# IBENS - Institut de biologie de l'ENS

Rapport Hcéres

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

Section des Unités de recherche

# Evaluation Report

## Research unit

## Institut de Biologie

## Ecole Normale Supérieure

March 2009

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

Section des Unités de recherche

# Evaluation report

## Research unit

## Institut de Biologie

# Ecole Normale Supérieure

Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

*Le Directeur*

Pierre Glorieux

March 2009

# Evaluation report

## The research unit :

Name of the research unit : Institut de Biologie

Requested label : UMR_S INSERM, UMR CNRS

N° in case of renewal :

Head of the research unit : M. Antoine TRILLER

## University or school :

Ecole Normale Supérieure

## Other institutions and research organization:

INSERM

CNRS

## Date of the visit :

21-22 January 2009

# Members of the visiting committee

## Chairman of the commitee :

M. Nils BROSE, Max Planck Institute for Experimental Medicine, Göttingen, Germany

## Other committee members :

M. Bertrand BLOCH, Université Bordeaux 2, France

M. Riccardo BRAMBILLA, San Raffaele Foundation and University, Milano, Italy

M. Alain BUCHETON, Institut de Génétique Humaine, Montpellier, France

M. Guillaume CHANFREAU, UCLA, Los Angeles, USA

Ms. Monica Di LUCA, University of Milano, Italy

Ms. Britta EICKHOLT, MRC Centre for Developmental Neurobiology, King's College London, UK

Ms. Marie FILBIN, Hunter College, New York, USA

M. Thomas GINGERAS, Cold Spring Harbor Laboratory, NY, USA

M. Lars HENNING, Swiss Federal Institute of Technology, Zurich, Switzerland

M. Adrian KRAINER, Cold Spring Harbor, USA

Ms. Ana POMBO, MRC Clinical Sciences Centre, Imperial College London, UK

M. Jean SALAMERO, Institut Curie, Paris, France

M. Miguel SEABRA, National Heart and Lung Institute, Imperial College London, UK

M. Evgeny ZDOBNOV, University of Geneva Medical School, Switzerland

## CNU, CoNRS, CSS INSERM, INRA, INRIA, IRD representatives :

M. Eric AGIUS, CoNRS representative, Toulouse, France

M. Jean-Vianney BARNIER, CoNRS representative, Gif sur Yvette, France

M. Jean-Philippe PIN, CSS INSERM representative, Montpellier, France

M. Lucas WALTZER, CoNRS representative, Toulouse, France

## AERES scientific representatives :

M. Erwan BEZARD

M. Philippe BOUVET

## University or school representative :

M. Yves GULDNER, directeur-adjoint Sciences, Ecole Normale Supérieure

## Research organization representatives :

M. Bernard BIOULAC, DSA SDV CNRS

Ms. Martine DEFAIS, SDV CNRS

M. Jean HOUMARD, ENS

Ms. Catherine LABBE-JULLIE, Chargée de mission INSERM

Ms. Chantal LASSERE, Chargée de mission INSERM

# Evaluation report

## 1 • Short presentation of the research unit

- Number of full time researchers : 53
- Number of researcher with teaching duties : 14
- Number of post doctoral fellows : 40
- Number of PhD students : 66 (oct 2008)
- Number of technicians and administrative assistants : 40.5
- Number of HDR : 45 of which 26 are advisors
- Number of students who have obtained their PhD during the past 4 years : 39
- Average duration : 4 years
- Number of PEDR : 8
- Number of "publishing" lab members : 91 out of 93

## 2 • Preparation and execution of the visit

The visit occurred on the 21st and 22nd January 2009. The preparation and execution of the visit was as specified in the Aeres guidelines. The visit went smoothly with all aspects of the evaluation covered satisfactorily. The committee splitted into two subcommittees for assesssing the Developmental Biology & Neurosciences departments and the Environmental and evolutionary genetics & Functional genetics departments, respectively.

Monday January 21 2009

Time : from 9:00 to 9:15
Welcome coffee

Time : from 9 :15 to 9 :45
Door-closed meeting: Committee members and AERES representatives

Time : from 9 :45 to 10 :15
Separate meetings of the two sub-committees

Time : from 10 :15 to 10 :45
Presentation of IBENS by the head of the unit, past activity and projects

Time : from 10:45 to 11:00
Coffee break

Time : from 11 :00 to 13:15
Presentations Developmental Biology & Neurosciences

| | |
|---|---|
| 11h00-11h15 : | General overview of the Developmental Biology section |
| 11h15-11h45 : | Développement et plasticité du cerveau |
| 11h45-12h15 : | Développement et fonctions des cellules ciliées |
| 12h15-12h45 : | Orientation du fuseau mitotique et détermination du devenir cellulaire |
| 12h45-13h15 : | Régionalisation nerveuse |

Time : from 11 :00 to 13:15
Presentations Environmental and evolutionary genetics & Functional genetics

11h00-11h15 : General overview of the Environmental and evolutionary genetics section
11h15-11h45 : Biominéralization et Morphogénèse
11h45-12h15 : Epigénétique et épigénomique végétale
12h15-12h45 : Biologie moléculaire végétale
12h45-13h15 : Discussion with the group leaders of the associated teams

Time : from 12 :15 to 13:15
Parallel presentation to part of the sub-committee(s)
Imaging facilities and visit of the department, if required, by A. Triller

Lunch from 13:15 to 14:15

Time : from 14:15 to 16:30
Presentations Developmental Biology & Neurosciences

14h15-15h00 : Régulateur de la neurogénèse
15h00-15h45 : Développement précoce
15h45-16h30 : Développement du système nerveux

Time : from 14 :15 to 16 :30
Presentations Environmental and evolutionary genetics & Functional genetics

14h15-14h30 : General overview of the Functional genetics section
14h30-15h20 : Biologie cellulaire de la transcription
15h20-15h55 : Imagerie de la transcription
15h55-16h30 : Expression des ARNm eucaryotes

Time : from 16:30 to 16:50
Coffee break

Time : from 16:50 to 18:55
Presentations Developmental Biology & Neurosciences

16h50-17h00 : Presentation of the future unit moving to College de France
17h00-17h30 : Biologie cellulaire des homéoprotéines
17h30-18h15 : Développement et neuropharmacologie
18h15-18h25 : General overview of the Neurosciences section
18h25-18h55 : Récepteurs NMDA

Time : from 16:50 to 18:55
Presentations Environmental and evolutionary genetics & Functional genetics

16h50-17h35 : Génétique moléculaire des ciliés
17h35-18h35 : Discussion with the group leaders of the associated teams

Time : from 18:55 to 19:30
Meeting of the sub-committee

<u>Thursday January 22 2009</u>

Time : from 8:30 to 10:30
Presentations Developmental Biology & Neurosciences

8h30-9h00: Transmission inhibitrice
9h00-9h30: Modélisation mathématqiue de la physiologie cellulaire
9h30-10h00 : Dynamique corticale
10h00-10h30 : Neuroéthologie du zebrafish

Time : from 8:30 to 10:30
Presentations Environmental and evolutionary genetics & Functional genetics

8h30-9h00 : Dynamique et organization des génomes
9h00-9h45: Réplication des chromosomes eucaryotes
9h45-10h30 : Génome de la levure

Time : from 10:30 to 10:50
Coffee break

Time : from 10:50 to 12:10
Presentations Developmental Biology & Neurosciences

10h50-11h35 : Neurobiologie et génétique de C. Elegans
11h35-12h20 : Cervelet
12h20-13h05 : Biologie cellulaire de la synapse

Time : from 10:50 to 12:10
General discussions, Institute facilities

10h50-11h10 : Transcriptome facility
11h10-11h30 : Proteomics
11h30-11h50 : Computing facilities
11h50-12h10 : Animal facilities

Lunch from13:00 to 14:00 with the team leaders

Time : from 14:00 to 18:30
General discussions

14h00-15h00 : Parallel meetings with committee's members
Meeting with engineers, technicians and administrative assistants
Meeting with the PhD students and postdocs
Meeting with researchers with permanent position

15h00-15h15 : Door-closed meeting : Committee members, AERES representative, ENS and Research Organizations

15h15-15h30 : Door-closed meeting : Committee members, AERES representatives, and A. Triller

15h30-18h30 : Door-closed meeting: Committee members, AERES representatives

# 3 • Overall appreciation of the activity of the research unit, of its links with local, national and international partners

The IBENS is a new proposed unit resulting from the fusion of four ENS (Ecole Normale Supérieure)-CNRS units and two ENS-Inserm units which should become a unique UMR (Unité Mixte de Recherche) ENS-CNRS-Inserm. The new unit will be divided into four sections : developmental biology, neurosciences, environmental and evolutionary genomics, and functional genomics.

IBENS is a world-class institution with excellent scientists at all levels of seniority and excellent projects. Senior groups with an excellent worldwide reputation are complemented by many junior groups, which have already shown that they can operate and contribute at a top international level. The new recruitments are excellent with regard to originality, quality, and potential. All sections are attractive and develop in general highly interesting and innovative projects. An indicator of their activity is the publication output with a very significant number of papers published in high impact factor journals. These sections are also active in teaching activities at all levels. Overall, the committee was impressed by the excellent quality of science in all sections. There is no question that IBENS deserves the strongest possible support of the funding agencies.

The following section is a group-by-group assessment of the constitutive IBENS teams. The corresponding paragraphs summarize the achievements of the individual groups, their strengths, their weaknesses (if any), and recommendations by the committee.

# 4 • Specific appreciation team by team and/or project by project

## Developmental Biology section

### Team : Régulateur de la neurogénèse

The ongoing research is largely shaped by questions regarding the functional analyses of transcription factors in the nervous system. A series of interesting studies into, for example, the role of Phox2 transcription factors provided compelling evidence of their importance during development of the visceral nervous system. Ongoing research involves the detailed characterization of the development, anatomy and evolution of this important - to date mostly understudied - circuit. The principal investigator continues collaborating with different labs in the Developmental Biology section, as well as at the national and international level, which resulted in a number of excellent publications with high impact. It is to be expected that future work in his lab will consolidate his position as a world expert in his field; his goals are well thought out, with clear lines of investigations and sets of interesting, yet feasible, experiments. The evaluation panel was particularly impressed with his research breadth as his ambitions do not stop at analyzing the development and evolutionary origin of neural circuits; they also embrace questions regarding the pathology of human syndromes. In summary, the team will be central to the success of the newly formed IBENS.

| Note de l'équipe | Qualité scientifique et production | Rayonnement et attractivité, intégration dans l'environnement | Stratégie, gouvernance et vie du laboratoire | Appréciation du projet |
|---|---|---|---|---|
| A+ | A+ | A+ | A+ | A+ |

### Team : Développement du système nerveux

The Developmental Biology Section within the newly formed IBENS is led by the principal investigator, who exploits different animal models in order to investigate the development of the nervous system. The principal investigator is continuing a series of exciting investigations into the role of the transcription factor Krox-20, a key regulator in a number of cellular processes controlling peripheral and central nervous system development. Recent work published by his laboratory identified transcriptional effectors and affectors of Krox-20 activity, unraveling the complex role of Krox-20 function during hindbrain segmentation, PNS myelination, and neural crest biology. Overall, the principal investigator impressed the evaluation committee as an engaged and very productive investigator who has taken the analyses of a single transcription factor intelligently into different important problems using the mouse, chick, or zebrafish as model systems. Of particular note are his continuing collaborations within the Developmental Biology section, as well as regular collaborations at national and international level, which resulted in an impressive list of publications of high impact. There are currently around 14 researchers in his laboratory (5-6 permanent staff) – The researcher who essentially single-handedly runs the project on forebrain development has recently been promoted to group leader (see next team assessment). The principal investigator laboratory forms a central part of IBENS contributing strong developmental and genetic approaches to analyze exciting problems in developmental neuroscience.

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| A+ | A+ | A+ | A+ | A+ |

**Team : Développement et plasticité du cerveau**

The principal investigator is a newly appointed group leader. The focus of her work is the molecular cues associated with cell migration and axonal guidance in the development of the dorsal thalamus - dorsal projection. She gave an outstanding presentation and is very productive, already having a last author paper in Cell. Although very new, she already has two PhD students and a number of technicians in her team. The principal investigator has great potential to be a very successful scientist and the committee had no doubt she will succeed. The principal investigator represents the ideal person to be given a group leader position within the department as she brings innovation, motivation, and enthusiasm. The department should be encouraged to nurture her growth and development. The committee found no weaknesses in this young group. Our only recommendation is that the principal investigator should attend more international meetings in order to bring more recognition to her group.

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| A+ | A+ | A | A | A+ |

**Team : Biologie cellulaire des homéoprotéines**

The work by this group has its origin in the analysis of the mechanisms by which homeoproteins are secreted and internalized through non-conventional pathways. Homeoproteins are a class of transcription factors that share the unusual property of intercellular transfer, involving the secretion of the protein from expressing cells followed by its internalization into adjacent cells. Both events rely on unconventional mechanisms due to the absence of classical secretion signals within homeoproteins and their accumulation in cytosolic and nuclear compartments following internalization. The group has characterized a minimal secretion sequence within the homeodomain of the Engrailed homeoprotein, based on the ability of synthetic peptides to cross an impermeant cellular barrier. This process is highly specific for homeoproteins as it requires both homeodomain internalisation (Penetratin) and secretion (Sec) sequences. For the next four years, the group plans to further analyze the possible link between the nucleus and the unconventional secretion process, and to investigate the role of lipids in unconventional secretion. The role of lipids in unconventional secretion will be further analyzed by modification of the intracellular lipid content in specific sub-cellular compartments and by studying mutant proteins deficient in lipid-binding. The principal investigator team is publishing at a reasonable level and collaborate nationally and internationally. Their projects are nicely focused on the key expertise of the team and adequate to its size. Their research focus is of great interest and should lead to the discovery of unsuspected mechanisms of the molecular transfer of information between cells within tissues. Biotechnological applications are within reach since the crossing of biological membranes remains a limiting step that restricts the use of therapeutic molecules. The group has developed a non-viral strategy allowing the cellular delivery and intracellular biological action of hydrophilic nucleic acid and peptidic molecules, based on the fusion to small peptide sequences, known as Cell-Penetrating peptides. Although mainly based on ex vivo models, the physiological significance of their studies will be continuously assessed through a close collaboration with the team "Développement et neuropharmacologie". In particular, the study of homeoprotein paracrine activity in the regionalization of the chick embryonic neuroepithelium provides an ideal context to analyze the functional consequences of quantitative or qualitative variations of homeoprotein secretion. While the team is addressing questions in the field of unconventional mechanisms of cell biology, it should also implement more 'conventional' investigations. Strong expertise exists at the IBENS as well as more generally in the field of cell biology of membrane transport (e.g. live-cell studies or ultrastructural studies employing microscopy techniques) should be taken into account in order to further examine the cell biology of homeoprotein secretion and transport. Also the search for specific molecular partners or machineries involved in homeoproteins pathways should be prioritized. Another concern is the level of independency of this group in the future. Most of its activities, although clearly focused on the cell biology processes of homeoproteins, are related, if not directly linked, to the group "Développement et neuropharmacologie", with regard to both past studies and future work. In the future, the team should make an effort to establish an independent research profile, while maintaining the strong and fruitful collaboration with the group of origin. They should also consider classical molecular and cell biology approaches, aimed at analyzing the subcellular localization, quantitative aspects of intracellular transport, and biophysics of homeoproteins.

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| A | A | A | A | A |

**Team : Développement et neuropharmacologie**

The principal investigator is world-leader in his area of research. Clearly the highlight is the discovery of a novel mechanism of signal transduction involving the intercellular passage of homeoprotein transcription factors. Also, the subsequent analysis of this process and of its role in brain development has led to important new insights and excellent publications. Together with the IBENS head, the principal investigator is one of the two leading figures within the IBENS.

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| A+ | A+ | A+ | A+ | A+ |

**Team : Développement précoce**

The past work of this team has allowed them to decipher the molecular mechanisms involved in the early development of the endoderm. They have unraveled the central role of Casanova and of the nodal signaling pathway in this process. The project concerning the characterization of new genes involved in endoderm development and the control of movement by Casanova is in line with their excellent expertise and very interesting. The project concerning the feeding behavior, although preliminary is particularly appealing and this line of research, even though very risky, is very promising and fascinating. The committee believes that the ratio between the number of PhD students and the number of tenured researchers in the team is low and encourages efforts to recruit new PhD students. In addition, the committee thinks that the team has spread its efforts a bit too broadly, which threatens to weaken the efficiency of the group. This group has a strong expertise in using the zebrafish embryo to investigate the complex question of endoderm development. The group is encouraged to focus their activities on the key projects, i.e. the projects concerning endoderm development and the feeding behavior in relation to taste bud development.

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| A | A | A | A | A+ |

**Team : Développement et fonctions des cellules ciliées**

This group, which has just joined the IBENS, presented an interesting project regarding the development of ependymal cells. Their focus is mainly on fundamental research with possible implications for adult stem cell research. Their work has led to remarkable technological advances in the study of the mechanical role of the cerebrospinal fluid on cell differentiation. This is a promising group that has to develop its research in the new environment. It is a junior group with great potential. The work is mainly concentrating on the development and differentiation of ependymal cells during embryogenesis. The group is operating in a very competitive field of research and all efforts should be made to recruit more postdocs and PhD students in order to reach critical mass. Given the importance of stem cell research in biomedicine, it is highly recommended to strengthen and extend projects with regard to translational implications.

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| A | A | A | A | A+ |

**Team : Régionalisation nerveuse**

The main interest of this team is in neurogenesis and neuronal patterning in cerebellum with a focus on the long-term influence of morphogens. One topic concerns the role of white matter progenitors in cerebellar interneuron differentiation. Another topic is the description of a non-conventional function of a caspase in the early differentiation of the neural tube. Another final aim is to describe the molecular control by transcription factors of the successive generation of distinct groups of GABAergic neurons. These projects have solid funding until 2012, and the group is involved in international networks. The group has internationally recognized expertise in its field and has regularly produced scientific publications in high-standard journals until recently. The projects are ambitious and original, but are carried by only two senior scientists who have published independently. One of them will retire soon. Thus, the size of the team seems to be too small to adequately respond to future challenges. Moreover, no young investigator has been identified who may benefit from the team's experience and who may develop and expand the research projects that were presented. Also, publication productivity has decreased over the last two years. This team is encouraged to focus on only a few selected projects in order to maintain the high level of research quality, and plan to either strengthen the group with young scientists in order to continue to develop independently within its own area of expertise, or to join another IBENS group in order to remain competitive.

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| B | B | B | B | B |

**Team : Orientation du fuseau mitotique et détermination du devenir cellulaire**

This group will join the IBENS soon. It presented an attractive project regarding mitotic spindle orientation and the link to cell cycle control in neurogenesis. The work presented represents a very nice descriptive analysis, which is required to set the stage of further investigations. To decipher the molecular mechanisms linking orientation of cell division and cell differentiation, future work will require working with mouse mutants, and the committee hopes that the new institute will provide all the required technical assistance to allow the proper development of this very interesting research field. Given that this is a new group, a particular effort should be made to recruit PhD students and postdocs in order to rapidly reach a critical size.

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| A | A | A | A | A |

## Neurosciences section

**Team : Cervelet**

This is a large group, with five permanent investigators and several PhD students and postdoctoral fellows. Despite its size, the group has a strong cohesion around a main scientific aim, i.e. neurotransmission in the cerebellum. Their analysis covers several levels of complexity, i.e. molecular, synaptic, and neuronal network analyses. Several interesting and important topics were proposed, with clearly identified sub-groups involved in their study. The first subject concerns network dynamics and its link to behavior. A recent successful approach was the development of the tetrode recording technique, which led to the demonstration that Purkinje cell activity is synchronized by a high-frequency population oscillation. A key new goal in this regard is to understand to what extent these high-frequency oscillations are involved in learning and memory of motor tasks and in motor control. Another aim is to simultaneously record several brain regions in order to investigate their respective roles in the integration of motor control. The second subject concerns the analysis of the role of the large fraction of silent synapses on the Purkinje cells and of the presynaptic NMDA receptor identified in parallel fibers. The third subject concerns the spillover of glutamate observed at the connections between cerebellar Purkinje cells and climbing fibres. This glutamate spillover creates the conditions for the coexistence and interactions between synaptic and para-synaptic glutamatergic transmission. The main goal here is to decipher molecular pathways activated by extra-synaptic glutamate and its role in parallel fiber coordination. This analysis will likely generate new concepts in neuronal transmission. The last issue concerns the cerebellar regionalisation and the role of functional modules. One key aspect in this regard is to decipher the genetic program controlling functional cerebellar regionalization and its relationship with zebrin modules and the internal circuitry. Altogether, this team has very interesting experimental models and very good projects, and it possesses a well-developed expertise to achieve the main goals they propose. The committee was impressed by the high quality of the recently obtained results and their publication in international journals with high impact, and also by the ambitious research program. With regard to the latter issue, the team may lack a strong expertise in imaging, which might be of importance in the future. However this problem can be addressed through the use of the imaging platforms within IBENS.

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| A+ | A+ | A | A+ | A+ |

**Team : Neurobiologie et génétique de C. Elegans**

This team has made major contributions, both at the technological and at the conceptual level. The group developed optimized ways to prepare samples for high-quality electron microscopic analysis of C. elegans morphology. They also developed new ways to generate mutants in this organism, as well as a simple strategy for making knock-out and knock-in animals. Using this animal model they identified important proteins and

mechanisms involved in the formation of cholinergic neuromuscular junctions. The group identified two important scaffold proteins, Lev9 and Lev10, that are required for the proper assembly of cholinergic receptors at the synapse. The observation that Lev9 is a multidomain protein composed of several CPPs reveals important new nervous system functions for such proteins, which are generally considered to be mostly involved in the complement reaction. In a real "tour de force", they were able to functionally express the levamisol receptor complex, and showed that this requires the co-expression of 8 genes, the 5 receptor subunits and 3 auxilliary proteins. This will help to identify the mechanism of action of levamisol. The strengths of the group are the excellent use of the C. elegans model, and the combination of anatomical, genetic, behavioral, and functional reconstitution approaches. The group has established excellent international collaborations, on well defined projects with excellent collaborators. The team is already well developed, and therefore meets all requirements for a long-term success. Projects are well supported by ongoing grants. There is a strong potential for further scientific development. Due to limited access to lab space and infrastructure, the potential of this team is somewhat limited. This issue should be addressed in the future.

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|---|---|---|---|---|
| A+ | A+ | A+ | A+ | A+ |

**Team : Dynamique corticale**

The team has the ambitious aim to study cortical sensory integration in vivo. The research of the team over the last four years has focused on the analysis of the overall organization (at the scale of tens to thousands of neurons) of neuronal activity in the brain (e.g. maintenance of spontaneous activity in small networks, spatio-temporal orchestration of activity between neighboring neurons, encoding of sensory parameters in cortical micro-columns). To do so, they developed a number of biological approaches and combined them with very original optical imaging techniques. They now have successfully met all the technical and biological challenges and are able to follow the activity of hundreds of cortical neurons, for example of the rat barrel cortex during controlled stimulation of whiskers. The group is one of the very first worldwide to have successfully set up this demanding set of techniques. Using this technique they have addressed a controversial question, i.e. whether cortical whisker barrel fields have a kind of map for directional sensitivity to whisker movement. Their work largely settles the controversy by showing the absence of existing directional maps in young animals and their presence in older animals. These findings led to the interesting concept that the late development of directional sensitivity in the barrel cortex might be related to increasing exploratory experience. The main strength of this team resides in its interdisciplinary activities. Due to their excellent background in physics, they can address challenging problems regarding the functional organization of the cortex, mainly through major technological developments, most notably in two-photon microscopy and brain imaging. In this regard, they have improved, and continue to improve, signal to noise ratio, depth of penetration. and temporal resolution in two-photon fluorescence microscopy. In the past, they focused on fast scanning two-photon fluorescence microscopy. They showed that the use of large aperture acousto-optic deflectors (AOD) allowed to access much larger fields of view than previously achieved. They built a unique setup, which allows them to record from freely selectable points-of interest at high speed (1 kHz), thus maximizing the signal to noise ratio. Following their previous work they now plan to implement the use of AOD scanners for in vivo recordings. To solve the recurrent problem of motion of the brain due to breathing and heartbeat, they propose a series of clever approaches, mainly pursued through close collaborations with Dieudonné's team at IBENS. A technological barrier to accurately image brain activity is the poor penetration depth, even in two-photon fluorescence microscopy (a few hundreds mm) and the multiple distortions, mainly due to the heterogeneity of the biological tissue (e.g. blood vessels). These distortions increase the size of the point-spread function, causing a blurring of the images. An increase in depth penetration would significantly increase the information provided by two-photon fluorescence microscopy. To extend the penetration depth of two-photon fluorescence microscopy, the team started with the challenging task to use adaptive optics. They are currently implementing a deformable mirror in one of their two-photon fluorescence microscopy setups and will explore different strategies using as a model the rat brain cortex labeled with an SR101 dye. This project is pursued in collaboration with Boccara (ESPCI), Beaurepaire (Ecole Polytechnique), and the French company 'Imagine Optics', and in collaboration with Denk (Heidleberg, Germany) through a joint PhD student. These are just a few challenging technologies that this team plans to develop, with a high chance of success. The number and the level of publications of the last three years are good. This rather new and young team is encouraged to better disseminate the very interesting and important results of their research.

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| A | A | A | A | A |

**Team : Transmission inhibitrice**

Although this is a relatively new team, it is well established with three senior researchers and young co-workers. They pursue a multidisciplinary approach to study aspects of inhibitory transmission in the brain. The team has had an excellent scientific production over the recent years. The projects build on the demonstrated expertise of the senior scientists of the group in investigating the physiology and pathology of inhibitory synapses, including human pathology. The research of the group will make important contributions to the general understanding of inhibitory transmission. The group has develped a set of interesting and original projects that involve several challenging technical improvements (including cell imaging and transgenic mice), stimulate collaborations (also with private companies), and are useful for other groups inside IBENS. The group has sufficient funds, is involved in high-standard networks, and has the facilities needed to further develop its projects independently.

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|---|---|---|---|---|
| A+ | A+ | A | A+ | A+ |

**Team : Modélisation mathématique de la physiologie cellulaire**

The main goal of the group is to model the properties of cellular and physiological behavior, to extract mathematical principles underlying cellular function, to analyze, both numerically and analytically, the derived equations, and to propose corresponding testable experiments. Their approaches are physical modeling, mathematical analysis, and computer simulations. The originality of the group relies on the idea that each project involves collaboration with an experimental group so that hypotheses and quantitative results can be experimentally validated in an iterative process. Until recently, they focused on modeling microdomains such as dendritic spines, the outer segment of photoreceptors, and synapses. More recently, they also studied cytoplasmic trafficking, where they analyze the motion of particles (ions, molecules, proteins, nucleic acids) in microdomains in order to identify the cellular microdomain function based on elementary chemical reactions. In the past, they developed a mathematical theory and numerical simulations to compute explicitly the time a Brownian molecule spends inside a microdomain and they now apply these techniques to estimate the mean time a Brownian receptor spends inside the post-synaptic density, which is a fundamental microstructure of synapses. Corresponding results are important to analyze the properties of the postsynaptic part of a synapse, which is involved in regulating synaptic plasticity. In the past three years, the group was successful with various projects including the quantitative analysis of various aspects of surface trafficking of proteins or the quantification of the amplification cascade occurring on the surface of internal disks in rod photoreceptors. Recently, they have modeled virus and DNA trafficking and obtained estimates for the probability and the mean time that a biological particle takes to reach a small exit site, e.g. a nuclear pore. Their quantitative analysis offers new perspectives to numerically simulate virus behavior in the cytoplasm and to analyze the role of the cytoplasmic parameters. The expertise of the group is an ideal component of IBENS. The principal investigator is a recipient of an ERC-starting grant and was previously granted as a 'chaire d'Excellence' (2004-2007), documenting his excellent expertise and potential. He regularly published in theoretical and biocomputational journals as well as on issues at the interface of biology and applied mathematics or biophysics. The spectrum of projects studied by the group is rather broad, which is in part due to the fact that the group depends on collaborations with experimentalists. Still, a slightly more stringent focus on the biological aspects of the

team's research would be helpful for the group itself and for the IBENS as a whole. Also, the choice of methodological approaches or models to tackle a given problem may be improved by extended comparative studies. The principal investigator's group is an essential part of the IBENS activities and is excellent. IBENS is encouraged to pursue the full integration of the group.

| Note de l'équipe | Qualité scientifique et production | Rayonnement et attractivité, intégration dans l'environnement | Stratégie, gouvernance et vie du laboratoire | Appréciation du projet |
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**Team : Récepteurs NMDA**

This team has made major contributions to the understanding of NMDA receptor function. They demonstrated that the "N-terminal domain" (NTD) of these receptors is involved in an allosteric tuning of channel opening. They first identified Zn as a key modulator of NMDA receptors (especially those containing the NR2A subunit, and to a lesser extent, those containing the NR2B subunit) and identified its binding site within the NTD. They showed that ifenprodil, an NR2B specific inhibitor, binds to the NTD. They developed an original approach to decipher the functional properties of triheteromeric receptors, which led to the functional identification of such receptor complexes in neurons. They revealed some structural features responsible for the allosteric transduction between the NTD and channel closure. These studies led to 5 major publications, which is an excellent outcome. Within the next four years, the group will work on three main projects. (i) The characterization of the quaternary organization (dimers of homodimers vs. dimers of heterodimers) of the NMDA receptor using AFM, as well as of the structural basis of the control of channel Popen and NTD; (ii) the identification of new ligands acting at the NMDA subunit NTD using a combination of modeling and medium throughput screening strategies; (iii) the characterization of the physiological role of Zn-inhibition of the NMDA receptor, by generating mice expressing an NR2A subunit that is insensitive to Zn. All these projects are well planned and supported by preliminary data. Such a program is in perfect line with the small size of this team. This is a well-focused small team with established multidisciplinary collaborations (medicinal chemistry, structural biology, mouse genetics, behavior), including collaborations with industry. They have produced high-quality and internationally recognized publications in a very competitive field. The questions tackled are important, especially when considering the involvement of NMDA receptor in synaptic plasticity and toxicity, and as a target for drug development. The program dealing with the identification of the physiological role of Zn acting at the NMDA receptor is well planned but highly risky. It will need important contributions from collaborator in analyzing physiological and behavioral data. The first project complex would need introduction of biophysical methods. This team is encouraged to recruit additional scientific staff and they should consider to introduce biophysical approaches (e.g. based on fluorescence imaging and FRET) in order to be able to analyze and validate the proposed conformational changes involved in receptor activation and modulation.

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**Team : Neuroéthologie du zebrafish**

This is a junior group that was recently formed at IBENS and in fact only consists of the group leader himself. The principal investigator has worked as a postdoc in the USA on zebrafish with an outstanding publication output. He showed how motor behavior is regulated at the cellular level. The ongoing projects, which will employ genetic manipulations in order to alter neuronal ensembles implicated in zebrafish behaviour, are extremely interesting and challenging. Simultaneous recording of several hundred neurons in the optic tectum of zebrafish correlated to the motor activity of the tail will allow to analyze the plasticity in rhythmic

activities. Specific light inactivation of inhibitory or excitatory cells in transgenic larvae expressing modified channels will permit deciphering the origin of rhythmic activity. Good starting grants are in place. It is going to be crucial for the group leader to recruit talented postdocs and PhD students. In order to compete efficiently, several approaches should be taken to genetically manipulate zebrafish. Since injection of drugs in vivo should be easy to perform, pharmacological approaches could well complement the genetic ones, providing more opportunities for success.

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**Team : Biologie cellulaire de la synapse**

This team has a long-lasting history in studies on synaptic biology and made major contributions to our understanding of the assembly and dynamics of the inhibitory synapse. Seminal studies, published in collaboration with D. Choquet, showed that receptors are not static components of the synaptic membrane but are continuously diffusing at the surface of the neuron and only transiently trapped at synapses. These observations have been strengthened through the original development by the group of the use of quantum dots for molecular labeling. This technique is now widely used in laboratories worldwide to study molecules that diffuse within membranes. In particular, the group focused on inhibitory glycine and GABAergic synapses, described key events in the structural organization of these synapses, and analyzed functional consequences of receptors diffusion. This is a consolidated team, that is highly productive, and world leading in their research area. Their studies led to several outstanding publications. In the coming four years they will follow three main lines of research: (i) Analysis of the assembly and molecular dynamics of inhibitory synapses (developing new approaches to model synaptic dynamics driven by lateral diffusion); (ii) analysis of synaptic structure using cutting-edge high pressure freezing techniques, correlative light and electron microscopy and electron tomography, focusing primarily on presynaptic assembly; (iii) integrative analysis of neuronal and microglial interaction. All the three lines of research are excellent, sound, and well planned for mid-term and long-term success. This is an excellent and very focused team, with collaborations at the national and international levels. They are considered worldwide leaders. The group is well funded by national and international agencies, and integrated in European networks. Important are the multidisciplinary approach they follow to address synaptic dynamics and modeling, and their capacity to develop new ideas through new technological approaches. They also make these new technologies accessible to their colleagues of the other IBENS teams. This is partly done through know-how transfer within the imaging platform, which is under the leadership of the head of this team. Consequently, the team is an attractive element in the context of IBENS because other groups involved in research at the interface between physics, biology, and mathematics profit from its presence. Furthermore, the team is extremely lively and includes many extremely promising young scientists. The team is encouraged to develop a better interaction with industrial partners, because their technological developments are certainly commercially interesting and have the potential to be applied in studies on diseases that involve synaptic failure.

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## Environmental and Evolutionary Genomics Section

This section regroups the three teams of the former UMR 8186 (Biologie Moléculaire des Organismes Photosynthétiques). Two of the group leaders have been working at the ENS for a long time while the third one arrived recently. Two other groups qualified as "associated teams" appear to maintain collaborative research with this section. It is clear that various projects developed in this section are related to those carried out in the Functional Genomics section. The committee encourages the members of the two sections to increase their relationships.

**Team : Biominéralization et Morphogénèse**

During the last four years, this team has established itself in the field as evident by extensive collaborations and networks. The team developed and set up various tools and enabling technologies for a novel diatome model species (transcript profiling, imaging). This work complements the extensive efforts of the other team working on diatoms and helps to create a critical mass for successful future research on diatomes at ENS. In contrast to most other teams at the department, this team follows an interesting transdisciplinary approach combining biology, chemistry, physics and modeling. Prospects exist for successful translational research and impact in nanotechnology and material science. The current projects are interesting and relevant, but the current team size (1 PI, 1 PhD student, 1 technician, 1 student) is at the lower limit for viability of the group. Several grant applications are currently under review, and the situation will potentially be somehow relieved in the near future, but it will be important to secure sufficient funding for the long-term viability of the group. In part because of its limited size and in part because of investments in tool and technology development, the publication record of the last four years was not entirely convincing. It will be essential during the next four years to demonstrate the group's productivity by major contributions in the field. Likewise, it will be important for the team to demonstrate its scientific independence from the team of the head of the section by publishing in addition to collaborative papers also independent papers.

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**Team : Epigénétique et épigénomique végétale**

This is a new group in the unit. It is composed of two CNRS researchers, one professor, one associate-professor, two post-doctoral fellows, one PhD student, one CNRS technician. The group develops quite an interesting project on chromatin-based epigenetic processes in Arabidopsis at the level of the whole genome. This activity should put new light on the old enigma on the transgenerational transmission of variations of characters not linked to differences in the DNA sequence. The head of this team has already proved his capacity to successfully develop this type of projects. The publication record of the group is excellent (15 papers, with a significant number in high impact factor journals (Nature, Nat. Methods, Science…), a large proportion of which are collaborative papers resulting in particular from a fruitful collaboration with a USA group) and its activity is largely funded by national and international grants. No doubt that this is outstanding science.

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**Team : Biologie moléculaire végétale**

This team is a world-leading contributor to diatome research. It was involved in one genome sequencing project and coordinated another one. It is extremely well connected in formal and informal community networks. It also contributes considerably to communicating science to the wider public. This activity will get a further boost with the start of the planned world-circling sailing boat expedition to gather environmental genomic data. In addition to the diatome research, there is also important and competitive work going on using Arabidopsis as a model species. For the future it will be important to sufficiently balance the two projects to maintain critical mass and viability of both. The PI might want to consider to let a senior researcher of the team take the lead of the Arabidopsis project.

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## Functional Genetics Section

This section includes seven teams corresponding mostly to the UMR 8541 (Laboratoire de Régulation de l'Expression Génique) with a number of modifications. One group became recently independent while another one from CGM-CNRS, Gif-sur-Yvette has been recruited and should start a new group in June 2009). An other group will move for another unit in the future. This section is primarily interested in understanding the processes of gene expression, using various biological models including yeast, xenopus, paramecia and human cultured cells.

**Team : Biologie cellulaire de la transcription**

This group is involved in four projects. These included 1) Genetic dissection of Cyclin T1/HEXIM1 binding, 2) recruitment of P-TEFb complexes on transcription sites, 3) investigation of sub-component interactions during transcription including the possible biological role of 7SK RNAs in this complex and 4) the role of non-protein coding RNAs (specifically snRNAs) in their association with RNA polymerase II.

His efforts over the last four years (2004-2008) have focused on extending his striking observation about the role of 7SK RNA (a small nuclear RNA-snRNA) in P-TEFb-driven transcription reported in Nature in 2001. During this time this group has worked to understand the transcription-dependent dissociation of P-TEFb-HEXIM1-7SK RNA that relies upon formation of the HnRNP-7SK RNA complexes and to dissect the RNA-protein interactions involved in polymerase II driven transcription (J Biol Chem. 2005, 280(34):30619-29 and Nucleic Acids Res. 2008 (7):2219-29). The progress made by the group in these areas is scientifically sound and has assisted those involved in mechanistic studies of the RNA polymerase II complex. Their efforts to characterize the protein subunit composition of the P-TEFb complex using Fluorescent Resonance Energy Transfer (FRET) tagging of each of the subunits and mutagenesis studies on components of the P-TEFb complex (e.g. HEXIM1) are noteworthy. However, it seems that a considerable portion of this work has not yet been published (see below). Additionally, recruitment of a CNRS researcher to develop the FRET studies has been instrumental in the advancement of these studies and points to thoughtful planning and management of the section. However, it should be noted that over the last four year period the head of the group has published 12 papers of which two are reviews, and he is either first or senior author on 3 of the remaining 10 research publications. This suggests that publication productivity of the group could be improved to assist in recognizing the work that has been achieved. Finally, although the section is entitled Functional Genomics Section, the bulk of the work that has been carried out thus far can best be described as mechanistic biochemical studies rather than genomic studies. It was surprising that both in the work performed over the last four years and contemplated to be conducted do not appear to ask if the mechanistic details worked out for specific genes in the genome.

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**Team : Imagerie de la transcription**

This team investigates the dynamic properties of gene transcription, using cutting-edge live-cell imaging methods. The team leader helped to develop this method at the laboratory where he did his post-doctoral work in New York. The team leader has successfully established the live-cell imaging methods and genetic engineering strategies at the ENS in Paris, first working in another team, and since early 2007 has started leading his own team on "Imaging of transcription". He is a partner of the Janelia Farm Single Cell Consortium, which has helped him maintain collaborative links with the laboratory where he did his post-doctoral training. He has also established collaborations with other teams in New York and at the ENS, some of which have already led to publications in international peer-reviewed journals. The research proposed is focused on the study of transcription, using imaging methods. This work involves the tagging of transcription factors, RNA polymerases and proteins that bind to nascent RNAs with fluorescent proteins and the measures the kinetic parameters of transcription. It is extremely important in understanding transcriptional regulation in living cells, and how gene expression is controlled at the single cell level.

There is a risk that the team leader will focus his work more on helping others to use the cutting-edge imaging methodologies that he has mastered on various model systems and problems, and less on developing his own theme of investigation that will distinguish him from his previous mentors. As this team matures, it will be important to consider the use of a wider breath of methodological approaches and the development of projects that are mostly led from within the team (i.e. making an effort to balance out the number of collaborations), towards becoming a main player in his highly competitive field of research.

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**Team : Expression des ARNm eucaryotes**

This team leader will be joining the Unit in June 2009 to head a team focusing on eukaryotic mRNA expression. Specifically, his focus will be on the exon-junction complex (EJC), which was originally discovered by the team leader during his postdoctoral studies in the U.S. Since then, the team leader successfully continued these studies as a productive member of a CNRS team in Gif-sur-Yvette.

The team leader discovery of the EJC was a very significant achievement in the field of post-transcriptional gene expression, as this complex appears to be at the heart of several linked mRNA pathways: splicing, export, localization, quality control, and translation. Recently, he effectively used biochemical reconstitution to define an EJC core and its interactions with other components, and he collaborated with an X-ray crystallographer to generate a high-resolution structure of the EJC core with bound RNA, which was published in Science.

Going forward, this team will generate and structurally and functionally characterize more complete versions of the EJC; study the mechanistic relationship between the EJC and translational control; attempt to develop an in vitro system for NMD; and study the formation of EJCs on different mRNAs in cells.

This is an ambitious set of goals, but given the proven track record of success of the team leader, one can be optimistic that he will continue to contribute major advances to the field. The structural project builds upon the structures he's already successfully obtained with biochemically reconstituted complexes; although he will now collaborate with a different structural group, this change was well justified in his presentation. The second aim is a relatively straightforward biochemical analysis based on mapping interactions and analyzing them in the context of functional translation assays; this approach should generate a lot of important new information. The third aim falls in the category of high-risk/high-return; while it is not known whether it will be possible to recapitulate NMD in a cell-free system, having such a system in hand would represent a major advance that would make it possible to address key mechanistic questions. The fourth aim involves a genome-wide experimental analysis of EJC association with mRNAs, which will be done both in Drosophila and human cells, in collaboration with a group at the Stowers Institute. This will allow rigorous testing of current models that have assumed that EJCs form at every exon-exon junction; it seems likely that interesting complexities and variations will emerge from the proposed systematic analysis.

In sum, the team leader is a highly productive young investigator, who has made key contributions to an important area of post-transcriptional gene regulation. His proposed research program is ambitious but well within his capabilities, and was deemed outstanding.

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**Team : Génétique moléculaire des ciliés**

This group is composed of three full time researchers, one engineer and two PhD students. Research activity focuses on the molecular biology and genome expression of Paramecium, in particular studying the unique features and rearrangements of the two distinct nuclear genomes (macronucleus and micronucleus). Some outstanding advances have been accomplished over the last four years on separate projects. Sequencing of the Paramecium genome has allowed several discoveries, for example the identification of a number of genomic features, including particularly small introns with a bias against stopless in-frame introns. Using this genomic information, the group has shown that some of these introns are spliced with suboptimal efficiency and that the nonsense mediated decay pathway participates in degrading these unspliced RNAs. Another axis of research has focused on the mechanisms involved in mediating developmentally regulated genome rearrangements. The group has recently identified several trans-acting factors involved in these processes, including Dicer like proteins and small RNAs. The number and impact of publications is outstanding with high quality research papers in Nature, Genes and Development. The group has published ten original research papers. Members of the group are senior authors in five of them. There is a high level of collaborative work with outside laboratories, as shown by the involvement in the genome project and the NMD/splicing project, and the group members are invited with a very high frequency to meetings. The group has attracted young researchers and should continue to be highly productive in the near future. In conclusion the quality and originality of the projects is outstanding and the group is clearly on an upward trajectory.

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**Team : Dynamique et organisation des génomes**

This group is composed of two full-time researchers, one research engeneer and three PhD students. The group has clear orientation on employing computational methods to approach biological questions, such as reconstruction of ancestral vertebrate genomes and identification of sequences under selection. The developed gene prediction software Exogean demonstrated one of the best performance in the EGASP'05 competition among the 20 other programs applied to ENCODE regions of the human genome. The group leader was distinguished by the bronze medal of CNRS in 2007, he is regularly invited to present on international meetings, and he is active in teaching and PhD student supervision. The group built up adequate computational resources that will allow them to embark on the fast expanding field of computational genomics.

However, the publication record falls short on reflecting the presented projects. There are 10 publications since 2004 that have attracted 482 citations (including the consortium publication of the Tetraodon genome sequence in Nature cited 426 times). There is little evidence of the effort to support collaborative research. The spectrum of the projects and productivity per person are somewhat lower expectations for a leading computational genomics laboratory. In conclusion, this group needs more innovative approaches to the projects of choice to distinguish themselves in the internationally highly competitive field of vertebrate comparative genomics. He should focus on publishing the results on achieved milestones. The group would strongly benefit from closer collaborations with experimental laboratories.

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**Team : Réplication des chromosomes eucaryotes**

This team is composed of two CNRS researchers, one CNRS technician, two post-doctoral fellows and two PhD students. The group has a long-standing interest in the field of DNA replication and is well recognised at the national and European level. The team leader is strongly implicated in the management of science and in conferences organisation. The composition of the team, although relatively small, is well balanced. They have set up innovative techniques to address the molecular mechanisms underlying the control of replication fork firing. More recently, they also incorporated theoretical modelling and genome-wide deep sequencing to their analysis.

However, the technical feasibility of the deep-sequencing analysis to map the human DNA replication origins is questionable. A lot of the projects are performed in collaboration in which the actual role of the team appears relatively limited and with a risk of dispersal. Finally, the publication record, although still satisfactory, could be improved. In conclusion, the team might consider refocusing its activity on its core projects.

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**Team : Génome de la levure**

This group is composed of five professor and full time researchers (with significant teaching duties) and one post-doc. Research has focused on genomic analysis of gene expression at the transcriptional and post-transcriptional levels using S.cerevisiae as a model organism. The group has made significant advances in identifying transcriptional networks that participate in various stress responses in yeast, incorporating comparative genomics to decipher the conservation and variation of these pathways across related yeast

species. A novel research area has been initiated to identify proteins that mediate the localized translation of mRNAs coding for mitochondrial proteins. While this project is more recent, significant progress has been made by identifying the involvement of the Puf3 protein in mediating the localized translation of these mRNAs, and is likely to yield additional examples of RNA protein interactions in the future. The number and rate of publications is quite good given the number of researchers associated with the group. The group has published 18 articles, 6 show members of the team as senior authors, the rest of the publications are collaborative papers. The quality of the publications is good, but there are no papers originating from the group itself in very high impact journals. However the collaborations with teams outside the ENS have resulted in higher impact publications such as Cell and Molecular Cell. There is a strong involvement in teaching in the group, given that the two senior members have teaching positions. Given the high teaching load of the senior members, this is to be considered when evaluating the production of the group. Regarding the future of the group, the move to another institute and the retirement of a senior member is also a question mark regarding the future directions of the group.

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## 5 • Appreciation of resources and of the life of the research unit

The organizational change that led to the termination of the classical 'units' and the establishment of IBENS is regarded by the committee as an excellent move. It will strengthen the institute in many ways as it will, for example, (i) foster stronger scientific interactions, (ii) facilitate the establishment of institute-wide platforms (e.g. by pooling instrumentation), (iii) strengthen the position of the institute in its endeavors to obtain funding or to implement infrastructural improvements, (iv) generate a stronger 'corporate identity', and (v) allow to rationalize management structures. The scientific and administrative organization of IBENS and the rules for decision-making are well thought through. The committee strongly supports the reorganization of IBENS and asks the funding agencies involved to support it fully.

The committee has had a meeting with the researchers of the IBENS. It appears that they work in excellent conditions and can find in the IBENS an exciting scientific environment, an intense scientific life and appropriate technical facilities. They have however two main concerns. The first one is that their level of autonomy (in particular author position in papers, and the possibility to write grant applications) is not very clear and varies depending on the teams in which they develop their activity. This is an important concern for persons who are actually senior scientists in many cases. The other one is that they feel that there is a lack of transparency in some decisions coming from their departments, and in the functioning of the technical facilities. The committee thinks that the direction of the IBENS might consider these points to increase the integration of the researchers in the decisions and underlines also that they appreciate developing their projects in an excellent Institute.

The IBENS, as a whole, has a relatively high number of technical staffs as compared to the number of permanent scientists. Yet, some platforms and common services, such as the "mouse facility", remain under high pressure. The committee strongly recommends that more staffs are hired to sustain uninterrupted and state of the art services. Also, as a consequence of the merge between the different units, a rationalisation of the different administrative services could be sought in close dialogue with the existing services.

Genomics facilities: The IBENS runs a genomics facility with extensive expertise in microarray analyses. Due to the lack of funds for the development of this platform to new high-throughput sequencing (HTS) technologies (such as Solexa-Illumina and Roche 454), and to the fast moving developments of this field, it has been decided to invest in analysis support for IBENS researchers. Of course this might have a significant impact in the productivity of IBENS scientists in the near future. The apparent strategy of waiting for others to optimise and decide which competing HTS technology will be 'better', without actively supporting the access of researchers to the technologies, may undermine the future success of several of the teams in the Functional Genomics and

Environmental and Evolutionary Genomics Sections. The committee thinks that, considering the present circumstances, the choice to re-direct the facility toward bioinformatics and statistical analyses, and the support to help researchers to prepare samples to be sent outside for sequencing, is reasonable. However, it is not clear how this strategy could be developed with the current staff, which is mostly trained in sample handling rather bioinformatics. The realisation of the presented strategy would ideally involve exchange of wet-lab personal for bioinformaticians. The strategic and academic management of the microarray/sequencing facility should be carefully reconsidered at the level of the Institute.

Imaging facilities: The IBENS also provides an excellent and very well equipped imaging platform. Several developments have been made by the platform or the IBENS departments, in particular a digital multiphoton microscope (DIM). It is important to notice that several developments by IBENS teams have been extremely beneficial for the whole Institute. In order to follow the rapid evolution of imaging technologies, the IBENS intends to acquire additional equipments to follow these new developments, in particular those related to DIM. They should find the support to buy these equipments in order to maintain the platform at the highest level.

Animal facilities: The IBENS runs two rodent facilities dedicated to the production and housing of mutant mice including an embryo transfer service. Some of the space problems have been recently solved but the animal facilities suffer from a lack of personnel. A significant increase of the personnel is absolutely required for a normal activity.

# 6 • Recommendations and advice

The committee was worried by the fact that an excellent institution like the IBENS is working in a very suboptimal infrastructure. The building is not really suited to accommodate top-class science and lab space is very limited. Given the top quality of IBENS, it will be necessary to improve the building, provide more modern lab space, and improve the instrumentation of various platforms (e.g. the transcriptomics platform). If IBENS is to continue its excellent scientific track record, it will be necessary that the ENS and the funding agencies involved in IBENS funding make a serious effort to continuously modernize the building infrastructure and instrumentation.

The committee was impressed with the overall quality of permanent scientific staff members not heading a lab. In the discussion with the permanent staff, several issues were identified that require the attention of the IBENS leadership :

- There should be guidelines on the policy of autonomy within a given group
- It should be defined whether a given staff member can apply for his/her own funding
- There should be a definition hierarchy as to whom to go to when things go wrong or need to be changed, e.g. in the imaging platform (e.g. the question whether it should be the lab head, or the chief of the platform etc.)
- The staff agreed that the platforms in general were working well except for a shortage of staff in the animal facility
- There should be a coffee room or social area where scientific ideas can be exchanged

The committee was extremely impressed with the quality, maturity, and competence of PhD students and postdocs. Obviously, IBENS is a research institute that has attracted a group of young scientists that are among the very best world-wide. In the discussion with the PhD students and postdocs, several issues were identified that would require the attention of the IBENS leadership :

1- Organization and representatives. There is no dedicated 'office for PhD students and postdocs (with an english-speaking person for foreigners) that can help with administrative tasks (e.g. contracts), assist foreign PhD students and postdocs (e.g. with visa, police formalities, health insurance, bank accounts), and provide bridging funds (e.g. between contracts). The group of PhD students and postdocs needs official support for the creation of a students and postdocs association. After the meeting with the AERES committee, the PhD students and postdocs decided to be more active and elect representatives for the institute council, but they need the support from the IBENS leadership.

2- Management of the PhD and postdoc projects and integration in the labs. There should be an IBENS thesis committee for each PhD student of the institute as a general rule, ideally composed of an independent tutor and a researcher from the institute with yearly meetings dedicated to providing scientific and management advice. There should be an equivalent support system for postdocs (e.g. an ombudsperson) that can help if scientific or administrative problems arise.

3- Interactions within the institute. The PhD students and postdocs would profit from an in-house seminar series where seminars are given by permanent researchers.

4- PhD students and postdocs need a common/social room to rest, meet, and/or eat, which would catalyze interactions between scientists from different groups/sections/fields/floors.

5- General in-house dysfunctions. There are several safety issues throughout the building that need to be dealt with (e.g. fire alarm, inefficiency of the existing check-in/check-out system outside working hours).

6- Technical platform management issues. There is a significant lack of organization (possibly due to the lack of dedicated responsible persons) and technicians to run several of the platforms (e.g. electron microscopy, photonic microscopy, animal facility), which is illustrated by the absence of (most of the) services during vacation times.

The committee fully supports these requests.

The committee also met with engineers, technicians, administrative staff, and other supportive staff at IBENS. Most, if not all, staff members of these categories acknowledged that they are working under rather good conditions and in a top-quality scientific environment. Overall, they had clearly liked their involvement and the way science was driven before the reorganization and establishment of IBENS. This is probably why they were somewhat worried about the future organization and their career development in this new organizational framework. The organizational change that is currently being implemented, and that is fully supported by the committee, may have to be communicated and explained more clearly to these staff members. They clearly are an asset to IBENS and it is necessary that they also fully support the IBENS reorganization.

| Note de l'unité | Qualité scientifique et production | Rayonnement et attractivité, intégration dans l'environnement | Stratégie, gouvernance et vie du laboratoire | Appréciation du projet |
|---|---|---|---|---|
| A+ | A+ | A+ | A+ | A+ |

**Département de Biologie**
Antoine TRILLER
Directeur du Départment

Madame la Directrice de l' ENS,
Madame la Présidente du CNRS
Monsieur le Directeur de L'inserm,

Paris le 3 Avril 2009

Nous avons reçu le rapport de l'AERES concernant l'évaluation de la recherche dans le Département de Biologie de l'Ecole Normale Supérieure. Ce rapport concerne l'évaluation scientifique des unités INSERM (789 et 784) ainsi que les UMR du CNRS (8542, 8544, 8186, 8541). Cette évaluation a été faite dans le cadre de la fusion de ces unités pour créer une structure globale INSERM, CNRS, ENS qui s'intitulera Institut de Biologie de l'Ecole Normale Supérieure (IBENS).

Je vous prie de bion vouloir trouver ci-joint, selon les instructions, un texte en anglais correspondant au « volet global qui sera adressé au rapport d'évaluation rendu public ». Le volet corrigeant les erreurs matérielles sera envoyé dans un fichier indépendant.

Je vous prie, Madame la Directrice, Madame la Présidente, Monsieur le Directeur, d'agréer l'expression de mes sentiments les meilleurs.

Antoine TRILLER
Directeur du Département de
Biologie de l'ENS

ÉCOLE NORMALE SUPERIEURE
46, RUE D'ULM - 75230 PARIS CEDEX 05
Tél : 33 (0) 1 44 32 35 47 - Fax : 33 (0) 1 44 32 36 54 - e-mail : triller@wotan.ens.fr

# Reply to the AERES report on the research units of the ENS Biology department

First of all we would like to thank the committee for the positive evaluation and for their recommendations. We appreciate that the committee was positive about the science and the general organizational changes that we have initiated. Some concerns have been expressed and some recommendations are made in the reports, most of them will be addressed in the new organization that will result in the "Institut de Biologie de l'Ecole Normale Supérieure", the IBENS. Specially the ones concerning the senior scientists in teams, transparency, and integration of researchers in the decision processes, implication of the technical and administrative staff as well as the rationalization of the organization.

The visit of the expert board was very positive as it boosted the PhD students and post-doc to built up an association and have representative of students and postdocs in our council (this was already in the project).

Concerning an IBENS thesis committee, we don't believe that this is needed. There are already thesis committees in all the PhD programs to which the teams are affiliated. However, we believe that it would be nice to have a tutor from the IBENS participating to these committees. This will be implemented

A common room for the students and scientists is planned in the reorganization of the building. This is indeed expected to increase conviviality and boost interactions.

Concerning the building, we are pleased that the visiting committee had pointed out the very bad shape of the building. Actually the ENS has started efforts to renew part of the building infrastructure.

We were quite surprised to see that some members of the committee had pointed « *a relatively high number of technical staffs as compared to the number of permanent scientists* ». Actually, after the departure of Alain Prochiantz at the Collège de France, the department researcher forces will be 68 permanent scientists (including assistant professors), 70-75 postdocs, 80-85 PhD students. The technical forces are 50 persons, 7 of them will be retired at 2010. Furthermore 26 of them are involved in platforms. The 24 remaining ones are within teams and as you can guess, many of them don't have technicians.

The total number of persons involved in the budget management is 9. Thanks to its good science, the department is successful in getting funding. Given the high number of contracts (ANR, CEE, HFSP, FRM, ARC, LRC, …), state budgets (CNRS, Inserm, ENS), and considering the global management of the department and research units, the situation is problematic. We hope to be able to rationalize this aspect with the IBENS structure, but the « gain of productivity » is not going to be tremendous. One would need at least 2 persons per scientific sections (that will be 8) and 3-4 for the IBENS organization. The total number should therefore be 11-12 persons

Under these circumstances it is often problematic to ensure the continuity of platform services. Yet we manage to do so and have all the instrumentation (including imagery facilities) available all the yearlong.

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