year plan and strategy

The projects continue from past activity and cover 3 main areas: (i) the number and behavior of synaptic receptors in single synapses; (ii) cell-autonomous regulation of synaptic glycine and GABA receptors accumulation by phosphorylation and Ca2+, in neurons, and (iii) non-cell autonomous regulation of these receptors via glia during inflammation and consequence on excitation/inhibition balance. These objectives will be achieved thanks to the development and use of super-resolution imaging techniques to characterize fast dynamics of the Gly and GABA receptors, and associated proteins (gephyrin and collybistin). They will also develop smaller quantum dots to access small volumes such as the synaptic cleft, and unnatural amino-acids to improve tracking of receptors with fluorescent tags. These are very interesting and innovative objectives, at the highest level of international competition. Although ambitious, this program is feasibile because of the resources, track-record and scientific quality of the team.

Conclusion:

As a whole, the team is of excellent quality. It is one of the leading international research groups in the field of cellular and molecular neuroscience. It has consistently demonstrated its ability to carry out research of the highest standard. The projects are excellent.

- Strengths and opportunities:

Ambitious and innovative research program to be performed by an excellent team.

- Weaknesses and threats:

None.

- Recommendations:

Maintain the level of excellence.

5 • Conduct of the visit

Visit dates:

Start: Monday, 28th January 2013 at 9:00 a.m.

End: Wednesday, 30th January 2013 at 7:30 p.m

Visit site(s):

Institution: IBENS

Address (no. street town): 46 Rue d'Ulm, Paris

Conduct or programme of visit:

The visit took place at the Ecole Normale Supérieure, 46 rue d'Ulm, during three full days, from 9:00 am to 7:30 pm, on the 28-30 January 2013. After a general introduction by the AERES representative and the chairman, a 30 min general presentation of the unit by the future director was given in the presence of most of the group leaders and some additional personnel of the unit, followed by 30 min discussion. Given the size of the IBENS, the visiting committee was divided into two parts that heard the oral presentation of the group leaders from the Functional Genomics/Environmental and Evolutionary Genomics, and Developmental Biology/Neuroscience sections, respectively. Each group leader presented the past activities and projects for 25 min followed by 20 min discussion in the presence of the team members. The team members left the room 5 min before the end to allow a "private" discussion between the AERES committee members and each group leader. Then 10 minutes discussion was allowed between the AERES experts to discuss and evaluate the quality of the team on the 6 different aspects requested by the AERES. At the end of the first two days, a door-closed meeting of 1-2 hours was conducted to qualify each team being evaluated during the day.

On day 2 of the visit the committee was split into three groups each having one hour discussion with i) the students and post-doctoral fellows, ii) the researchers with permanent position, excluding the team leaders, and iii) the technicians and engineer staff. Furthermore, a 30 minute meeting with the head of each section of the IBENS was held on day 3. Half an hour exchange with the representatives of the university Pierre et Marie Curie (UPMC), the research organization (CNRS and INSERM) was held before the final door closed meeting.

Two technician representatives of INSERM (CSS6) and CNRS (section 22) were present on site during the visit. They attended the presentation and discussion of most teams, but did not participate in the discussion. They also organized a general discussion with the Engineers and technicians, in preparation of the one with the AERES committee representatives.

Specific points to be mentioned: None

The president wants to thank all experts from the committee for their very active participation during the discussion, their constructive questions and remarks to the team leaders, bringing about a very nice humanee and scientific atmosphere, optimal for such a unit evaluation.

The committee regrets to not have had the possibility to visit the laboratory and the platforms during the 3 days of the visit (in particularly the animal facility).

6 • Statistics by field: SVE on 10/06/2013

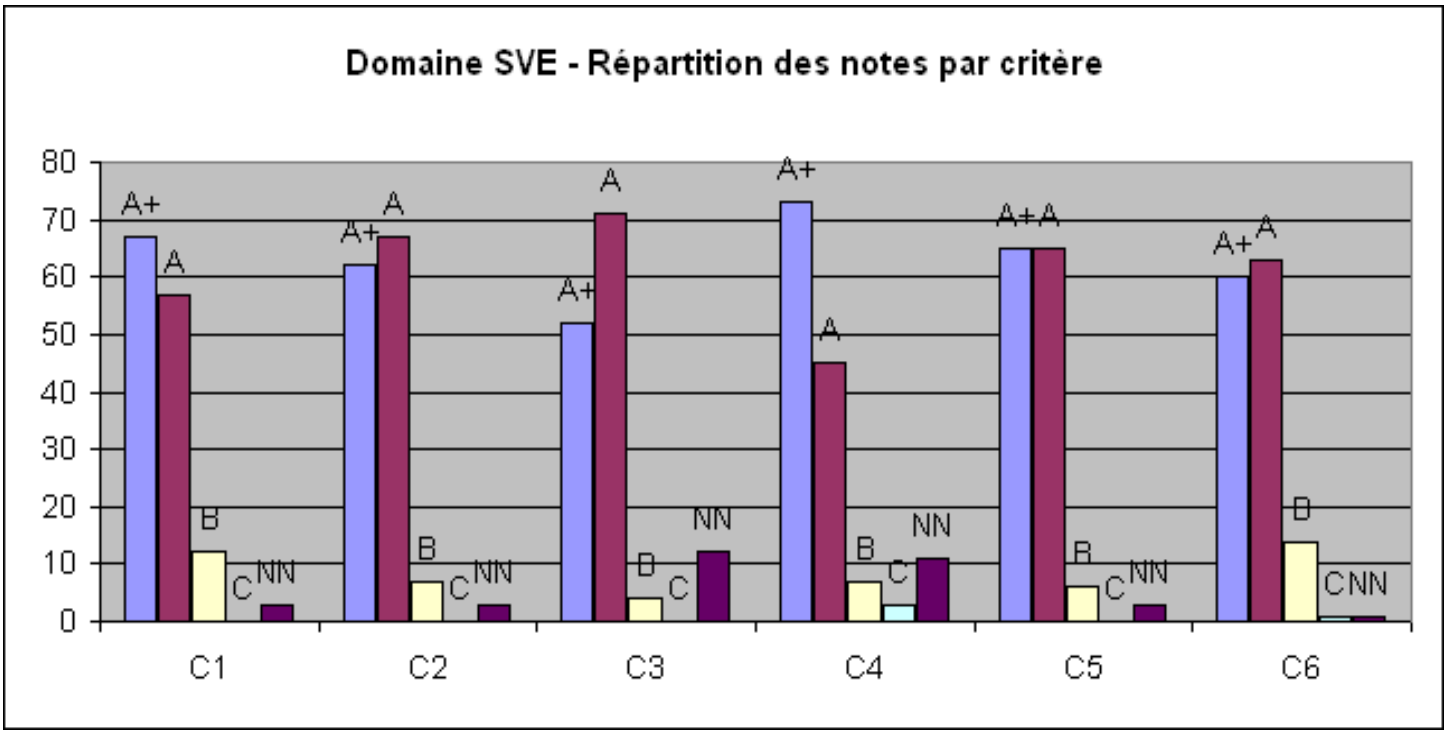
Notes

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	67	62	52	73	65	60
A	57	67	71	45	65	63
B	12	7	4	7	6	14
C	0	0	0	3	0	1
Non Noté	3	3	12	11	3	1

Percentages

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	48%	45%	37%	53%	47%	43%
A	41%	48%	51%	32%	47%	45%
B	9%	5%	3%	5%	4%	10%
C	0%	0%	0%	2%	0%	1%
Non Noté	2%	2%	9%	8%	2%	1%

Histogram



7 • Supervising bodies' general comments

IBENS
Institut de Biologie de l'Ecole Normale Supérieure

Antoine Triller
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Paris le 25 Avril 2013

Commentaires Concernant l'évaluation AERES de MemoLife

Commentaires Généraux:

We are grateful to the committee for there extensive evaluation. There commentary will be very helpful to improve IBENS quality.

Commentaires spécifiques:

We were surprised by the statements in page 7 & 8 :
- *"the working conditions described for the housing of Xenopus in the -2 sub-basement appear unacceptable."*
- *"Despite past efforts renovation is clearly necessary. (...) there are serious worries about the working conditions in the Xenopus breeding station."*

The Xenopus husbandry was completely renewed during the 2006-2009 quadriennal contract and is endowed with modern equipments that are run by qualified personnal. All team leaders using this husbandry and their collaborators are satisfied with it and have not been informed of serious dysfunction or working conditions problem by the technician working there. To our knowledge the AERES Committee has not visited this intallation and has not formulated any remark during the presentation of this platform or during the rest of their visit. It is therefore unclear to us what the above-mentioned "serious worries" might be.

Concerning some factual apsects:

Team of Pierre Paoeletti was created in 2007, not in 2010,

4 important publications should be added to the publication list:

- Allosteric signaling and dynamics of the clamshell-like NMDA receptor GluN1 N-terminal domain. (2013) Zhu S, Stroebel D, Yao CA, Taly A, Paoletti P. ***Nature Structural & Molecular Biology***. 20:477-85.

- Expanding the genetic code in Xenopus laevis oocytes. Ye S, Riou M, Carvalho S, Paoletti P. (2013) ***ChemBioChem***. 14: 230-5.

- Visualization of structural changes accompanying activation of N-methyl-D-aspartate (NMDA) receptors using fast-scan atomic force microscopy maging. (2013) Suzuki Y, Goetze TA, Stroebel D, Balasuriya D, Yoshimura SH, Henderson RM, Paoletti P, Takeyasu K, Edwardson JM. ***Journal of Biological Chemistry***. 288:778-84.

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- NMDA receptor subunit diversity: impact on receptor properties, synaptic plasticity and disease. (2013) Paoletti P, Bellone C and Zhou Q. ***Nature Reviews Neuroscience***. 2013. In Press

Team of David Holcman

Concerning weaknesses and threats: *"The team lacks interaction with the commercial sector."* : This team has already mentioned that BioNewmetrics is our developing web-site to promote our algorithms toward the private sectors. This is not mentioned in the AERES Repport.

A new reference to be added: N.Hoze, C. Amuroso, M. Ruault, A Taddei, D. Holcman, Dynamics of telomere clustering in the nucleus.(2013) Molecular Biology of the Cell. In Press

Team of Sonia Garel:

3 important publications

Lokmane L, Proville R, Narboux-Nême N, Györ I, Keita M, Mailhes C, Léna C, Gaspar P, Grosschedl R and Garel S. (2013) Sensory map transfer to the neocortex relies on pre-target ordering of thalamic axons. ***Current Biology**, in press*.

Deck M, Lokmane L, Chauvet S, Mailhes C, Keita M, Niquille M, Lebrand C, Yoshida M, Yoshida Y, Mann F, Grove E, Garel S (2013) Pathfinding of corticothalamic axons relies on a rendezvous with thalamic projections. ***Neuron**,* **77**: 1-13.

Mire E, Mezzera C, Leyva-Diaz E, Paternain AV, Squarzoni P, Bluy L, Castillo-Paterna M, Lopez MJ, Peregrin S, Tessier-Lavigne M, Garel S, Galceran J, Lerma J, Lopez-Bendito G (2012) Spontaneous activity regulates Robo1 transcription to mediate a switch in thalamocortical axon growth. ***Nature Neurosci***, 15:1134-43.

Team of Xavier Darzacq

This team has developed strong interactions with industry especially Nikon and Imagine Optique with the co-development of new equipments for single molecule imaging and Vivatech with whom new cellular models relevant to cellular differentiation are being developed.

Team of Denis Thieffry

- Weaknesses and threats:
There appears to be a need to strengthen the staffing in this group at the postdoctoral level, once they have occupied their new lab space.
Thieffry's team currently includes one PU, one MCU, two postdocs, one PhD student and two predoctoral students. The statement below appears thus somewhat abusive in this regard.

Their future plans are certainly feasible but arguably lack novelty from the computational point of view.
The section 3 of the research project is fully devoted to the development of novel computational methods and tools, but the committee has apparently completely overlooked that part of the project, which has been only superficially presented orally, due to time constrains.

- Recommendations:
The committee noted that the team appears to emphasize collaborative projects at the expense of developing new tools/algorithms and recommends they guard against this.
This is somewhat contradictory with the content of the section "Assessment of scientific quality and outputs", where the committee states:

Both their past and future work are organised into distinct but complementary areas. The group's work to establish qualitative dynamical modeling methods, and the development of associated software, has been original and important work, as illustrated by the range of applications. Their recent work developing software for the analysis of ChIP-seq data may also have a broad impact given the explosion of epigenomic studies.

New publications (2013):
Comet JP, Noual M, Richard A, Aracena J, Calzone L, Demongeot J, Kaufman M, Naldi An Snoussi EH, Thieffry D (2013). On circuit functionality in Boolean networks. ***Bulletin of Mathematical Biology***, in press.

Darbo E, Lecuit T, Herrmann C, Thieffry D, van Helden J (2013). Transcriptional and epigenetic signatures of zygotic genome activation during early drosophila embryogenesis. ***BMC Genomics***.

Bérenguier D, Chaouiya C, Monteiro PT, Naldi A, Remy E, Thieffry D, Tichit L (accepted with minor revisions). Dynamical modeling and analysis of large cellular regulatory networks. ***Chaos***.

Team of Hughes Roest-Crollius

It is difficult to understand the actual day-to-day functioning of the group, as most of its members are either graduate students or Postdocs.

The group currently comprises 3 permanent staff (CNRS research engineer, senior CNRS research scientists (CR1), CNRS research director (DR2)). Together with 4 non-permanent staff (post-docs, PhD students and undergraduates) this provides a good balance between permanent and temporary staff.

There is no information here as to the number of people who have been trained over the past several years […] Nonetheless, the team currently has two Ph.D. students and four postdoctoral fellows and thus appears to be a very good site for bioinformatics training.

During the period of the report, the group has trained 10 undergraduate students (L3, M1, M2) and all have pursued their studies successfully. The full list was made available to the committee in the Annex to the PI's CV. The "Alumni" page of the group's website shows that during the period of the report, 4 PhD students have graduated and have joined renowned laboratories (Stanford University, Ensembl group at the EBI, Paul Flicek's group at the EBI) or joined private companies.

The PI states "in the last few years, our group has pursued many interests in the field of genome and molecular evolution." It is possible that they have pursued too many interests […]They certainly have developed the necessary tools to make major contributions and the committee is highly optimistic about their future.

The many interests that have been pursued have all led to publications, always in medium to high impact journals either as main authors or co-authors (Bioinformatics, Genome Biology, Plos Genetics, Science, Nature Genetics,…). This shows that the group has developed bioinformatics tools and skills that are adaptable to different subjects and are in demand by collaborators. The group remains committed to answering other biological questions when interesting and relevant opportunities arise.

Conclusions (weaknesses and threats): Diversification, too many projects. Limited scientific output.

Owing to an oversight on our part, one important publication was missing in the list provided to the committee. This publication is the following:

- Cusack, B.P., Arndt, P.F., Duret, L., Roest Crollius, H. (2011) Preventing Dangerous Nonsense : Selection for Robustness to Transcriptional Error in Human Genes. PLoS Genetics 7(10): e1002276. (Impact Factor 8.7)

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Several results were submitted at the time of the final AERES report, and have since been published. Four articles have been published during the 4 months since the report, including 2 after the committee's visit in January 2013. These comprise articles in Nature, Nature Structural and Molecular Biology, NAR and Methods, where our group is main author or co-authors. One article from our group is currently under consideration by Plos Biology.

Antoine Triller

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