Epilepsie et cognition

Rapport Hcéres

▶ **To cite this version:**

Rapport d'évaluation d'une entité de recherche. Epilepsie et cognition. 2011, Université Aix-Marseille 2, Institut national de la santé et de la recherche médicale - INSERM, Centre national de la recherche scientifique - CNRS. hceres-02035172

HAL Id: hceres-02035172

https://hal-hceres.archives-ouvertes.fr/hceres-02035172

Submitted on 20 Feb 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

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

Section des Unités de recherche

AERES report on the research unit

Brain Dynamics Institute

From the

Université Aix-Marseille 1

Université Aix-Marseille 2

INSERM

February 2011

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

Section des Unités de recherche

AERES report on the research unit

Brain Dynamics Institute

From the

Université Aix-Marseille 1

Université Aix-Marseille 2

INSERM

Le Président de l'AERES

Didier Houssin

Section des unités de recherche

Le Directeur

Pierre Glorieux

February 2011

Research Unit

Name of the research unit : Brain Dynamics Institute

Requested label : UMR_S INSERM, UMR CNRS

N° in the case of renewal : UMR_S_751

Name of the director: Mr. Patrick CHAUVEL

Members of the review committee

Committee chairman

Mr. Christoph MICHEL, University of Geneva, Switzerland

Other committee members

Mr. Olivier BERTRAND, University of Lyon, France

Mr. Nathan CRONE, John Hopkins University, Baltimore, USA

Mr. Alain DESTHEXE, CNRS, Gif-sur-Yvette, France

Mr. Uwe HEINEMANN, University Charité, Berlin, Gemany

Mr. Stefano SERI, Aston University, Birmingham, UK

Ms. Angela SIRIGU, University of Lyon, France

Mr. Herbert WITTE, University of Jena, Germany

Mr. Claude FEUERSTEIN, University of Grenoble, France, CNU representative

Mr. Florian LESAGE, University of Nice, France, INSERM CSS representative

Observers

AERES scientific advisor

Ms. Thérèse JAY

University, School and Research Organization representatives

Mr. Pierre CHIAPPETTA, University Aix Marseille 1

Mr. Alain ENJALBERT, University Aix Marseille 2

Ms. Catherine LABBÉ-JULLIE, INSERM

Mr. Bernard POULAIN, CNRS

Mr. Jean-Charles REYNIER, CHU

Report

1 • Introduction

- Date and execution of the visit

The visit took place on February 24th and 25th, 2011. The first step was a closed-door meeting of committee members with the AERES representative to agree on the mission and timetable of the visit.

A series of presentations in the presence of all Institute members followed. The first presentation was given by the director of the Institute who explained the scientific motivation underlying the creation of the Institute and outlined the global research plan. The deputy director was also briefly outlining his role in the Institute and one of the Institute members summarized the integration of the Institute in international research consortia. After this introduction each head of the group presented his/her team and the research activities and plans. Each presentation was followed by a productive discussion with committee members.

The committee also had the opportunity for an in-depth discussion with two vice-presidents of the University, a representative of the Chief Executive Officer of the Hospital, as well as regional and national representatives of CNRS and INSERM. In addition, discussions with the PhD students, the postdocs, the permanent researchers and the engineers and technicians took place in three parallel sessions. During the second day, the committee met for a closed-door session followed by a final private discussion with the Director who provided complementary information regarding the emergence of the structure at the Institute and his vision concerning the development and the future of the Institute.

The committee highly appreciated the quality of the oral presentations and the frank and competent discussions with all members of the Institute and the representatives of the University, Hospital and Research Institutions.

- History and geographical localization of the research unit, and brief presentation of its field and scientific activities

The Brain Dynamics Institute represents the consolidation of three independent and physically separated research entities under the same umbrella: the unit U751 “Epilepsy and Cognition” at the Faculty of Medicine, the “Theoretical Neurosciences” team of the unit UMR6233 at the Faculty of Sciences, and some of the members of the Mediterranean Institute of Cognitive Neurosciences (INCM) at the CNRS campus of Joseph Aiguier. Members of these three units as well as individual members of other research laboratories in the area joined the BDI, which will be located at the Faculty of Medicine and the La Timone Hospital.

The scientific rationale for this merge is bringing together researchers from different background working on brain network dynamics in the Marseille area and to establish a multidisciplinary research environment. Based on existing research interest of many of the members of the BDI, epilepsy was chosen as a unifying model to investigate brain network dynamics, as well as specific aspects of cognitive and sensori-motor behavior. This will offer the opportunity to apply knowledge acquired with intra and extra-cranial recordings of brain electromagnetic activity and behavior more broadly to human and non-human primates. It is envisaged for research to encompass molecular and genetic experimental studies on the one hand, and theoretical large-scale network modeling on the other, emphasizing the translational nature of the research at BDI.

Given the importance of the temporal aspects of brain network dynamics the methods of the BDI focuses on neurophysiological techniques. These methods range from electromagnetic recordings and stimulation in humans (EEG, MEG, TMS), recordings of local field potentials in humans and animals, up to recordings of multiunit or single

unit neuronal activities in animals. Comparison with metabolic activity and studies of the electro-metabolic coupling in vitro and in vivo are also planned.

- Management team

The BDI activities will be overseen by a Director, P Chauvel and a Deputy Director, Viktor Jirsa . The Deputy Director is also head of one of the BDI groups while the Director is integrated in a different group without directly leading it.

The scientific and organizational decisional body of the BDI is the Directorial Board composed of the leaders of the four groups, and the director, totaling 5 members.

All members of the Institute belong to the Institute Council; this is intended to meet 2-3 times a year.

An international scientific advisory board will be established.

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	8	11
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	5	11
N3: Number of other researchers including postdoctoral fellows (Forms 2.2, 2.4 and 2.7 of the application file)	11	5
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	7	10
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.8 of the application file)	3	
N7: Number of staff members with a HDR or a similar grade	9	15

2 • Overall appreciation on the research unit

- Summary

The expert committee unanimously considered this Institute as excellent and unique in the world. It is directed by an outstanding personality with a worldwide reputation in the epilepsy community, both for his clinical expertise and his scientific competence. His leadership provides the unifying vision of the Institute. This became obvious in his enthusiastic introductory presentation and in the final private discussion. While the integration of some of the new groups that join the Institute might appear as a challenge, the committee is confident that the team spirit that was felt during the various discussions with researchers will make this integration not only possible but also very fruitful.

The scientific production of the members of the Institute is very good in their respective fields. The patient-oriented research, being it clinical studies or experimental studies using the SEEG technology resulted in publications in the highest-ranking journals in the field, as did the modeling work of the theoretical neuroscience group. Also the recent functional imaging studies of the junior group are excellent and show the potential of this young emerging group. Some of the new groups joining the DCP group have a very good publication record while others joining the PHYSIONET have somewhat been hampered by challenges related to new technical developments and hardware and software installations. These new technologies are however now fully functional and it is legitimate and reasonable to expect growing productivity from this group, additionally boosted by the integration in a larger dynamic group.

The clear strength of the Institute is its multidisciplinarity, which is the foundation for a truly translational research, from patient studies to cellular research and from modeling to signal processing. The University and Hospital representatives made it very clear that the multidisciplinary approach of the Institute has the full support of the respective Institutions, and that Neuroscience is one of their few thematic priorities. More than 300 m2 within the Hospital will be made available to the theoretical neuroscience group, as well as an extension of the laboratory at the Faculty of Medicine, confirming the concrete commitment of the Institutions.

- Strengths and opportunities

The Institute will profit from the excellent leadership. The enthusiasm, competence, and national and international reputation of the director and the deputy director in their respective domains will be the driving force of the Institute and will guarantee international visibility.

The long-lasting successful collaboration of some of the key players of the Institute will assure high-quality cross-disciplinary research.

The location of the Institute within and in close proximity to the Hospital will guarantee close contacts between researchers and clinicians and good working conditions. The support of the Hospital and the University is excellent.

The Institute has excellent competence in a diversity of fields, which favors multidisciplinary translational research.

The access to a large number of intracranial recordings in humans and the combination of these recordings with MEG, EEG, and fMRI is unique and makes the Institute a worldwide center of excellence in this research domain.

- Weaknesses and threats

The expert committee could not identify clear weaknesses or threats that could hamper the productivity of the Institute as long as appropriate support is provided. Given the diversity of the scientific and methodological approaches, the support of technical and engineering staff is crucial. This point particularly concerns system engineers for the computer clusters, and technicians and engineers for the imaging platforms (MEG and MRI). The commission considers this need particularly important to assure that the promising head of the junior group (Dynamap) is not relegated to the role of support engineer for the other teams.

The availability of the common space for the whole Institute will take 1-2 years from now, which might delay the integration of some groups. However, the clearly formulated willingness of all members to share some of the existing space to facilitate early integration of the new groups convinced the committee of the definitive commitment of all (old and new) group members.

The BDI provides excellent education at the systems neuroscience level and care must be taken that this is made available to the PhD students who want to engage in this promising field. Support of PhD students is at present distributed at a regional level and not research unit directed. This could be compensated by giving some PhD student salaries to the Institute and by encouraging applications for post-graduate education. It is a general observation that due to the need to publish in high-impact journals PhD students may not quickly publish the 2-3 good papers that normally make them competitive for high quality post-doctoral positions. It would be helpful if provisions were made to support extensions of PhD student grants if required.

- Recommendations

The Committee considers the integration of the theoretical neuroscience group with the other groups as a crucial requirement and should receive highest priority. It is recommended that a detailed roadmap be formulated to achieve this objective. The achievements of the milestones of this roadmap should be evaluated continuously by the directorial board, with the help of the Scientific Advisory Board.

The Committee considers the junior group DynaMap as the most important link between the different groups, particularly between the theoretical neuroscience group and the human experimental groups. The committee was impressed by the versatility, scientific ability, and flexibility of the junior group. However, the Committee considers the group by far too small to be competitive, and strongly recommends a consolidation of this group by pro-actively attracting additional researchers and engineers.

The Committee strongly supports the creation of an international scientific advisory board and recommends that this board becomes rapidly functional and establishes a roadmap together with the directorial board.

- Production results

(cf. http://www.aeres-evaluation.fr/IMG/pdf/Criteres_Identification_Ensgts-Chercheurs.pdf)

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	11
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	11
A3: Ratio of members who are active in research among staff members [(A1 + A2)/(N1 + N2)]	1
A4: Number of HDR granted during the past 4 years (Form 2.10 of the application file)	0
A5: Number of PhD granted during the past 4 years (Form 2.9 of the application file)	9

3 • Specific comments

- Appreciation on the results

The BDI will be a union of excellent research teams. The director of the BDI is one of the leading figures in clinical epilepsy research worldwide. His clinical unit is the international center of reference for frontal lobe epilepsy and one of the most active epilepsy surgery centers in Europe. His work on mechanisms of seizure propagation is outstanding and has laid the foundation for models of brain network dynamics. He has established a very productive research team and has promoted many talented young researchers that in the meanwhile have become well-established excellent principal investigators in their own right.

The most relevant research of the epilepsy group has come from their sophisticated analysis of intracranial recordings in epileptic patients. It has allowed them to characterize the electrophysiological properties of the epileptogenic zone and the mechanisms that lead to propagation of this activity through networks with abnormal functional connectivity. In collaboration with a research team in Rennes, many pioneering papers on this topic have been published.

More recently, the epilepsy group has become interested in the advanced analysis of scalp EEG using source imaging and the combination of EEG with fMRI. Some interesting studies have already resulted from these applications. With the recent installation of the MEG, this research aspect will become even more relevant.

The second pillar of the BDI is the group "Dynamics of Cognitive Processes" (DCP). The head of this group is a highly recognized and experienced researcher with an excellent CV. The long-lasting tight collaboration with the epilepsy group over more than two decades has led to a number of important studies on spatio-temporal dynamics of auditory perception and other cognitive functions using intracranial recordings in epileptic patients. This work has recently led to new insights in the dynamics of different memory functions and the functional properties of mesio-temporal brain structures. Besides intracranial recordings, the group has also used non-invasive techniques such as fMRI and EEG and has demonstrated their proficiency in these methods by a number of interesting studies on memory and language functions. The cognitive neuroscience group will be greatly strengthened by two researchers from the INCM, one working on the motor system using EEG and TMS, the other on language and music using EEG and fMRI. Both groups have solid knowledge in their respective fields and have published several interesting studies.

The third pillar of the new BDI will be the "Theoretical Neuroscience Group" (TNG). It will be constituted from four different research groups that were located in three different Institutes in Marseille. Two of them have already been working and publishing together in the UMR6233. The head of the TNG is one of the leading scientists worldwide in computational neuroscience and author of many outstanding and pioneering papers, published in journals of the highest impact. He co-edited a book on Network Connectivity that became one of the classics in this domain. He is internationally very well integrated and has long-lasting collaborations with the key players in this field. Their work on the dynamics of large-scale neuronal network connections at rest was pioneering and the work on phase flow coding in complex systems has been published in one of the top-ranking journals. The two other groups that will join the TNG are thematically closely related to the first group and will bring new approaches to characterize network dynamics into the team. Both groups have a permanent scientific output. They will clearly very much profit from their integration into a larger multidisciplinary team.

Besides these three basic teams that represent the majority of the BDI, new groups with new research topics will be integrated in order to provide a translational aspect to the BDI. One of these new groups brings in the competence of intracranial recordings in monkeys and expertise on the fronto-parietal system. Another team, actually already integrated in the U751, studied epileptogenesis in rodent models of temporal lobe epilepsy and discovered an important genetic factor that is involved in circuitry reorganization that lead to epileptic activity in this animal model. This work resulted in a continuous flow of high-level publications. The last group that will join the BDI has been working on the molecular properties and function of glycine receptors and on the direct measurement of chloride concentrations in biological preparations. The number of publications resulting from this work in the last four years is somewhat modest compared to the other groups, partly due to the development of a new device for in vivo chloride measurement. The group will surely profit a lot from the integration into a larger collaborative research team.

In summary, the scientific output of the key members of the BDI is excellent. The U751 published 80 papers between 2006-2010 with a steady increase year on year. Around 50% of the papers were published in excellent journals such as Brain, J. Neuroscience , Cerebral Cortex, Neuroimage. There is a healthy mixture between clinical and experimental studies, demonstrating the strong clinical embedding of this research group. The UMR6233 has an impressive record of high-level publications on mathematical models of brain connectivity. Papers in Nature Reviews in Neuroscience and PNAS demonstrate the scientific recognition of this work. Most of the other joining groups and individuals have a

solid scientific background but more variable production of publications. They will strongly benefit from the attachment to the leading teams.

The partnership between the clinical epilepsy group and the cognitive neuroscience group is very well established and has resulted in many joint publications. On the other hand, the partnership with the fundamental neuroscience group is somewhat weak, and a partnership with the theoretical neuroscience group does not exist yet. There is thus no strong history of joint collaboration between these groups before the creation of the BDI.

- Appreciation on the impact, the attractiveness of the research unit and of the quality of its links with international, national and local partners

The senior researchers of the BDI have outstanding international reputations, demonstrated by their membership in Editorial Boards of high-level scientific journals, presidency or council membership in national and international scientific organizations, membership in scientific evaluation committees, invitation to keynote lectures in large international conferences, and the reception of prizes and distinctions. Several strong and stable collaborations within national and international networks have been established, most importantly the participation of the TNG in the international consortium Brain Network Recovery (Brain NRG). The list of extramural grants that the different groups have raised is impressive, including highly doted European grants.

Five permanent researchers have been recruited and at least 25% of the researchers of the Institute are from abroad. Over 30 Masters students and over 40 PhD students and postdocs have been trained. Many of them have found positions in foreign labs, demonstrating the attractiveness and the training capabilities of the Institute and the socio-economic role of the Institute in the area. The fusion of the different groups and the installation of a common research environment will surely increase the appeal of the Institute. This is particularly due to the availability of a state-of-the-art technological platform including electrophysiological and imaging facilities on all levels. The translational aspect of the Institute is convincing, particularly with respect to the clinical application of the research results.

- Appreciation on the management and life of the research unit

The Institute is divided into four research groups. Together with the Director and Deputy Director, the group leaders represent the Directorial Board. The sizes of the groups are very heterogenous. The group PHYSIONET has the size of a Department while the DynaMap group consists of only 2 scientists. The reason for this heterogeneity was discussed with the director and with the head of the PHYSIONET. It became clear that the request of several groups from other centers to join the BDI led to the fast growth of the PHYSIONET. The head of PHYSIONET explained that the definitive integration of these new groups will be based on a 1 year test period. He also made clear that the PHYSIONET is considered as a launching platform and that the subgroups have their own projects with their own publications.

A certain percentage of grant money gathered by the different research teams will be given as “overhead” to the Institute. This will allow supporting the needs of smaller groups or investing in common platforms.

The Institute has a plenary research meeting once a week which all researchers attend, including the clinicians of the Institute. Similarly, the basic researchers regularly participate at the clinical staff meetings where patients and clinical issues are discussed. These common meetings are essential for the planned translational research and are very much valued by the researchers and the clinicians.

The scientific environment is excellent due to the diversity of competence within the different research groups. More than 20 advanced permanent researchers guarantee the competent supervision of PhD students. However, the number of foreign researchers and postdocs is relatively low in some of the groups.

The teaching activities of the researchers are quite high. The majority of the researchers teach around 200 contact hours per year in pre- and postgraduate levels in multiple disciplines and faculties. The Institute is strongly involved in the Neuroscience Masters program of the Universities and will play a key role in the planned PhD in Neuroscience program.

The University and Hospital strongly support the Institute and particularly appreciate the translational aspect and the multidisciplinarity. The epilepsy and surgery program of the Institute is declared as a clinical research center with support from both, the University and the Hospital.

The fusion of the three Aix-Marseille Universities will further strengthen the support of the Institute. The MEG platform is supported by the University as well as by INSERM and CNRS.

- Appreciation on the scientific strategy and the project

The scientific vision of the Institute is very coherent and focused on the common goal of better understanding brain network dynamics. Taking epilepsy as a model system for studying network dynamics is convincing given the outstanding competence of the group.

The total number of sub-projects is large and the relevance of some of the sub-projects in the global context needs to be carefully analyzed. Prioritization will be necessary after the first research period.

The idea of the cross-cutting research themes to foster the collaboration between the groups is original, but their value needs to be continuously evaluated. This particularly concerns the EpiMonk project, which is considered as a high-risk project but with a reasonable chance of success due to the previous experience of the Institute Director in this animal model of epilepsy. Monkey MRI facilities are urgently required for the success of this project.

The Committee considered the multidisciplinary aspect of the project very strong. In contrast to many other centers where either the fundamental or the clinical aspect is too weak, the tight linking between theoretical, experimental, and clinical research in this project has the potential to make it uniquely productive in the scientific fields of epilepsy, cognition, and systems neuroscience.

4 • Appreciation team by team and/or project by project projet

- Title of the team: “Physiology & Physiopathology of brain networks” - PHYSIONET
- Name of the team or project leader : Christophe BERNARD

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		5
N3: Number of other researchers including postdoctoral fellows (Forms 2.2, 2.4 and 2.7 of the application file)		7
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		3
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.8 of the application file)		
N7: Number of staff members with a HDR or a similar grade		6

- Appreciation on the results

The subproject aims at understanding formation of networks from the molecular to the systems levels in particular with respect to generation of epilepsy. Various members of this subproject have relatively recently joined the team. Hence the work must be judged on the basis of previous work in other units. Moreover, the labs for experimental work at the INSERM U751 were only finished in 2009 resulting in a strong decline of work efficacy for the experimentalists who had moved from INMED to U751 in 2006. Experimentalist work at U751 was further impeded by loss of mice strains due to contamination of the animal labs. Taken these aspects into account the members of the group publish regularly in excellent and very good scientific journals and the published work is utterly relevant to the new approach. PHYSIONET is divided in several subprojects.

Subgroup 1 deals with human epilepsies. The head of the group is an expert in analyzing the temporal and spatial participants in the networks from which an epileptic seizure emerges. This has of course also clinical consequences including potential new operation techniques such as disconnection by gamma knife approaches. The subgroup leader has published some 140 articles and many deals with the organization of networks in single seizures. This is a patient dependent approach and this is in fact one of the strength of this group. They use intracranial and intracerebral EEG measurements and a number of algorithms to analyze the evolvement of seizures in relation to the clinical picture of a given series. The group is world leading in this approach. More recently they focused on the relationship between interictal spikes and rhythmic activities. They are well embedded in the clinical and theoretical environment and have many papers together with others now included in PHYSIONET but also outside the group. Most important is the interaction with the group in Rennes and in the future with TNG. They also used increasingly fMRI data to corroborate their hypotheses on network formation

underlying generation of seizures. This includes well published work in Brain and other journals and finally some clinical analysis of gamma knife surgery. Considering the interaction quality locally and nationally as well as internationally and the productivity of the group this is an excellent team with high productivity in the past. This group will in future also use animal models and thereby profit from the expertise of the experimentalists and from techniques which have been transferred from G Buzsaki's lab through a recently hired postdoc.

Subgroup 2 deals with network dynamics and learning. Present ideas on mechanisms of learning and memory formation move away from classical LTP models where high frequency stimulation is used to alter the efficacy of synaptic coupling. This is in part due to the fact that neurons in higher centers fire sparsely in order to counteract the convergent input risk of pathological summation. In sparsely firing networks synaptic plasticity and learning can only occur if and when synaptic activity is coincident between pre and postsynaptic elements. This requires formation of network oscillations. Disturbances of such network oscillations will then result in missed learning or no learning at all. The group is headed by a monkey neurophysiologist who analyses learning mechanisms in monkeys on the basis of observations made by others. This is an interesting approach and the head of this unit has published some 40 papers in excellent and very good journals on this matter. This group will set up an aluminia cream model of focal epilepsy and thereby be able to analyse epileptogenic neuronal ensembles in more depth than it is possible in humans using high resolution techniques of multi site recordings as well.

Subgroup 3 moved 4 years ago from INMED to U751. The head of this subgroup and speaker for PHYSIONET is an excellently educated neurophysiologist with a strong interest in cellular and molecular mechanisms of neuronal excitability and on network oscillations. He coined the term of acquired channelopathies as a way in which single neurons can change their excitability profile and how this will change their oscillatory potency. He has paid with his cooperation partners much attention on the regulation of HCN channels, which provide for a strong theta resonance that likely contributes to generation of theta oscillations. His publication record was excellent but suffered from the relative long interruption of experimental work associated with the move from INMED to Inserm U751. His expertise is acclaimed by making him a section editor on neurobiology of disease in the prestigious J Neuroscience. He also won the prestigious Michael prize for epilepsy research and is since a number of years member of the Commission of neurobiology of epilepsy of the International league against epilepsy. The members of this group have stable interaction locally and on the national levels. As a member of EpiCure the group is well connected to Italian and German partners. There is also a close connection to American colleagues such as D Johnston and T Baram. Important is the idea of factors involved in epiletogenesis, which regulate a cohort of proteins in their expression.

Subgroup 4 has recently joined this team by moving from INMED to U751. The head of this subgroup is the best quoted scientist in PHYSIONET. He is an excellent biophysicist who has a strong interest in regulation of glycine receptors. It recently turned out that in contrast to previous ideas glycine receptors are also functional in adult tissue. In his work in Inmed and before that, he focused on regulation of expression. By developing new tools for signaling of Cl new measurements became possible which also address the question how Cl is regulated. This is of relevance since one of the most studied and still controversial issues in epileptogeneis is the question whether Cl levels inside cells provide for depolarizing actions of GABA and glycine. This is important with respect to the question how the developing brain mobilizes formation of networks. An important aspect of the group is work on metabolism. This is important with respect to the question how the brain cares for energetics as the oxygen levels in afferent arteries to the brain are rather low during fetal life and astrocytes are not yet mature etc.

Subgroup 5 is run by an experienced and rather brilliant morphologist, a very devoted neuroscientist studying the developing profile of gabaergic circuits in temporal lobe structure and their alterations under pathological conditions. She is very constant in her publication record, which is excellent. More lately she has moved into the monkey field, which is of high relevance because of the proximity to human studies. She has since many years steadily contributed to the success of the group with publications in internationally well respected journals and symposia and has a stable activity record within the local group.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The head and spokesman of PHYSIONET received the well-known international Michael Prize, which is the most prestigious award in epilepsy research. He became member of the J Neuroscience editorial board where he is now a managing editor. He is often invited to organize symposia and was in the past involved in organization of different workshops on neurobiology of epilepsy supported by other members of the team. He is a member of the Commission of Neurobiology of the International league against epilepsy. He has attracted a number of valuable interactions with colleagues both on the local national and international level.

The recently recruited team around subgroup 4 is led by an international well recognized biophysicist who is very clear in his loyalty to scientific partners. He is a good bridge to the rich Russian biophysicist community. He is the most experienced senior scientist in the whole group which makes discussions on science and management of the team and well as mentoring of younger scientists very valuable.

The head of the human epilepsy group is frequently invited to international symposia particularly with regard to the discussion on the idea that epileptogenic networks rather than local alterations underlie epilepsy and that these networks become momentarily active under specific conditions. A member of the team pioneered gamma knife surgery and as such is often invited to surgical conferences.

The group is attractive for students both from inside France but also from around the world. There are quite a number of non-French postdocs and students in the group who clearly enrich this group strongly. I wonder though how easy the access to gifted students is, and which mechanisms exist to recruit them into successful scientific work. On the postdoctoral level there are many non-French postdocs and attempts have been made to attract also group leaders from abroad.

All group leaders have successfully raised grant money either on the EU levels or from ANR and from other foundations. The grant income of the group shows its strength very well

Although the work is primarily related to basic research there is considerable social and medical perspective in the work. This applies not only to epilepsy and epileptogenesis but also to mechanisms of learning and memory formation.

- Appreciation on the scientific strategy and the project

The overall approach of the PHYSIONET group is to understand network behavior under physiological and pathophysiological conditions. This is a valid approach as it is more and more realized that epilepsy is only one of the many diseases in which networks function abnormally under some conditions. This also applies to Schizophrenia, Alzheimer´s disease, diseases with tremor, motor disabilities etc.

The level of analysis reaches from monkey and human behaviour down to the single cell level taking not only morphological basis of networks but also functional connectivity into account. An important aspect of studies in this group is the coupling between metabolic and neuronal activities and effects which alterations in such studies have. This is also of relevance how neurovascular coupling is altered which is the basis for many diagnostic and system level analyses of freely behaving monkeys and humans. There is a link between human epilepsy research to rodent experimental research by establishing a monkey model of epilepsy. This is based on the aluminia cream focus model. This model is of particular interest be cause the epilepsy develops on the basis of rarification of synaptic input to dendrites and reduction in bifurcation patterns and has some proximity to Alzheimer disease for this matter. They profit from the clinical setting in which they work and it is of advantage that many scientists have their lab space close to or within this setting.

Group 1 specializes on analysis of the epileptic brain by use of different techniques, which are in part invasive. The goal is in the near future to understand more of the interictal state with particular emphasis on localizing disturbances that eventually form the basis for generation of seizures. The other aim is to understand some of the different psychopathological alterations, which can be of significance for the patient and his/her social interaction. This relates also to the influence of brain states on the emergence of epileptic seizures and may ultimately result in an integrated behavior related treatment program of epileptic patients. It offers also the chance to get more insight into pathophysiology of psychiatric disorders in general. The planned experiments are state of the art and will result in considerable progress in understanding seizures the epileptic brain and the pathophysiology of emotional and psychiatric disturbances associated with epilepsy.

Group 2 deals with network dynamics and learning as well as their alterations within the epileptic focus established in the parietal cortex. Much of the work in this group relates to work done by others in humans with the advantage that more invasive and higher resolution techniques can be employed. In a first approach they will analyse the so-called resting state and then use perturbation by TMS and eventually locally to get a better insight into effects of different aspects of resting state on learning. This approach is novel as it is not primarily hypothesis driven. A second aspect will continue work related to intermodality transfer of information studies for which the group is well known. Finally they will record neuronal activity in frontal cortex and most importantly also in the cingulate gyrus a structure where enteroception is strongly analysed to determine effects of non reward or errors on learning and network alterations. Using LFP and single unit recordings this will be a strong program which will profit from the close proximity to human studies and the manipulative possibilities which rodents offer. By setting up a monkey model of epilepsy they bridge the gap between clinical and experimental work and this permits to analyse also the course of disease leading to the state for epilepsy surgery is a last resort of therapy.

Group 3 will use rodents to analyze the formation of functional neuronal networks in rodent brains. They will work on five tasks using multicontact electrodes and analysis of single units as well as high-resolution imaging and recording techniques from single cells within such networks. In task 1 they will study the information flow under different conditions in the rodent brain and more precisely in task 2 the information flow between hippocampus and entorhinal cortex under different working conditions. In task 3 alterations in network behavior will be related to alterations in single cell behavior with emphasis on acquired channelopathies. In task 4 epigenetic factors will be studied which influence the emergence of an epileptic network and in task 5 they will study the metabolic aspects of such work. The preliminary work is well under progress and the expertise in the group is highly relevant for performing such work.

Group 4 will deal with mechanisms of chloride homeostasis and with metabolic aspects as well as regulation of glycine receptors and more recently also of GABA receptors. This involves new technology for recordings of Cl inside cells. Also in this subgroup preparatory work is well under way.

Group 5 will build the morphological basis of inhibitory networks that are crucial for understanding brain rhythms and mechanisms by which the brain can switch from one working mode to the next. Although this is a rather competitive field they have shown that they can keep up with progress in the field. One novel aspect is the analysis of alterations in hypothalamic and particularly supramamillary input to the hippocampus in normal and pathological conditions. This aspect is highly innovative. In task 3 the role of interneurons in different network oscillations will be studied in normal and altered nervous tissue. Finally aspects of neurogenesis will be studied as well.

- Conclusion :

  - Summary

In general the group PHYSIONET will use a multilevel approach to understand network behaviors and their behavioral significance in normal and epileptic brains. The expertise of the group varies between excellent and very good. The scientific approach is very convincing and involves many different techniques profiting largely also from the expertise in other groups. The publication record is excellent and the productivity of the group is very good.

  - Strengths and opportunities

The multispecies approach and the different levels of recording techniques offer possibilities far beyond the molecular and cellular approaches which govern many aspects of neuroscience in these days. They have the chance to translate cellular alterations in understanding of alterations on the systems level. The already established interaction between clinicians neuropsychologists and theoretic neuroscientists carries already now and the results which will evolve on the basis of these interactions will be extremely important. Particularly the possibilities to use monkeys for this research makes this group extremely remarkable as this approach is only now feasible again after many years in which epilepsy research has shifted from the in vivo to the ex vivo and in vitro level. The scanning possiblities for monkeys and rodents and the attention paid to metabolic aspects of neuronal function and ultimately on neurovascular coupling in the group are also of considerable interest. This is of importance as recently first examples were published in which a physiological vasodilation during seizures was locally converted into ischemia inducing vasoconstriction. Including measures on local blood flow by optodes,

near infrared spectroscopy and NADH and FADH2 measurements will further strengthen the international visibility of the approach.

- Weaknesses and threats

Important will be attraction of good students. At present they are dependent on funds that are centrally distributed to many different institutions and faculties. It would be important to have funds available to attract students from abroad on one hand and to support students that are closely affiliated to the research team as well. There is a string hunger for high-level publications in part of the group, which may delay sometimes appearance of the work to the public. A good mixture of high level and excellent level publications would be helpful. There is the risk that necessary technical help will not be stable due to retirement of engineers and technicians.

- Recommendations

This rather big team might separate into three teams in the next granting period. The scientific advisory board should help students and younger scientists with career advice and monitor the management of this big team.

- Title of the team: Theoretical Neuroscience (TNG)
- Name of the team or project leader Victor K. JIRSA

    - Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		4
N3: Number of other researchers including postdoctoral fellows (Forms 2.2, 2.4 and 2.7 of the application file)		3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		1
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.8 of the application file)		
N7: Number of staff members with a HDR or a similar grade		2

In total 15 group members

- Appreciation on the results

The group's research efforts and achievements can be classified as excellent. The quality of publications with regard to content, independent of the journal's impact-factors and other bibliometric indicators, is outstanding as well as pioneering. According to the bibliometric indicators (in the last five years >30 % of the articles were published in excellent and very good journals), the team is one of the emerging research groups of excellence in the field of theoretical/computational neuroscience. By the use of new analysis and modeling approaches, the studies of the group members have provided essential contributions to brain dynamics and connectivity analysis. Previous research conducted by the sub-group leaders is substantially relevant and thus the potential contribution to the overall aims of the group will be significant.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The TNG is one of the essential structural branches of the multidisciplinary BDI which is composed of four different research groups with no common history of collaboration. Previous scientific contributions of the TNG are in the fields of theoretical neuroscience, dynamics of motor learning and plasma surface, i.e. all in all a rather inhomogeneous structure. It is intended that the TNG shall cooperate with the other BDI groups. These groups have been assembled from different clinical and scientific facilities. The overlapping fields should allow substantial potential for inter-group collaboration within the BDI.

The TNG is well integrated into international research networks in the fields of theoretical and computational neuroscience. The output of these scientific collaborations has been consistent. TNG is an active branch of the international consortium Brain Network Recovery (Brain NRG). The list of third-party funded projects is impressive. The research projects will be funded with a total of approximately 200 M€ until 2015.

During the last four years the group has organized two international conferences, three international workshops and one international summer school; such a level of active organization/participation can be considered as excellent.

The group has not only attracted world-class scientists and professors, but also richly talented post-docs and PhD-students. The PhD-students are satisfied with the quality of the supervision. The scientific atmosphere has been rated as stimulating. The PhD-group is composed of international, innovative and motivated individuals.

- ## Appreciation on the scientific strategy and the project

Virtual Brain Project(s) (individual group and cross-cutting project): "Virtual brain" is the methodological "backbone-project" of the BDI. The principle scientific aims of these projects were recently described by the Brain Network Recovery Group in Arch Ital Biol 148(2010), 189-205. Methodological approaches involving the multiscale complexity of the brain are given and preliminary results are shown by using measured data (Cocomac database). The authors describe the scientific challenges and remaining open questions of such an ambitious endeavor. The relationship between structural and functional networks is one of these open questions; complex structural networks can generate different functional patterns. Interaction analysis and modeling can be helpful by providing a more precise answer to this question. The measurements of inter-regional fiber pathways (DTI, DSI and related methods) and of the activations of brain regions (fMRI, MEG, EEG) provide only a raw framework for these investigations.

Spatiotemporal determinants of brain dynamics: In the recent past the TNG has produced excellent results in the field of modeling and analysis of large-scale (EEG/MEG) data. However the currently planned research aims are in the field of modeling discharge patterns of single neurons and small neuron populations. By means of well-known neuron models (Hindmarsh-Rose, FitzHugh-Nagumo) temporal bursting patterns of neuron populations were simulated. Building on this, the project "Spatiotemporal determinants of brain dynamics" is designed as a "bottom-up approach". Preliminary results were given by using both an excitatory and an inhibitory subpopulation composed of heterogeneous neural networks.

Emergence of brain function: This project is based on the methodology of non-linear dynamic systems, self-organization and synergetic and will provide the methodological basis for the cross-cutting project PhenoFunk. The cooperation with the DCP group is planned and in this way computational approaches will applied to experimental data. In both project descriptions the theoretical basics for analysis and modeling are outlined. The project may be considered as largely applicable to other fields (translational aspects).

- ## Conclusion

  - ### Summary

The BDI's leadership should be encouraged to carry on constructing a really multidisciplinary institute. This requires to support intergroup cooperation between theoretical and experimental groups in terms of Systems Neuroscience approaches, i.e. the research should be organized as an integrated process of computational analysis and modelling, systems analysis, technological development for experiments, and quantitative experiments. It is crucial that analysis and modelling approaches are linked at various spatial and temporal scales for their application to both scale-bridging and scaling-up perspectives. Moreover, the development of simulation models could give rise to more focused and efficient model-driven data collection. The establishment of "kick-off projects" should be supported.

- Strengths and opportunities

The TNG is essential for the BDI because the simplest cognitive tasks depend on the interaction, or dynamic coupling, between active neural structures. These interactions cannot be directly measured, but require appropriate analysis methods and modelling that use measured brain activity data as input. It is evident that improved signal processing and modelling tools are needed to fully exploit the spatio-temporal information provided by modern electrophysiological and brain imaging techniques. Joint projects between all teams are planned to strengthen the BDI's mission as a multidisciplinary institute.

The TNG members have already demonstrated their methodological competences to concentrate more on adaptation of real-world problems to formal models. If the model is not so complex (e.g. if the number of coupled differential equations is not so high) then the model parameters can be determined on the basis of data (optimization approach). The solution of these data-adapted equations provides a realistic signal simulation. For modelling BOLD signals a neuronal connectivity model must be combined with a model which emulates the hemodynamic response (e.g. Balloon models). Such models enable the explanation of the dynamics of the measured signals and their underlying neuronal generator networks (sources). This strategy seems to be very promising especially for the investigation of isolated aspects of the space-time structure of coupling.

- Weaknesses and threats

A content-driven cooperation program between the TNG group and the junior research group "Dynamical Brain Mapping" is still lacking. Furthermore, a networking between TNG and the experimental and clinical projects of the BDI is not clearly outlined.

- Recommendations

It is intended that the BDI will act as a scientific "melting pot" to integrate a number of existing, successfully working research groups from the fields of clinical, experimental and theoretical (computational) neuroscience to meet today's challenges which are associated with the investigation of brain dynamics. The structure of the BDI resembles a virtual research centre, i.e. it might be possible that this structure hampers the team fusion. Therefore, the following recommendations should be considered:

The move into the new TNG labs must proceed as rapidly as possible.

Every effort should be made to establish cooperative projects between the TNG and the other BDI groups. However, first joint projects between DYNAMAP and TNG as well as between PHYSIONET and TNG are already planned. In particular the cooperation between TNG and DYNAMAP should be strengthened. Advanced concepts of data fusion should allow the integration of effective connectivity and synchronisation phenomena. A beneficial relationship between both groups may provide synergies for the whole institute.

TNG and DYNAMAP both need cluster computing power, and also need common research themes to be strengthened, so the committee strongly recommends that a common cluster computing facility is created for all teams of the BDI (or that existing platforms are merged) A specifically qualified engineer is required to provide support for all users of the BDI.

The neuroinformatics type of approach should be made in cooperation with similar projects done at the INCF (International Neuroinformatics Coordinating Facility); a methodological benefit can be expected.

To carry out all its missions, the committee recommends that the TNG allocates a post-doc position with a strong focus on research in the field of data-driven modelling (EEG, SEEG, MEG, fMRI).

- Title of the team: Dynamics of cognitive processes (DCP)
- Name of the team or project leader Catherine LIEGEOIS-CHAUVEL

    - Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		6
N3: Number of other researchers including postdoctoral fellows (Forms 2.2, 2.4 and 2.7 of the application file)		2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		1
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.8 of the application file)		
N7: Number of staff members with a HDR or a similar grade		6

    - Appreciation on the results

The « Dynamics of Cognitive Processes » team is devoted to the study of a variety of brain/behavior topics such as memory, music processing, and sensorimotor integration. The team, a mix of scientists and clinicians, is run by a Research Director from Inserm, and by three co-PIs (a clinician [PUPH], two CNRS research scientists [CR1, DR2]), each heading a specific research group. Overall there are 2 CR1, 2 DR2, 4 PUPH, 3PH, a research engineer, 2 post-doc, 6 graduate students. Some of its members come from the previous Unit 751, others from INCM.

The team's members investigate brain functions mostly in human subjects, both normal and pathological, using techniques ranging from fMRI, EEG, TMS, SEEG. The pathological model is extremely interesting especially the one referring to patients suffering from epilepsy and having deep electrodes implanted in their brain. Such research is actually at the core of this team's projects and constitutes a scientific marker of the previous lab (headed by the Director) and of the future lab. During these past 4 years the team has produced interesting research published in good journals. Different studies have focused on the role of the medial temporal structures in spatial memory, retrieval and recognition processes as well as hemispheric specialization for visual and verbal encoding. The role of anterior and medial temporal regions has been also explored in the domain of language perception and understanding. Past research has also addressed the role of the amygdala and the hippocampus in emotional processing of multi-modal stimuli. A huge amount of research was also devoted to characterize oscillatory activity and their relationship to transient activity. Concerning this aspect the team has also contributed to improve EEG methods.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

Concerning scientific production, the team has published 51 original papers in journals ranging from good (Neuroimage, Neuropsychologia) to excellent (Cerebral Cortex, Brain, J.Neuroscience). The team has also obtained several national (ANR, PHRC) and European grants (FP7).

- Appreciation on the scientific strategy and the project

For the forthcoming new Unit the team's planned research projects are of potentially high impact. Three lines of research will be investigated: (1) Spatio-temporal dynamics of memory in the healthy and brain-damaged subjects (2) Sensorimotor grounding of language and music (3) From intention to action. The first, in continuity with previous studies on memory, is aimed at understanding the spatiotemporal dynamics of memory processes, by focusing on long-term memory consolidation and functional connectivity of medial temporal cortex with interconnected structures. This line of research represents a laudable attempt to leverage the combined resources of the DCP team members to investigate the impact of both epilepsy and AD on memory systems. The intracranial studies of epilepsy patients provides an outstanding platform to validate the noninvasive studies that can be done in normals and patients at risk for AD. The cross-sectional and longitudinal studies using fMNRI and fcMRI in normals, patients with epilepsy, and patients at risk for AD are quite ambitious and have the potential to make an important impact. Another high-risk, high-impact project within this line of research is the attempt to characterize the spatiotemporal dynamics of recollection memory in patients with early AD. The excellent spatiotemporal resolution afforded by intracranial EEG has been exploited very effectively by this group to investigate the ventral sensory pathways and mesial temporal lobe structures relevant to the proposed experiments. Although epilepsy patients may be at risk for developing AD in the future, it would be impractical to make any inferences from this population. Instead, the investigators plan to use electrophysiological markers derived from intracranial studies of epilepsy patients to investigate memory processes in patients with MCI or isolated age-associated memory impairment. These patients will presumably be studied noninvasively with scalp EEG and MEG. The most challenging aspect of this study will be to noninvasively detect the electrophysiological markers discovered from intracranial EEG studies. The Dynamap group could make an important contribution here. It may be useful to supplement this study with intracranial recordings of epilepsy patients with and without memory impairments and/or MTL pathology to further develop a model of memory circuitry that can be applied to noninvasive studies. In the experimental paradigm for this study subjects will be instructed to use different strategies (familiarity vs.recollection) for recognition memory. It will be important to design stimuli and tasks that necessitate only one strategy or strongly favor one strategy over another in order to achieve more rigorous behavioral control.

The second line of research (Sensorimotor grounding of language and music) will track in an original way, the behavioral and brain dynamics of lexical representations when learning a new language, the role of the dorsal stream in the imitative vocal processes and plasticity in congenitally deaf children with cochlear implants. This is a particularly strong proposal because it builds on the outstanding track record and existing theoretical and experimental strengths of the group. It is also most likely to benefit from comprehensive SEEG sampling of potentially relevant perisylvian cortical regions. The artificial language learning experiment is extremely innovative and is expected to have a very high impact on the field. The lexical production experiment could provide critical neurophysiological data to constrain evolving functional-anatomic models of visual object naming and thus could also have a very high impact in the cognitive neuroscience literature. The approach of varying the ordinal position of objects within a semantic category to elicit variations in response latencies and in the latency of lexical access in cortical networks is innovative and could help elucidate the cortical networks involved during lexical access. Because of the parallel (or cascading) activation of multiple levels of representation during naming, it may also be useful to vary the difficulty of perceptual analysis. Because of the difficulty of recording EEG noninvasively from the ventral stream of visual object processing, SEEG studies will again provide crucial information that can be used to validate noninvasive EEG or MEG results.

In the proposed studies of imitative vocal processes, the hypothesis that the connectivity of the audio-motor system can be influenced by the level of imitability is very exciting. Presumably this would be tested in part by the proposed experiment in cochlear implanted adults and children, comparing repetition of sentences after listening to and reproducing rhythms that match or mismatch the metrical structure of the sentences. If this could also be done with SEEG, the results could be particularly compelling. Perhaps noise or other sources of interference could be used to increase the difficulty for subjects with normal hearing. It will be particularly interesting to test whether TMS of motor cortex can interfere with auditory perception. Some of the experiments here may have the most direct applicability to the dynamical systems models investigated by TNG, particularly with respects to models of audio-motor entrainment.

Finally, the last topic will explore the functional changes of primary and non-primary motor area when movements are under cognitive constraints. The PI of this subgroup has already published remarkable results showing how top-down processes such as intention to act or to inhibit a movement modulate cortico-spinal excitability. Parallel SEEG studies could be useful to validate the results obtained from this study. For example, a parallel invasive "perturb-and-record" approach could be used in which SEEG recordings are made during direct cortical stimulation through the implanted electrodes. This can elicit cortical-cortical evoked potentials (CCEPs), which have been used to probe the

functional connectivity of cortical networks. These results could be compared with the results of TMS-EEG. Would it also be possible to use TMS with SEEG as is planned for EpiMonk ?

- Conclusion :

  - Summary

In conclusions this is a very good team, headed by a PI well known in both clinical (epilepsy) and neuroscientific domain (mostly for her studies on EEG and SEEG in patients). The committee must underline the arrival of two PIs, the first working in the domain of language and music processing and the second on the neural basis of higher motor control, both having produced very good research in their own labs and importantly they are known and respected in their domain of expertise. Last but not least, the inclusion of a co-PI clinician who contributes with a neuropsychological approach in both stroke and degenerative disease is important to preserve continuity between the experimental and clinical worlds.

  - Strengths and Weaknesses

Combined experimental and clinical approaches, long time expertise in EEG and SEEG methods, new and yet unexplored lines of research. The weakness may be in the variety of topics and questions addressed by each subgroup which can lead to clear-cut research boundaries reflecting the expertise of each PI. Nevertheless the committee thinks this criticism can be overcome by the emergence of transversal projects fostered by the (new) members' geographical and scientific proximity.

- Title of the team Dynamical Brain Mapping (DynaMap)
- Name of the team or project leader: Christian BÉNAR

    - Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		1
N3: Number of other researchers including postdoctoral fellows (Forms 2.2, 2.4 and 2.7 of the application file)		1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		2
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.8 of the application file)		
N7: Number of staff members with a HDR or a similar grade		0

In total 15 group members

    - Appreciation on the results

A fair evaluation will need to take into account the recent establishment of this team within the BDI to account for relatively limited evidence of outputs and of structured synergies between this and the other groups.

The DYNAMAP group has wide local collaborations which span from research and clinical teams to an SME (Microvitae Technologies). National collaborators include the team of Inserm U642 in Rennes, with whom the team has track record of shared publications. The international positioning of the team is somewhat weaker, with the most relevant collaboration being with the laboratory at McGill in Montreal, where the group leader obtained his PhD and worked with the commercial spin-out of the Montreal lab. The group quotes as collaborators the Cuban Neurosciences Centre, but it was not possible to assess the nature or extent of the collaboration.

The past research seems to have been focused on time-series analysis and use of established analysis strategies and/or software platforms (EEG-MEG source analysis, simultaneous EEG-fMRI analysis). In this area, the contribution of the group in terms of novelty and originality of analytical methods seems somewhat limited. Much more interesting, at least in principle, is the proposed framework for integrated multimodal imaging subserving a program of work on the characterization of oscillatory properties of epileptic networks, as well as the link between transient and oscillatory activities in the functional organization of brain networks. Part of this has recently received funding for a 4 year program (€113.865) starting in 2010.

It is probably still too early to evaluate progress on this. The strive for excellence and innovation in the DYNAMAP group has given rise to collaboration with industry to develop electrodes for simultaneous MEG-SEEG acquisition. This is valuable both as an example of vision to contribute to the financial sustainability strategy of the Institute and has an intrinsic merit as an example of direct translation of biomedical research to product development. Unfortunately it is not yet clear how the management of intellectual property has been structured at BDI and whether part of the governance strategy includes pro-active exploitation of this potentially crucial opportunity. Furthermore, it is not possible to evaluate in detail the originality of these new electrode development compared to those developed by other companies for the same use.

The quality of publication is of international excellence, at least in terms of the journals in which results have been published. The crude number of submitted outputs (11 papers in the last 4 years and a total of 16 papers, 6 of which with the team members as first or last authors, mostly the team leader) seems somewhat limited; given the mismatch with potential wealth of available data, The committee is inclined to consider it in the context of the necessary initial investment in time and resources to develop collaborative networks.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The group has been involved in the Neuromath (FP-6 COST ACTION 603) project and has actively contributed to the development and sharing of innovation with EU partners. Benar has been invited to present his work at Arenberg Castle Katholieke Universiteit Leuven, Belgium on an international workshop. It was not possible to find specific reference to invited lectures of other team members. The group, both due to the profile of its members and the environment, is in a privileged position to attract students and post-docs form abroad. External funding is still limited therefore growth will probably be steady but slow in the absence of strategic investment in this group. One might argue whether growth is best achieved by keeping the group separate. Collaborations listed in the document seem suitable for integration of DYNAMAP in a national research network. At international level, closer synergies with EU partners seems crucial and might stem from participation to NEUROMATH COST action.

- Appreciation on the scientific strategy and the project

The scientific project seems well grounded, as it relies on the availability of unique intracranial data from one of the most productive surgical program in Europe. Such synergy has already been demonstrated to some extent, and can only be improved by the creation of a coherent strategy such as the one presented for the BDI. The limited size of the group compared to the other members of BDI will pose some challenges in terms of critical mass and consequent ability to exploit the potential offered by the diversity and wealth of potential collaborations within BDI. Looking at the global strategy, it is apparent that the expertise of this group is central to the deliverables of DCP and PHYSIONET, and that TNG will most likely have to rely on computational input. In the short to medium term this might pose challenges given the limited number of scientist in the group compared to the others. The multimodal imaging element is difficult to evaluate in detail in this context in terms of relevance. There are numerous groups who have established themselves as leaders with structured strategies and software platforms. In the absence of evidence of novelty and originality of approach, it is difficult to evaluate the cost-effectiveness of entering is such a competitive and structured field with comparatively limited human resources.

- Conclusion :

  - Summary

This is a relatively new group, of limited numerical representation. Given this consideration, its outputs are well in line with what would be expected in terms of ability to attract grant funding and produce research outputs.

  - Strengths and opportunities

The scientific profile of the team members and the positioning and collaborations at local and national level is a definite strength. The collaboration with industrial partners seems the strongest point to be encouraged and supported at BDI level with managerial input to systematic exploit the added value of the research produced in DYNAMAP.

  - Weaknesses and threats

Given the size of international competitors, it will be difficult for DYNAMAP to be a significant player at international level as analysis platform developer. The scientific community is moving to a polarization with SPM, EEGLab, FieldTrip being the most commonly applied analysis tools. The development of an integrated platform for multimodal imaging is an enormous undertaking and in its current membership it might absorb most of the resources of the group. The group seems spread quite thinly across too many large scale developments. One member of the group has been heavily absorbed in supporting the MEG platform both as systems manager and as engineer. The latter is probably not the most cost-effective use of his unique expertise and the Group will need technical/engineering support to allow the major team members to focus on developing their scientific strategy.

  - Recommendations

Improve through a central strategy opportunities for collaboration with industry. There needs to be a start-up investment in at least one post-doctoral position to allow senior team members to focus on strategic developments.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
EPILEPSIE ET COGNITION	A	A+	A+	A	A+
DYNAMICAL BRAIN MAPPING [CHAUVEL-BÉNAR]	A	A	Non noté	A	A
PHYSIOLOGY AND PHYSIOPATHOLOGY OF NEURONAL NETWORKS [CHAUVEL-BERNARD]	A	A+	Non noté	A+	A+
THEORETICAL NEUROSCIENCES [CHAUVEL-JIRSA]	A+	A+	Non noté	A	A+
DYNAMICS OF COGNITIVE PROCESSES [CHAUVEL-LIÉGEOIS-CHAUVEL]	A	A+	Non noté	A	A

C1 Qualité scientifique et production

C2 Rayonnement et attractivité, intégration dans l'environnement

C3 Gouvernance et vie du laboratoire

C4 Stratégie et projet scientifique

Statistiques de notes globales par domaines scientifiques

(État au 06/05/2011)

Sciences du Vivant et Environnement

Note globale	SVE1_LS1_LS2	SVE1_LS3	SVE1_LS4	SVE1_LS5	SVE1_LS6	SVE1_LS7	SVE2 _LS3 *	SVE2_LS8 *	SVE2_LS9 *	Total
A+	7	3	1	4	7	6		2		30
A	27	1	13	20	21	26	2	12	23	145
B	6	1	6	2	8	23	3	3	6	58
C	1					4				5
Non noté	1									1
Total	**42**	**5**	**20**	**26**	**36**	**59**	**5**	**17**	**29**	**239**
A+	16,7%	60,0%	5,0%	15,4%	19,4%	10,2%		11,8%		12,6%
A	64,3%	20,0%	65,0%	76,9%	58,3%	44,1%	40,0%	70,6%	79,3%	60,7%
B	14,3%	20,0%	30,0%	7,7%	22,2%	39,0%	60,0%	17,6%	20,7%	24,3%
C	2,4%					6,8%				2,1%
Non noté	2,4%									0,4%
Total	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

*** les résultats SVE2 ne sont pas définitifs au 06/05/2011.**

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

• SVE1 Biologie, santé
- **SVE1_LS1 Biologie moléculaire, Biologie structurale, Biochimie**
- **SVE1_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes**
- **SVE1_LS3 Biologie cellulaire, Biologie du développement animal**
- **SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie**
- **SVE1_LS5 Neurosciences**
- **SVE1_LS6 Immunologie, Infectiologie**
- **SVE1_LS7 Recherche clinique, Santé publique**

• SVE2 Ecologie, environnement
- **SVE2_LS8 Evolution, Ecologie, Biologie de l'environnement**
- **SVE2_LS9 Sciences et technologies du vivant, Biotechnologie**
- **SVE2_LS3 Biologie cellulaire, Biologie du développement végétal**

UNIVERSITÉ DE LA MÉDITERRANÉE
AIX-MARSEILLE II

Objet : Réponse au rapport d'évaluation - **S2UR120001660 - Epilepsie et Cognition - 0131843H** - de l'unité Epilepsie et Cognition

Observations d'Aix-Marseille Université

Observations to assessment of publication quality:
University would like to call the attention to the inhomogeneity of the terms used to qualify the quality of scientific production among the different teams.

In particular, the qualification used for the DCP team's production was less favorable than that of the other teams although the *same proportion of papers (> 40%)* has been published in the same journals named "excellent" in the introductory part of the report, and in the other specific reports:
Please compare:

p.8 : "In summary, the scientific output of the key members of the BDI is excellent. The U751 published 80 papers between 2006-2010 with a steady increase year on year. Around 50% of the papers were published in *excellent* journals such as Brain, J. Neuroscience , Cerebral Cortex, Neuroimage"

to: p.18/19 : "During these past 4 years the team has produced interesting research published in *good* journals. [...] Concerning scientific production, the team has published 51 original papers in journals ranging from *good* (Neuroimage, Neuropsychologia) to *very good* (Cerebral Cortex, Brain)"

Remark : a paper published in J. Neuroscience by the DCP team (Catherine Liegeois-Chauvel as the last author), based on a work made in her lab, has been omitted.

In comparison:
Team Physionet

p. 10, last paragraph : "Taken these aspects into account the members of the group publish regularly in *excellent* and *very good* scientific journals
The publication record is excellent."

Jardin du Pharo . 58 Boulevard Charles Livon . 13284 Marseille cedex 07 . France
Tél. : +33 (0)4 91 39 65 00 . Fax : +33 (0)4 91 31 31 36 . www.univmed.fr

Team TNG

p. 15, 3rd line, first paragraph : "According to the bibliometric indicators (in the last five years >30 % of the articles were published in *excellent* and *very good* journals)"

En accord avec les deux autres établissements d'Aix-Marseille

Le Président
de l'Université de la Méditerranée

Yvon BERLAND

Le Vice-président du Conseil Scientifique
de l'Université de la Méditerranée

Pierre CHIAPPETTA

UMR 751 INSERM

Directeur : Patrick Chauvel

Yveline GRAFF
Inserm
Département de l'Évaluation et du Suivi
des Programmes
101 rue de Tolbiac
75654 PARIS Cedex 13

Marseille, April 14th, 2011

Dear Madam,

We have read with attention the report established by the AERES Committee, who visited our Unit on February 24th and 25th. We are grateful to the Chairman and the members of the Committee for the time they have spent on the analysis of our activities and project. In addition, we have especially appreciated the quality of their work and the in-depth evaluation of each team and of the global strategy of the Unit. Our impression is that the Committee did perceive the essential scientific objectives of the association of these four teams into a group really functioning as a Unit.

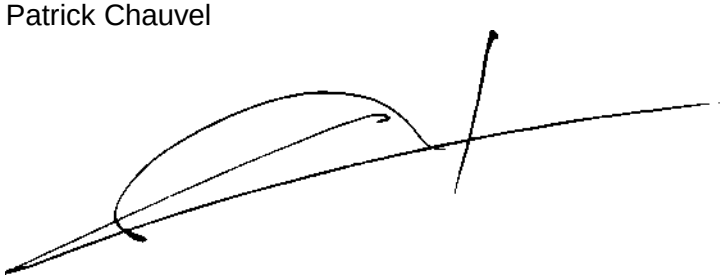
We have clearly understood the recommendations made by the Committee to set up the Unit and to pay attention to strengthening the links between Physionet, DCP, TNG (in particular) and Dynamap in order to help building up the size of the latter. We share their comments on the need in this important field to recruit or attract new researchers from outside. We also share their comments on the necessity to reinforce the technician and engineer support for the MEG lab.

We will install an international scientific advisory board as soon as the Unit is created.

You will find attached some corrections which should be made in the final report. Besides a few factual errors, our main concern regards the use of different qualifying terms applied to the publications of one team (DCP) in comparison with the others.

Sincerely,

Patrick Chauvel



Faculté de Médecine de la Timone - 27 Bd Jean Moulin - 13385 Marseille cedex 05. France
Tel : + 33 (0) 4 91 29 98 10 - Fax : + 33 (0) 4 91 78 99 14
Email : veronique.ayala@univmed.fr

Instituts thématiques Inserm
Institut national de la santé et de la recherche médicale

FACULTÉ DE MÉDECINE DE MARSEILLE
UNIVERSITÉ DE LA MÉDITERRANÉE AIX-MARSEILLE II

APHM

UMR 751 INSERM

Directeur : Patrick Chauvel

Corrections to assessment of publication quality:

I would like to call the Committee's attention to the inhomogeneity of the terms used to qualify the quality of scientific production among the different teams.
Because AERES has defined ranks differentiating the journals, systematically utilizing this ranking would be fair.
In particular, the qualification used for the DCP team's production was less favorable than that of the other teams although the *same proportion of papers (> 40%)* has been published in the same journals named "excellent" in the introductory part of the report, and in the other specific reports:

Please compare:
p.8 : **"In summary, the scientific output of the key members of the BDI is excellent. The U751 published 80 papers between 2006-2010 with a steady increase year on year. Around 50% of the papers were published in *excellent* journals such as Brain, J. Neuroscience , Cerebral Cortex, Neuroimage"**
to:
p.18/19 : "During these past 4 years the team has produced interesting research published in *good* journals. [...] Concerning scientific production, the team has published 51 original papers in journals ranging from *good* (Neuroimage, Neuropsychologia) to *very good* (Cerebral Cortex, Brain)"

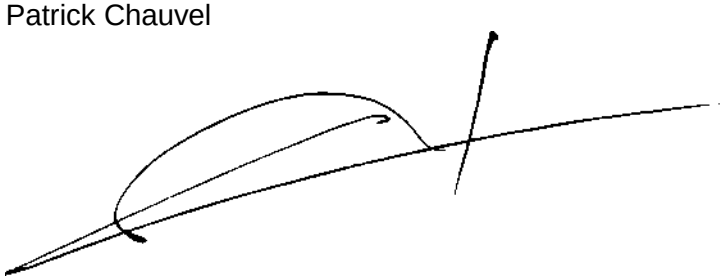
Remark : a paper published in J. Neuroscience by the DCP team (Catherine Liegeois-Chauvel as the last author), based on a work made in her lab, has been omitted.

In comparison:

Team Physionet
p. 10, last paragraph : "Taken these aspects into account the members of the group publish regularly in *excellent* and *very good* scientific journals
The publication record is excellent."

Team TNG
p. 15, 3rd line, first paragraph : "According to the bibliometric indicators (in the last five years >30 % of the articles were published in *excellent* and *very good* journals)"

Patrick Chauvel



Faculté de Médecine de la Timone - 27 Bd Jean Moulin - 13385 Marseille cedex 05. France
Tel : + 33 (0) 4 91 29 98 10 - Fax : + 33 (0) 4 91 78 99 14
Email : veronique.ayala@univmed.fr