



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

Section des Unités de recherche

Evaluation report

Research unit

Développement Evolution et Plasticité du Système
Nerveux

CNRS



April 2009



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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

April 2009



Evaluation report

The research unit :



Name of the research unit : Développement Evolution et Plasticité du Système Nerveux

Requested label : UPR CNRS

Number in case of renewal : UPR 2197

Head of the research unit : M. Philippe VERNIER

Institution and research organization :

CNRS

INRA

Other university or school :

University Paris 11

Dates of the visit :

16-17 February 2009



Members of the visiting committee

Chairman of the committee :

M. Philip W INGHAM, Institute of Molecular and Cell Biology, Singapore

Other committee members :

M. Jacques DEMONGEOT, Laboratoire TIMC-IMAG, La Tronche, France

Ms. Agnès HEMAR-de DARUVAR, Université Bordeaux 2, France

M. Charalambos KYRIACOU, University of Leicester, UK

M. Bertrand LAMBOLEZ, Laboratoire de Neurobiologie des Processus Adaptatifs, Université Paris 6, France

Ms. Nancy PAPALOPULU, University of Manchester, UK

Ms. Sylvie SCHNEIDER-MAUNOURY, Laboratoire de Biologie du Développement, Université Paris 6, France

Ms. Vanessa SOUBEYRE, Université Pierre et Marie Curie, France

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

M. Frederic NAGY, CNRS representative

M. Xavier COUSIN, INRA representative

Observers

AERES scientific representative :

Ms. Jocelyne CABOCHE

University or school representatives :

M. Alexandre REVCOLEVSCHI, University Paris 11

M. Jacques BITTOUN, University Paris 11

Research organization representatives :

M. Bernard POULAIN, CNRS representative

M. Florian GUILLOU, INRA representative



Evaluation report



1 • Short presentation of the research unit

The Unit is composed of five teams that perform comparative analyses of the development of the nervous system in a variety of chordate species. The Unit was established on January 1st 2000 following the division of the Institut Alfred Fessard into four Research Units. It has been renewed twice (in 2002 and 2006) and is now reaching the end of its current contract. As part of the review process the committee was asked to consider the proposal to establish a new Unit based upon UPR2197, through the absorption of the two remaining Teams from Unit UPR2216 “Neurobiologie Génétique Intégrative” and the recruitment of additional two Team Leaders.

- Number of lab members : 69 including
 - 20 researchers
 - 3 researchers with teaching duties
 - 12 postdoctoral fellows
 - 11 PhD students
 - 13 engineers, technicians, administrative assistants, including 5 paid on research contracts
- Number of HDR : 15, 11 being student advisor
- Number of students who have obtained their PhD during the past 4 years : 12
- Average length of a PhD during the past 4 years : 3.8 years
- Number of lab members who have been granted a PEDR : 0
- Number of “publishing” lab members : 21

2 • Preparation and execution of the visit

Ten days prior to the site visit, the members of the Visiting Committee (VC) were provided with a comprehensive written report on the past work and accomplishments of each research team, together with a summary of their future plans and the overall strategy of the Unit.

The meeting started with a closed doors session at which the chairman assigned to each committee member the task of leading the questioning of a specific team leader. The overall aims and achievements of UPR2216 “Neurobiology Integrative Genetics” (NGI) and UPR2197 “Développement Evolution et Plasticité du Système Nerveux” (DEPSN) were presented by their respective Directors. The latter also set out the rationale for the formation of the proposed new Unit, “Neurosciences and Development”. Following these overviews, each of the leaders of the nine teams of the proposed new Unit gave 30 minute presentations of their past achievements, current research and future plans, followed by 10 minutes of questioning by the members of the VC. After the final Team presentation on Day 1, the members of the VC split into two groups, one of which met with members of the technical and administrative staff whilst the other met with the Postdoctoral fellows and PhD students. Following these meetings, the members of the VC were taken on tours of the AMAGEN and the Multi-photon microscopy facilities.

On day 2, following the final three presentations by individual Team leaders, the VC had meetings with the Researchers, first with those who are not Team leaders and second with the Team leaders themselves. Finally, the VC had a one hour meeting with representatives of the University and Research Organisations before retiring behind closed doors to discuss their final evaluations.



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

The DEPSN Unit has, over the past decade, established a reputation for its comparative analyses of nervous system development, accumulating significant expertise in the laboratory culture and manipulation of a number of aquatic species, notably ascidians (*Ciona intestinalis*), zebrafish (*Danio rerio*), Medaka (*Oryzias latipes*), cave fish (*Astyanax*) and *Xenopus* along the way. Initially, much of the work of the Unit was descriptive, combining classical histological analysis with the contemporary modern techniques of in situ hybridisation and immuno-histochemistry to identify and compare brain regions and specific neuronal populations within and between species. Over the past few years there has been a significant shift in emphasis towards more functional analyses. This trend has been reinforced by the addition of three new Teams that have broadened the research interests and technical expertise within the Unit. Collectively, the five teams of the current Unit have published 74 original research papers during the period under review, a reasonable output for a group of this size. The majority of these have appeared in good quality specialist journals; somewhat disappointingly, however, no papers have been published in any of the major high impact journals, such as *Nature*, *Science* or *Cell* though one Team has consistently published in *PNAS*. Most of the Team leaders have also published one or more review articles, again in specialist journals, and all have been invited to a number of international and/or national meetings.

The members of the visiting committee were generally impressed by the presentations given by each of the Team leaders and by the progress and achievements of these Teams over the past four years. They recognized the unique character that the constellation of research interests and expertise of each Team has given to the Unit. The committee was particularly impressed by the Unit's technical accomplishments in the areas of transgenesis and in vivo imaging, exemplified by the AMAGEN and BioEmergences technical platforms. The future development and exploitation of these platforms should give the research Teams a significant competitive edge in the coming years. The committee was pleased to learn that its enthusiasm for the AMAGEN platform is shared by INRA, whose representative expressed very strong support for its continuation and recognized its key importance for INRA agronomic research.

The Visiting Committee recognised the strong link between the Unit and the Université Paris-Sud 11 (Orsay), through both the training of PhD student and the significant contributions to undergraduate teaching by a number of Unit staff. It was also clear to the committee members that Orsay is appreciative of the strategic importance of the Unit, regarding it as one of the strongest in the Gif-Orsay axis and seeing its research activities and focus as being a good fit with the vision for the Saclay Plateau. The committee noted the strong commitment to placing more University appointments within the Unit, a policy that can only serve to strengthen its ties with the local community. Each of the Teams has established at least one strong collaboration with a national or international partner. In addition, two Team Leaders have played key roles as co-ordinators of EU 6th Framework projects: "Embryomics", "BioEmergences" and "Plurigenes". Taken together, these indicate a healthy level of external interactions.

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

Team 1 Neurogénétique du poisson zébré

This Team is currently based at the Helmholtz Zentrum in Munich from where it will relocate in the coming months. Over the past 7-8 years, the Team has established a significant international reputation for its work on neural stem cells (NSCs) using the zebrafish as an experimental model system. A key achievement has been the identification of the Her5 and Her 11 proteins as factors required for the maintenance of pools of long lasting neural progenitors in the embryonic CNS, the role of miR-9 in regulating Her5 activity and the identification of neural stem cell pools in the adult brain. This work has led to a consistent stream of quality publications in the leading specialist journal *Development* as well as one paper in the high impact journal *Nature Neuroscience*. More recently, the Team has performed pioneering studies of behaviour in the zebrafish, establishing robust assays for emotional and cognitive behaviour. A particularly exciting aspect of these assays is their potential application in large scale forward genetic screens. This potential has already been realised by this team through the isolation of 6 mutations that modulate the reward response as well as the isolation of a mutant exhibiting hyper-aggressive behaviour. The molecular identification of the latter as an hypomorphic mutation in the FGF receptor-1 is particularly intriguing, pointing to a potential link between the control of



NSCs in the adult and the regulation of behaviour through the 5HT system. Such links between adult neurogenesis and behaviour, together with the analysis of the origin of adult NSCs using state of the art lineage tracing techniques, will form a major theme of the Team's future research, positioning it at the forefront of research into neural development and function.

The Visiting Committee note that the move to Gif will see a significant reduction in this Team's human resources, particularly in the number of animal technicians at its disposal. It will be important to ensure that the level of resource does not fall below the minimal threshold required to maintain the Team's leading and groundbreaking position within the international community.

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 2 / Neurobiologie Intégrative du Tronc Cérébral chez l'Embryon

This team investigates hindbrain respiratory centres, from the specification of underlying neuronal networks to the emergence of respiratory rhythms in the embryo, and their maturation at early postnatal stages. This question of central physiopathological importance is addressed using a truly original and cutting-edge combination of approaches including genetic dissection of cell lineage, electrophysiology and imaging in the embryo, and postnatal respiratory physiology. During the last 4 years, the team made important contributions to establishing the key role of dual pre-Bötzinger and parafacial oscillators as generators of respiratory rhythms (31 PR articles, including 2 J Neurosci. papers rated "F1000 Must Read", 5 PR reviews, 5 book chapters). The team is very well funded through EU, ACI, and ANR (coordinator) grants.

The very ambitious and original project focuses on : 1) demonstration of identified molecular determinants specifying the embryonic pre-Bötzinger (Dbx1) and parafacial (Krox20) oscillators, 2) chemosensitive ambition of the embryonic parafacial oscillator based on demonstrated Phox2b positive cells and TASK2 channel selective expression, 3) connectivity synchronizing the oscillators ipsi- and contra-laterally (Robo3 signaling), and 4) characterization of the unique mouse model of Central Congenital Hypoventilation Syndrome (Phox2b27A1a human mutation). The team has the required competence and established collaborations to fulfil this ambitious project.

Altogether, this is an outstanding project with high impact potential and clear link to postnatal respiratory pathologies. A major strength of this Team is its unique expertise in physiology of embryonic and adult neural networks, which attracts collaborations with world leaders in developmental genetics, axon path-finding and respiratory physiology. There is excellent synergy between team members with established complementary expertise. A potential weakness is the reliance on mouse genetic models obtained through collaborative agreements; it may be advisable in the longer term to establish closer association with developmental geneticists.

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 3 Génétique Moléculaire des Rythmes Circadiens

Over the past four years this team has consolidated its international position as one of the leading groups working on the neurogenetic analysis of the *Drosophila* clock. In 2004, the team published a Nature paper that established a paradigm shift in the field, which is being copied by groups all over the world. This paper dissected the neuronal basis of the clock into the so-called M and E oscillators. Further work on the clock network (published in PLoS Biol in 2007), revealed how the M oscillator was inhibited by light while the E oscillator was activated by it and provided a fundamental understanding of how the two oscillators cooperate to provide seasonally rhythmic behaviour in temperate latitudes where photoperiods become increasingly exotic. Although their identification of a new gene, clockwork orange (*cwo*) and the designation of its central role in the clockworks was pre-empted by two competitor groups, this Team's study is certainly more comprehensive and is already highly cited. This illustrates how the Team continues to make a very significant European contribution in an extremely competitive field dominated by large groups from the USA. The current projects are focused on how the clock is entrained, both in adults and larvae, by temperature and light, with a particular emphasis on the molecules cryptochrome and the rhodopsins as the input to the clock neurons, and PDF for the output. Other studies focus on the development of the clock and on a ubiquitin ligase encoded by *dtrip12* that is involved in posttranslational control of the positive regulator CLK. Finally a large scale RNAi screen has identified a number of new clock genes.

The Team is large with six researchers and a number of technical staff and post-docs, PhDs and visitors. It disseminates its work through participation in conferences both internationally and nationally. Its members also make significant contributions to both undergraduate and graduate teaching. The external income is considerable. The Team is involved in the major EUCLOCK consortium of the EC. While the publication quality is extremely good in terms of IF, the committee felt that the output (5 peer reviewed papers) was on the low side. Having said that, the type of fly work performed is extremely demanding and labour intensive, and for high quality publications in this field, it is important not to publish prematurely. Nevertheless the committee noted that one of the researchers has not published at all, and does not appear to be close to publishing.

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	B	A+

Team 4 Développement et Evolution de la Neurotransmission

This team is composed of 8 members: 2 researchers, 1 engineer, 2 post-doctoral fellows, 2 PhD students and 1 undergraduate student. The size of the team is maintained relatively small by the team leader because of his heavy administrative load, which was considered sensible by the members of the committee. Nevertheless, the team have succeeded in raising funding from various agencies and foundations, and have published numerous papers in good quality specialist journals. The Team performs original and significant research focussing on dopaminergic neurons: their specification and organization in the central nervous system of chordates and how this organization influences the functions sub-served by neurotransmitter systems, using zebrafish, ascidians, eels and mouse as model systems

The specific projects are :

Comparative study of the distribution of the two paralogues of tyrosine hydroxylase, TH1 and TH2 and dopamine receptors in zebrafish and avian brains.

Analysis of the genetic and cellular mechanisms controlling neurogenesis and differentiation of dopamine neurons and the implication in modelling human diseases.

Origin and regionalization of the hypothalamus and the differentiation of intrinsic dopamine neurons.

The team is collaborating with different groups of the Unit and has already published with some of them. This underlines its central role in the coherence of both the current and proposed Units. The visiting committee appreciates and congratulates the research and the management of this team.



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 5 Rétinogénèse

This will be a new team for the Unit, headed by a young investigator originating from the CNRS research Unit UPR 8080. It consists of 3 researchers, 4 technical staff, 1 post-doc and 2 PhD students. The team studies stem cells and neurogenesis in the retina of the amphibian, *Xenopus laevis*. There are two main research axes, retinal stem cell proliferation and cell fate determination. The *Xenopus* retina is an excellent model system to address these questions, because it generates several specific cell types in a well-characterised sequence and it continues to grow through the maintenance of a stem cell zone, the ciliary margin, at the periphery of the retina. In addition, *Xenopus* is a particularly good model system for these questions, as it offers a number of modern tools such as the possibility of large scale expression and functional screens, a sequenced genome and molecular tools for knocking out gene expression. The team leader has contributed to the development of methodology for knocking out gene expression in small clones in the retina via lipofection. Through external collaborations, they are using a number of innovative tools such as systems to express or inactivate Wnt signalling in the post-embryonic retina.

The team is well known for their work in dissecting the effects of Hedgehog (Hh) signalling in the cell cycle kinetics of the retina, which was published in a high impact journal (*Genes & Development*) and raised the international profile of the team. Their future plans include projects to continue elucidating the mechanistic detail of signalling as well as large-scale high throughput projects to uncover novel molecular players in eye development; these should fuel further projects and allow the team to expand further. There is identifiable synergy with the other teams in the Unit, particularly with Team 8 in the analysis of stem cell maintenance in the tectum of Medaka, and with Team 4 on the specification of neuronal subtypes elsewhere in the CNS.

The visiting committee noted that there is currently no space for this team to move in. It is important that suitable space is found as soon as possible, as interactions from a distance are always more difficult.

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 6 Développement et Evolution du Cerveau Antérieur

This team studies the development and evolution of the forebrain by using a comparative approach in a number of species, namely the mouse, *Xenopus*, Medaka, *Astyanax*, and zebrafish as well as more primitive organisms such as the lamprey. There are two main research axes : the evolution of the telencephalon, and in particular corticogenesis, and the evolution of midline signalling. This team is fairly recent and consists of one group leader and 6 members, that is 2 post-docs, 2 students and 1 technical staff. The Team leader trained within Unit 2197, in Team 4, and has been leading an independent Team for just the last 4 years. There is a strong evolutionary undercurrent in the research of the Unit and team 6 fits with this very well. There is clear potential for synergy with other teams, both current and incoming.

The quality of the work is excellent, and the publication output is good. However, most publications are in medium impact or specialised journals. It was felt that the work carried out by this group is important, and has great potential, but given the small size of the team, it would be advisable to focus on a smaller number of projects albeit temporarily, until the group size increases. In turn, this will allow each question to be pursued



in greater depth, which should result in publications with greater impact. The committee does not wish to be prescriptive in choosing projects, as this decision rests with the group leader, but it was noted that mouse corticogenesis, while strategically important is also an extremely competitive area.

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 7 Réseaux Génétiques et Morphodynamique

This team has done impressive work since it was established three and a half years ago. It has developed a very original 4D image workstation through the collaboration of computer scientists specialized in image processing, applied mathematicians and bio-informaticians dedicated to complex systems and systems biology, and software engineers coming from a private company. This workstation acquires (in biphotonic microscopy) and manipulates very huge data-bases (of several petabytes), which store images recording the individual trajectories of the cells involved in differentiated lineages during the embryogenesis of the zebrafish. The Team leader has managed as coordinator two collaborative European projects, BioEmergences and Embryomics, bringing together one dozen laboratories in a very active network devoted to the individual reconstruction of the cell fates in the tissues history during the 4 first days of the embryogenesis.

The Team has solved very difficult problems, starting from the reconstruction of the spatio-temporal behaviour of cells and tissues and progressing to the representation of these dynamical phenomena at different scales : in vivo genetic expression, nuclei segmentation, mitosis backtracking to the earlier sphere stage, individual cell motion and global tissue dynamics (like gastrulation). The Team has definitively validated the subduction scenario for the presumptive forebrain morphogenesis.

The publications are good on the computer science side (journals like *Kybernetika* and *Electrical Engineering* and well ranked computer science conferences) and promising on the biological side. The initial high-risk but potentially high-impact ambitions of the project (to explain in what place and at what time differentiated cell lineages appear, grow and move) are only partly achieved, but the present state of the research suggests that after the complete statistical exploitation of the acquired data and the definition and simulation of a mechanistic in silico modelling, the team will reach its final goal of in silico virtual morphogenesis, explaining further the major steps of the in vivo development.

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 8 Morphogenèse du Système Nerveux des chordés

Team 8 is the largest of the former DEPSN and will be one of the largest in the proposed new Unit. Research activity has focused on two major themes :

- 1) understanding the emergence of circum ventricular organs in chordates using the anterior placode of the prochordate *Ciona* as a simple model species.
- 2) deciphering genetic network controlling cell proliferation in the Medaka optic tectum.



During the course of this latter project, participation in a EU funded project “Plurigenes” promoted the shift of the group interests to the identification of neural stem cells. Analysis of the very marginal zone of adult optic tectum proliferation zone reveals the presence of slowly cycling cells likely neural stem cells (NSC). An in situ screen was performed focusing on genes expressed in these NSCs, leading to the identification of candidate genes.

The Team has also made notable technical advances, becoming one of the very few groups capable of breeding Ciona under laboratory conditions, as well as improving transgenesis methods through the use of meganucleases. This latter accomplishment led to the establishment of the AMAGEN platform, which aims at providing fish and Ciona transgenesis services for the research community.

In the coming years, involvement in projects using Ciona will be reduced (focusing on identification of neuropeptide coding genes) in favour of projects pursuing the analysis of the control of neural cell proliferation: identification of pluripotent associated genes in tectum NSC, identification of genes that could provoke dedifferentiation of neural cells and identification of cis-regulatory elements in genes expressed in proliferating cells, cell cycle exit and stem cells.

Given the size of the group and the high level of funding, the committee felt that the publication level could have been higher. At the same time, it acknowledges that systematic screens require significant expenditure of energy and resources with no guarantee of significant returns. The committee recognizes that the contributions of this Team will be pivotal in the future N&D Unit with human resources devoted to the research community (production of tools) and opening to internal collaboration.

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 9 Développement et Evolution de la Crête Neurale

This is a relatively small team whose permanent members, the Group leader, a “Professeur Emerite” and a Research Engineer who runs her own scientific projects, have a long-standing interest in the study of the neural crest (NC). In addition to the three researchers, the team is composed of one post-doc and two PhD students.

During the last four years the team studied the function of the cranial neural crest (CNC) in brain morphogenesis in avian embryos, using chick-quail chimeras and functional analyses by in ovo electroporation. They uncovered a function of the CNC in dorsal brain formation and demonstrated that this function is achieved by BMP antagonists expressed in the neural crest. They also used a cell culture assay they had developed previously in order to study the multipotency and stem cell properties of NC cells. These two projects led to the publication of several papers in high quality journals (notably PNAS and Development).

The projects of Team 9 include : 1) the characterisation of the molecular mechanisms involved in CNC formation and in its function in brain morphogenesis, by in ovo functional experiments; 2) the molecular characterization and the purification of multipotent NC cells in culture.

The strength of Team 9 resides in their excellent knowledge and experience in the research field, and in their strong international notoriety. The committee recommends that the team increases its potential, both in terms of funding and personnel, in order to be able to develop ambitious and innovative projects in the best conditions.



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

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

The total non-salary support for the Unit between 2005-2008 was €2.82m, equivalent to ~ €700K per annum for five Teams. This is an adequate though not generous level for a Unit of this size. The Committee noted that the majority of this support comes from external sources, and in particular from the European Union. The Unit Director and his colleagues deserve congratulation for their efforts in securing such a high level of outside support.

Time constraints prohibited a tour of the general laboratory areas, but the facilities for the two technical platforms were inspected. The BioEmergences platform seemed to be very well equipped with two multiphoton confocal microscopes and a prototype digital scanned light sheet microscope (DSLMS). The aquaria facilities are quite compact and though adequate for current usage will clearly require significant expansion with the arrival of the new Team using zebrafish.

— Technical and Administrative staff

Most of the Technical and administrative staff (19) have permanent positions, with just a few (5) on short term contracts. In general, the ITA appear happy with working conditions within the Unit. They appreciate the stimulating and friendly atmosphere within the labs, participate in lab meetings and journal clubs, have the opportunity to attend national or international meetings and are included as co-authors of papers to which they have contributed. They also have easy access to information regarding training sessions and are free to apply to attend these. They have their own representative in the lab Council and feel supported by their group leaders/head of unit. One concern, however, is that internal advancement (promotion au choix) would become harder as the Unit enlarges.

The technicians and engineers working on the technical platforms seem happy with the way it is managed. However, they expressed concerns about their future and advancement. Their involvement within the platforms (especially AMAGEN) has precluded significant involvement in research projects. The ITA with permanent contracts hope that once the platform is running smoothly, they will interact more on research projects (part-time on the platform/part-time on research project). However, those with short term contracts are concerned that their very specialized skills acquired working on the platforms will not be easily transferable.

— PhD Students and Post doctoral Fellows

Of the 14 students and 13 post-doctoral fellows that met with the Visiting Committee, 4 and 5 respectively came from overseas. There was agreement that the level of resource within the Unit is generally good, with adequate funding to perform experiments and to attend national and international meetings. There are good interactions and collaborations between labs. Communication is also good, facilitated by weekly meetings of the entire Unit, alternating between research reports and journal clubs. Presentations at these meetings are generally delivered in English by foreigners, but usually in French by francophones. The committee questioned whether this is in the best interests of staff and students, given that English is the prevailing scientific language.

Few PhD students complete their thesis within 3 years. When questioned about the motivation for doing a PhD one respondent suggested it was essential to be employable. More than 50% of the PhD students aspire to go on to do post-doctoral training. Most of the post-docs would like to pursue a career in research but the majority appeared very pessimistic about their chances of doing so, at least within France. Nevertheless, fewer than 50% said they would be willing to go overseas to pursue a research career. In general there was a high level of



satisfaction with their team leaders - all expected to have a major contribution to the preparation of their work for publication.

— Researchers (non-Team leaders)

The majority of the Researchers are French nationals with only one from outside France. All but one trained elsewhere and joined their current teams after post-doctoral research. In general, they seem content with the direction and management of the Unit and with their interactions with their team leaders. Only a minority aspire to become team leaders themselves and most consider their current positions to be a good career option. Their main concern is with the management of space allocation and the perceived problems arising with the arrival of new teams.

— Researchers (Team leaders)

There was general enthusiasm for the establishment of the proposed new Unit amongst the Team Leaders, with one in particular opining that it would have a major impact on the progress of his research through closer interactions, and all believing there would be significant synergy within the new grouping. In particular, it was felt that the technical platforms will be exploited by most of the groups to better effect. The importance of developing links with outside institutions was recognized - for instance the Institute for Complex Systems has expertise which will be invaluable in developing the 4D imaging platform. There was also recognition that translation of basic science to the clinic requires closer interaction with clinicians. In this regard, members from the Institut du Cerveau et de la Moelle Epinière had visited the Unit recently to discuss areas of common interest, while collaborations with the human geneticists at Pitié-Salpêtrière are being established by the Unit Director. However, there was an acceptance that it is currently very difficult to attract clinicians into basic research labs (because of career training conflicts and differences in levels of remuneration between researchers and clinicians).

6 • Recommendations and advice

— Strong points :

The proposal to merge the existing DEPSN and NGI Units to form a new Unit of Neurobiology and Development was considered to be a bold, imaginative and exciting proposal by the members of the visiting committee. Such a Unit will address the next frontier in developmental neurobiology - the link between ontogeny, physiology and behaviour - by building upon the strong foundations of evolutionary and developmental biology within DEPSN and in genetics and physiology within NGI. This integration will generate a dynamic new grouping with several crosscutting themes, notably behaviour, neural stem cells and evolution and will undoubtedly be enhanced by the recruitment of the two additional teams. Both of these teams have excellent international reputations for their cutting edge research. The visiting committee considers the recruitment of Team 1 as being of particular importance to the strategy of the proposed Unit and is pleased to learn that this view is shared by the CNRS.

— Weak points :

While the overall publication rate is good, the proportion of publications in high impact journals is low. This lack of high visibility almost certainly contributes to another weakness identified by the Team Leaders themselves, namely the difficulty of attracting good PhD Students. The Visiting Committee was also struck by the dearth of Post-doctoral researchers with independent fellowships (such as EMBO, HFSP). Such independent post-docs are the life-blood of successful research institutes. The visiting committee also noted some variation in the output of individual Researchers between Teams.

The allocation of space is recognized as being imperfect at present and is constrained by historical circumstances as well as by its availability.

Although there seems to be some scope for changes in the usage of communal space within the INAF, such initiatives appear to be inhibited by the lack of overall executive control.



— Recommendations :

Space :

In the future it will be important to have a transparent space allocation model but it is pointless to introduce this at present as there is not enough space to accommodate all of the existing groups. Such a model can however be introduced once the proposed extension of the building is completed, which the Review Committee recognizes to be a high priority. In the meantime, it is essential that temporary accommodation be refurbished and made operational as soon as possible.

It would also be worth considering giving the Director of INAF more powers to take decisions on the use of existing communal space.

Recruitment :

One problem identified by the Team leaders is their ability to recruit good PhD students. While it was recognized that this is a global problem, there was a feeling that local circumstances mitigated against successful recruitment in Gif when competing with institutes in central Paris. One suggestion would be to become more proactive in recruiting from abroad - there are several sources of sponsored students (eg. the Gulbenkian Institute in Lisbon, and various Middle Eastern countries operating Government scholarships). It is also important to recruit talented post-doctoral researchers from outside France. This will add diversity and vitality to the Unit and help to raise its international profile. Publishing more papers in higher impact journals will certainly help with recruitment. The importance of a website in projecting the Unit's research strengths and training opportunities should also not be underestimated.

Collaborations :

The fusion of the two units will present opportunities to develop new lines of investigation based upon synergies between groups, several of which have already been identified. Another possible area of mutual interest may perhaps be the analysis of the circadian system of *Astyanax* and its links to eye development.

It is noted that Team 3 collaborates with another Team within the INAF that has developed an elegant aequorin-GFP reporter that allows visualization of neuronal activity in flies. Inclusion of this Team would buttress the neurobehavioural aspects of the new Unit, as well as specifically helping to add some weight to the invertebrate component.

Administration :

With the proposed enlargement of the Unit, it is essential that the vacant secretarial post be re-filled.

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+



Philippe VERNIER, Directeur

Gif, le 23 avril 2009

Tel.: 33 1 69 82 34 30

Fax : 33 1 69 82 34 47

E-mail : vernier@inaf.cnrs-gif.fr

**Mmes et Mrs les membres du Comité
d'évaluation de l'AERES**

Remarks on the Report from the visiting committee.

The teams leaders and anticipated director of the research unit, the creation of which is requested at the CNRS, sincerely thank the visiting committee and its Chairman for the depth of the analysis and suggestions made in the report. We also appreciate the precision and clarity of the wording and the detailed overview of the activity of our teams and methodological platforms, as well as of the scientific policy of the Unit. This report both recognizes the wealth of efforts made by the teams along these last few years but also encourages and stimulates us for improving the originality of our research and the quality of its published outcome.

We generally acknowledge the remarks and suggestions made in the reports. We would like to make the following comments:

1- The visiting committee has examined essentially the project of creation of an entirely new unit, which is in part the merging of two pre-existing Research Units of the same institute (INAF), with the addition of two external teams. However, the third part of the Report (Overall appreciation of the activity of the research unit...) presents the past activity of one of the pre-existing Research Units only (DEPSN, UPR2197), but not that of the other Unit (NGI, UPR2216), neither that of the Unit from which Team 5 is coming from (UMR8080). This is probably due to the fact that the Committee did not receive the corresponding documents, which were otherwise transmitted to the University and AERES. Thus, the previous scientific policy of these two Units has not been evaluated, except for their current merging into the proposed new Research Unit.

2- The Report is noting our lack of publication in very high impact journals (the Cell-Science-Nature trinity) for these last four years. This is a fact. However, we would like to stress that a few papers have been published in other very high standard journals (Genes & Dev., Nature Neuroscience, Plos Biology, PNAS...etc) and that the overall level of publication quality has significantly improved for most -if not all- of the teams over the last four years, with more than seventy papers published in journals with

Impact Factor >4 and High Cited Half-Life >10 among 140 published by all the teams together. Thus, the dynamics is good, and we will aim at maintaining this progression.

3- The Report states our difficulties in recruiting “good PhD students”. This is a bit misleading since the PhD students we currently have in our groups are very good and even outstanding in some cases. The problem we have is more to attract new students in general. But we feel that this is rather a common problem in biology labs in France, currently. Thus, the suggestions made by the committee in that matter are very useful.

These are very minor remarks and, again, we would like to warmly thank the visiting committee for its sharp and fair review of our project. We also hope that many of the suggestions made by the committee in its report will encourage our supporting institutions for helping and accompanying the evolution of our Unit in the next few years.



Philippe VERNIER