LBPC-PM - Laboratoire de biologie physico-chimique des protéines membranaires

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Physical and chemical biology of membrane proteins

Under the supervision of the following institutions and research bodies:

Centre National de la Recherche Scientifique

Université Paris 7-Denis Diderot

December 2012

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

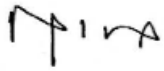
Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head



Pierre Glaudes

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

Grading

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

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

With respect to this score, the research unit concerned by this report received the following grades:

- Grading table of the unit: Physical and chemical biology of membrane proteins

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

Evaluation report

Unit name:	Physical and chemical biology of membrane proteins
Unit acronym:	UMR 7099
Label requested:	Renewal of UMR label
Present no.:	7099
Name of Director (2012-2013):	Mr Bruno MIROUX
Name of Project Leader (2014-2018):	Mr Bruno MIROUX

Expert committee members

Chair: Mr Jean-Luc GALZI , Strasbourg

Experts:

Ms Agnès GIRARD-EGROT, Lyon (representative of the CNU)

Mr Erik GOORMAGHTIGH, Brussels Frei University, Belgium

Mr Peter GRAUMANN, Marburg University, Germany

Ms Carola HUNTE, Freiburg University, Germany

Ms Véronique TREZEGUET-BUSQUET, Pessac (representative of the CoCNRS)

Scientific delegate representing the AERES:

Mr Jacques BARATTI

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

Mr Marc BENEDETTI, Life Sciences delegate, Université Paris Diderot

Mr Gilbert DELEAGE, Directeur Scientifique Adjoint, CNRS

1 • Introduction

History and geographical location of the unit:

The UMR 7099 entitled Physical and Chemical Biology of Membrane Proteins is affiliated to the Centre National de la Recherche Scientifique (CNRS) and to the Université Paris Descartes (Paris VII). It is hosted by the Institut de Biologie et Physicochimie (IBPC) located 13 rue Pierre et Marie Curie in Paris (75005). It is a unit with a single team that was renewed in 2009. At that time, the former director of the laboratory (Mr Jean-Luc POPOT) gave way to Mr Bruno MIROUX, researcher at the institut national de la santé et de la recherche médicale. The research unit is recognized for its expertise in membrane protein functional architecture.

Management team:

The laboratory is headed by Mr Bruno MIROUX.
He is assited by a financial manager

AERES nomenclature:

SVE1LS2 and SVE1LS1

Unit workforce:

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1	1	1
N2: Permanent researchers from Institutions and similar positions	9	9	9
N3: Other permanent staff (without research duties)	6	6	1
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)			
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	2	2	
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	**18**	**18**	**11**

Percentage of producers	***100 %***

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	10	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit*	5	
Number of Research Supervisor Qualifications (HDR) taken	4	
Qualified research supervisors (with an HDR) or similar positions	3	3

2 • Assessment of the unit

Strengths and opportunities

The research done by members of the unit is globally of very high quality in both basic and translational science. The marked reorganization of the unit following departure of scientists and recruitment/attraction of new ones is a success.

Because of historical reasons and also due to the connection with the other laboratories in the institute, the unit is highly specialized in membrane protein biochemistry, biophysical characterization and structural biology.

It is in addition clearly a leader in the field of amphiphilic polymers and in their chemistry, for which it has worldwide reputation.

The coupling of cell free expression of proteins with NMR is established and controlled, especially with the use of amphipols to favor refolding.

The Laboratory is located in an exceptional environment for both high quality basic science and applied science. Funding is globally sufficient, international collaborations and networks are quite numerous (including the LabEx and EquipEx affiliations), the connection with the University provides well-trained and motivated students.

A number of high quality technical facilities are available, which in particular cover nearly all aspects of the structural biology process.

Overall, there are excellent opportunities for translational science with the envisaged applications of amphipols as tools for basic research, but also for vaccine strategies and other health applications.

Weaknesses and threats

There is a risk linked to the partial loss of expertise in biophysics of amphipols and chemistry.This field should not be weakened for too long to remain at the forefront.

The solid state NMR theme benefits from well-established scientists. The methods are good but the group may fail to address the biological question, in particular regarding the structure-function relationship issues, because the control of ion channel functional state will be extremely complex to achieve.

The modest size of the unit is a risk because of the absence of critical mass around very competitive topics such as the determination of GPCR-bound ligand structures.These issues may benefit from alternative technologies currently actively developed.

Recommendations

In its future strategy, the laboratory should consider enlisting the skills of an additional chemist and a biophysicist to make the best possible use of the competitiveness on amphipols.

The unit should worry about how to make the best possible use of the new mass spectrometer, as no expert is present in the unit to develop concepts and applications.

Events especially devoted to the scientific participation of PhD and post-doctoral fellows may be organized to improve their integration in the unit.

3 • Detailed assessments

Assessment of scientific quality and outputs

Globally during the past five years the laboratory published 51 articles (on top of which 15 are from new researchers and are not counted here) and 5 invited reviews or book chapters. Fifty per cent of the articles were published in journals with IF >4 (JBC, Faseb J. Langmuir, Biophys J, BBA …) and the number of publications in journals with IF>10 is fairly high (10 articles in PNAS, JACS, Annu rev biochem, Annu rev biophys, Nature methods). More than half of the published articles and reviews are issued from the laboratory as can be judged by analyzing authorships (first or last author). Several members of the laboratory have published highly cited papers in their current field of research, such as for the structure of COX (920 citations), over-production of proteins in bacteria (900), functional characterization of the uncoupling protein (560), membrane protein folding (650) for the most notable ones.

Laboratory members gave 60 invited conferences at national and international congresses and gave another 60 talks/seminars in research institutes. Research themes are globally original (super complex structure resolutions, In Cell NMR …), and some groups are clearly leaders in their field at the international level. The theme by theme analysis (below) shows heterogeneity in the average amount and quality of publications.

The laboratory is clearly a world leader in the field of amphiphilic polymers. It can be ranked top 10 in this field of physical chemistry.

Assessment of the unit's academic reputation and appeal

Some indicators of the Laboratory reputation have been detailed above, such as the number of invited lectures at international conferences and research centers.

The coordination of collaborative studies (3 ANR grants), laboratories (LabEx Dynamo) and facilities (2 EquipEx Cacsice for SAXQ, MS and 700MHz NMR, and Paris en resonance for 800MHz NMR) also clearly demonstrate the pivotal role played by the unit in the national and european communities. The reputation of the group on amphiphilic polymers largely encompasses european borders as shown by the integration in NIH funded programs (e.g. amphipols as vaccine adjuvants with USA and Canada).

The laboratory succeeded in attracting two young scientists, two senior investigators and a new director during the past 4 years.

Post-docs represent approximately 20% of the work force of the Laboratory.

The laboratory organizes highly frequented workshops and schools on membrane proteins purification, folding and biohysical characterization. The use of amphipols is promoted during these training sessions, and this leads to their increasing and widespread use in the community.

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

During the past 4 years the laboratory globally obtained 1.3 M€ in grants (among which european grants, 1 NIH grant to be compared to the 0.1 M€ of institutional support). The academic grants were obtained by applications to both french and international calls. In most cases the funded studies were collaborative involving teams of the laboratory and external teams. In more than 50% of the cases, funding through collaborative grants was obtained from institutional french agencies (ANR, FRM ..). Members of the laboratory are often principal investigators of collaborative studies. The laboratory also received support from the “initiative d’excellence” a governemental program for large equipments (NMR, MS, and for a laboratory of excellence (8 M€ equipment, 0.4 M€ running costs and 2 M€ for fellowhips).

Amphipols are patented and a licence for production and distribution has been given to Affymetrix/Anatrace.

Assessment of the unit's organisation and life

Credit should be given to the Laboratory for its successful change in management which was conducted in the past four years. The task was certainly not simple as 6 researchers and technicians left the laboratory during the past five years. Despite these important changes, the management could convince 9 scientists (5 researchers and 4 engineers and technicians) to join the laboratory and to build a promising new team.

It appears quite evident that the members of the laboratory are happy to work in the laboratory and to take advantage of the rich scientific and technological environment of the campus, which provides support in the form of multiple "investissements d'avenir" successful initiatives.

The current head of the laboratory has been chosen to continue his function for the term to come. He is appreciated by colleagues, technicians and students.

Inter-theme technical collaborations illustrate how the choice of having a single team unit with scientists dedicated to projects rather than to groups allows flexibility and efficient internal communication.

Assessment of the unit's involvement in training through research

The laboratory is very active in the field of training, albeit having very limited staff from the university.

The unit has trained more than 50 students with levels ranging from high-school to master, PhD and post doctorate. 12 graduate students are currently supervised, 7 PhD theses were defended since 2009.

Altogether, the laboratory staff provides more than 350 hours of lectures in several universities, mostly in Paris, in biochemistry, biophysics and structural biology mainly.

Researchers have also organized three international workshops worldwide, as well as one CNRS school and one research groups (GDR).

Assessment of the five-year plan and strategy

The laboratory develops an integrative approach starting from atomic structures up to higher levels of organization that is ambitious and risky enough to warrant breakthroughs.

To ensure success, the unit has established solid cooperations as illustrated by its participation (and co-direction) to two EquipEx programs, CACSICE (analytical MS, NMR 700 MHz and vizualization wall at IBPC) and PARIS EN RESONANCE (800MHz NMR-DNP at the ENS) and one laboratory of excellence DYNAMO (dynamics of energy transducing membranes). All these programms provide leading edge equipments and support for laboratory running costs and doctoral and post doctoctoral fellowships. Researchers of the laboratory are also establishing new national and international networks, in particular on technologies exploiting amphipols in GPCR studies (Copenhagen) or other membrane proteins (Francfort, Basel, NIH …) which help develop new concepts and technologies.

One ambitious program of the laboratory is the crystallography of supercomplexes. The laboratory has full equipments and skills to tackle this issue both in terms of complex membrane protein purification and in crystallography.

The escalation of levels of organization is facilitated by the recent recruitement of researchers working in bacterial physiology and would be further improved by joining expertise in cellular biology.

The single team, with multiple themes structure, appears very efficient in terms of intra-laboratory concepts and protocol exchanges, and thus deserves that the laboratory keeps a small size. As a corollary, attention must be paid to avoid programs that would be remote from each other in terms of techniques or concepts.

4 • Theme-by-theme analysis

Theme 1: Energy coupling and supramolecular organization of respiratory complexes

Manager's name: Mr Daniel PICOT

Workforce

Theme workforce in Full Time Equivalents	As at 30/06/2012	As at 01/01/2014
FTE for permanent professors	1	1
FTE for permanent EPST or EPIC researchers	4	4
FTE of other permanent staff without research duties (IR, IE, PRAG, etc.)		
FTE for other professors (PREM, ECC, etc.)		
FTE for postdoctoral students having spent at least 12 months in the unit		
FTE for other EPST or EPIC researchers (DREM, etc.) excluding postdoctoral students		
FTE for other contractual staff without research duties		
FTE for doctoral students	2	
TOTAL	7	5

• Detailed assessments

Conclusion

• Overall opinion of the theme:

The function of the cytochrome b/Rieske complex in electron transport during photosynthesis and the action of mitochondrial carrier proteins at a molecular level are highly interesting and relevant topics. The scientists involved have great expertise on the biochemistry of membrane proteins, and on the physiology of mitochondrial carriers. The scientists are able to answer the fundamental biological and chemical questions of how electrons are transported within the membrane, how molecular supercomplexes are set up at an atomic level (interaction surfaces), and how mitochondrial transporters (uncoupling proteins) operate at a molecular level. The scientists have generated high impact publications in the past and will continue to do so in the future. The expertise of theme leader has been crucial for a recent key PNAS publication. Taken together, the research proposals have a high potential to yield novel insight into fundamental questions, so the overall opinion is a positive one.

● Strengths and opportunities:

The laboratory develops an integrative approach starting from atomic structures up to higher levels of organization that is ambitious and risky enough to warrant breakthroughs.

To ensure success, the unit has established solid cooperations as illustrated by its participation (and co-direction) to two EquipEx programs, CACSICE (analytical MS, NMR 700 MHz and vizualization wall at IBPC) and PARIS EN RESONANCE (800MHz NMR-DNP at the ENS) and one laboratory of excellence DYNAMO (dynamics of energy transducing membranes). All these programms provide leading edge equipments and support for laboratory running costs and doctoral and post doctoctoral fellowships. Researchers of the laboratory are also establishing new national and international networks, in particular on technologies exploiting amphipols in GPCR studies (Copenhagen) or other membrane proteins (Francfort, Basel, NIH …) which help develop new concepts and technologies.

One ambitious program of the laboratory is the crystallography of supercomplexes. The laboratory has full equipments and skills to tackle this issue both in terms of complex membrane protein purification and in crystallography.

The escalation of levels of organization is facilitated by the recent recruitement of researchers working in bacterial physiology and would be further improved by joining expertise in cellular biology.

The single team, with multiple themes structure, appears very efficient in terms of intra-laboratory concepts and protocol exchanges, and thus deserves that the laboratory keeps a small size. As a corollary, attention must be paid to avoid programs that would be remote from each other in terms of techniques or concepts.

All scientists involved have all necessary expertise to reach their very ambitious goals: the 3D structure of a super complex of membrane proteins, the mode of the uncoupling activity of UPC1, and the identification of the function of UCP2. The latter protein is involved in various diseases, so this project has also medical relevance. The b6f complex is similar to complex III of the respiratory chain, which is central to energy generation in animal cells, so the work on b6f will give vital insight into the molecular activity of these electron-transporting complexes. The laboratory has the capacity to solve all these questions. The topic of membrane protein supercomplexes is highly actual and timely. Given that the research unit is highly interactive within, and also has many collaborations, combination of the different expertises will be fruitful. Thus, the difficult task of crystallizing a super-complex of already large membrane protein complexes needs to be tackled now. Both, NMR and X-ray crystallography are available in the group, whose complementarity may well increase the efficiency of structure determination and the identification of the interaction surfaces. Work in the subteam is in full swing and will be further boosted by the expertise on biochemistry of membrane proteins available in the research unit.

The function of the cytochrome b/Rieske complex in electron transport during photosynthesis and the action of mitochondrial carrier proteins at a molecular level are highly interesting and relevant topics. The scientists involved have great expertise on the biochemistry of membrane proteins, and on the physiology of mitochondrial carriers. The scientists are able to answer the fundamental biological and chemical questions of how electrons are transported within the membrane, how molecular supercomplexes are set up at an atomic level (interaction surfaces), and how mitochondrial transporters (uncoupling proteins) operate at a molecular level. The scientists have generated high impact publications in the past and will continue to do so in the future. The expertise of theme leader has been crucial for a recent key PNAS publication. Taken together, the research proposals have a high potential to yield novel insight into fundamental questions, so the overall opinion is a positive one.

● Weaknesses and threats:

As for any ambitious project, the goals may not be reached. The structure determination of supercomplexes may prove to be too challenging, or complexes too weak to be captured. This threat is no weakness, because intermediary steps to be solved are approached: the function of the chlorophyll group in the b6f complex will be determined, as an example for an important gain of knowledge on the function of the complex. The involvement in signalling will also be an interesting point.

- Recommendations:

Both projects are on a good way. The PI is encouraged to also publish small (but significant) results, even if greater endeavours are aimed at. As a general recommendation to the group, based on the comments from the PhD students, it is recommended to have more opportunities for students to present the progress of their work more often (at least once a year) in front of the group, and to hold a journal club to learn to present work from the literature.

Theme 2: Molecular signalling of GPCRs

Manager's name: Mr Laurent CATOIRE

Workforce

Theme workforce in Full Time Equivalents	As at 30/06/2012	As at 01/01/2014
FTE for permanent professors		
FTE for permanent EPST or EPIC researchers	3	3
FTE of other permanent staff without research duties (IR, IE, PRAG, etc.)		
FTE for other professors (PREM, ECC, etc.)		
FTE for postdoctoral students having spent at least 12 months in the unit		
FTE for other EPST or EPIC researchers (DREM, etc.) excluding postdoctoral students		
FTE for other contractual staff without research duties		
FTE for doctoral students	1	
TOTAL	4	3

• Detailed assessments

Conclusion

● Overall opinion of the theme:

GPCR signalling is a complex process that is subject to active research worlwide. Several disruptions, mutations, or defects lead to various disorders including cancer. The underlying molecular processes are investigated in theme 2 in different ways:

1) solving the structure of bound agonist ligands: ligand binding to, and activation of BLT2, the leukotriene receptor involved in chemotaxis of granulocytes and macrophages are studied. NMR spectroscopy is used to determine the 3D structure of the agonist to the receptor. Another aspect of the project is the study of BLT2 reconstituted in nanodiscs under a native form to falicitate structure-function studies. Interesting results are obtained about the interaction of LTB4 and 12-HHT with the receptor. However NMR techniques applied to large molecules and used to decipher molecular mechanism involved in signal transduction may not prove competitive.

2) solving the structure of proteins and protein complexes involved in the Hedgehog signaling pathway. The focus here is a soluble complex downstream of Smoothened in *Drosophila*, named HTC and consisting in Fused, COS2 and Ci, the first two participating in Ci conversion from an inactive to an active form. The approach is based on structural studies of these proteins. They are produced in *E. coli*. The subject is very competitive. The molecular mechanisms underlying signaling pathways are less studied worlwide than the structure of the receptor. There are thus potentialities in focusing on this issue.

- Strengths and opportunities:

The group has acquired expertise in expressing fully (2H) labeled proteins in bacteria, purifying and refolding them using mixtures of detergents and amphipols. NMR study of the soluble GPCR is then carried out and combined to molecular dynamic studies to obtain the structure of the leukotriene bound receptor. This project has led to important publications (JACS, J biomol NMR, Trends biotechnol). Fallouts are expected in inflamatory response in the long term. Additional receptor-ligand complexes might be examined using this approach. PI expertise is acknowledged in France and abroad (4 invited conference).

The structure solution of the Hedghog transducing complex acting downstream of the GPCR, Smoothened, was introduced in the unit in 2010 with the arrival of a new researcher. It aims at solving structures of protein complexes acting downstream of the receptor and organized around the protein SUFU whose structure was solved in the group. The understanding of Hh signaling at the molecular level could lead to the discovery of interesting drugs by bioinformatic analyses. The topic offers opportunities to settle internal collaborations

- Weaknesses and threats:

The structure of 12-HHT in its bound state was solved (unpublished data) though the flexibility of 12-HHT constrained the analyses. So far there is no BLT2 targeted drug and these results could open the way to in silico drug design. However 12-HHT structure is still lacking for molecular modeling.

No publication yet on the Hh project. Positioning of the unit in this field has still to be established.

- Recommendations:

- The group shoud collaborate with pharmacologists and medicinal chemists to develop new ligands based on the solved structure in order to test robustness of the approach, expecially if the activity of the receptor were to be regulated by the new ligands.

- Hasten publication on the Hh topic. Apply for short term grants (Ligue contre le cancer, Cancéropôle, ...). Because the study of soluble proteins is not in the frame of the unit, the unit should think about orienting towards the study of Smo or Ptc as soon as possible.

Theme 3: Transport and membrane dynamics in bacteria

Manager's name: Mr Philippe DELEPELAIRE

Workforce

Theme workforce in Full Time Equivalents	As at 30/06/2012	As at 01/01/2014
FTE for permanent professors		
FTE for permanent EPST or EPIC researchers	2	2
FTE of other permanent staff without research duties (IR, IE, PRAG, etc.)		
FTE for other professors (PREM, ECC, etc.)		
FTE for postdoctoral students having spent at least 12 months in the unit		
FTE for other EPST or EPIC researchers (DREM, etc.) excluding postdoctoral students		
FTE for other contractual staff without research duties		
FTE for doctoral students	2	
TOTAL	4	2

• Detailed assessments

Conclusion

● Overall opinion of the theme:

Research in this theme aims to elucidate how substrates are transported across the bacterial envelope in molecular up to atomic detail, an interesting and relevant topic. The focus is on heme transport and on the bacterial response to mechanical stress. The implementation of cell-free production and of development of isotope-labeling for the mechano-sensitive channel MscL was achieved during the reporting period. These methods are important for the proposed structural and mechanistic studies of MscL. They may also be helpful for further characterization of bacterial heme transport. The interesting model system for the latter was brought into the unit by a new researcher who joined in 2011. The successful and systematic previous work with this model provides a very good basis for promising future studies. In general, the proposed research in this theme has the potential to answer fundamental questions in the area of membrane transport.

- Strengths and opportunities:

Specific strength of the theme is noted in the expertise of preparation of isotope-labeled membrane proteins for structural studies especially in combination with solid-state NMR, which permits analysis of membrane proteins in natural lipid environment. Furthermore, in a fairly unique combination of expertise, theme 3 and 1 aims to explore a challenging interdisclipinary project in which production of membrane proteins in a specific *Escherichia coli* overexpression strain under conditions that stimulate abundant formation of internal membranes (theme1) is employed to analyse membrane proteins structurally by in-cell solid state NMR.

- Weaknesses and threats:

MscL seems not be ideal as a model system. Research on structure and mechanism of MscL is in serious competition with large, strong groups on an international level. In addition, it seems of limited use to exploit the power of solid-state NMR for the analysis of conformational changes and dynamics, as these structural changes are difficult to trigger and maintain under experimental conditions.

- Recommendations:

An additional model system might be considered, in which conformational changes can be triggered by ligand binding, covalent modification, or other events, so that the newly developed NMR methods such as in-cell NMR directly provide answers to biologically important questions.

Theme 4: A toolbox for the membrane protein chemistry

Manager's name: Mr Fabrice GIUSTI

Workforce

Theme workforce in Full Time Equivalents	As at 30/06/2012	As at 01/01/2014
FTE for permanent professors		
FTE for permanent EPST or EPIC researchers		
FTE of other permanent staff without research duties (IR, IE, PRAG, etc.)	5	5
FTE for other professors (PREM, ECC, etc.)		
FTE for postdoctoral students having spent at least 12 months in the unit		
FTE for other EPST or EPIC researchers (DREM, etc.) excluding postdoctoral students		
FTE for other contractual staff without research duties	1	
FTE for doctoral students		
TOTAL	6	5

• Detailed assessments

Conclusion

● Overall opinion of the theme:

Theme number 4 is presented as “a toolbox for membrane protein chemistry”. This transversal theme is by itself a first class research activity. It is also the cement that makes the other activities particularly original and efficient. The quality of this theme is outstanding as indicated by the publications in the best possible journals (Langmuir, Biophys J, Nature Methods, Anal Chem), the international grants obtained (European and from the American NIH), the very large number of national and international collaborations, the patents obtained and the industrial collaborations. Theme 4 is entirely dedicated to achieve the design and synthesis of new molecules with an in-depth knowledge of the properties of membrane proteins.

● Strengths and opportunities:

The keywords are originality and efficiency:

1) Originality: the design of original surfactants called amphipols is probably the single most important achievement of the team that explains its world-wide recognition. Handling membrane proteins remains a challenge and the design of new molecules that help solubilize membrane proteins is recognized as a major breakthrough. Furthermore, these molecules have been shown to help fold and stabilize membrane proteins, either nascent or during refolding procedures. Overall, hundreds of researchers have learned the benefits of this class of molecules and much start using them. Their appearance on the market will certainly further increase their reputation. The outstanding originality of these molecules is the key of their current success. New surfactants are constantly designed, synthesized and tested for their biological properties.

2) Efficiency: the team is very dynamics and the needs of the other themes results in frequent requirement for new amphiphilic molecules. The original amphipols have already been modified in a number of ways for instance, to immobilize membrane protein on surface-sensitive support like SPR sensor. The skills to make the synthesis of these molecules, encapsulated in "theme 4", are unique. The key feature here is that all the members of the group work in close collaboration.

The everyday discussions within the lab result in constant re-evaluation of the design of amphiphilic molecules. The process is ongoing and the opportunities are more numerous than ever. Just to quote a few that is already on track: synthesis of perdeuterated molecules for NMR studies or functionalized with various kinds of tags, labeling with various fluorescent dyes, vaccination, cell-free in-vitro membrane protein synthesis, membrane protein refolding, and membrane protein crystallization.

● Weaknesses and threats:

No weakness could be identified nowadays. Threats are related to the small number of scientists in charge of the chemistry aspect of the research. Every mean should be used to maintain and increase the number of chemists able to design and synthesize new molecules. The success encountered so far relies heavily on the presence of the chemists, biochemists and biophysicists within the same lab.

● Recommendations:

The number of applications is rapidly growing. The industry buys licenses and is already offering some of these products on the market. It appears to be willing to offer more molecules. This is a real opportunity that neither the lab nor French research as a whole should let escape. According to the foreign experts of the panel, it is essential to re-enforce theme 4 by at least one additional engineer.

5 • Conduct of the visit

Visit dates

Start: december 14, 2012 at 8h30.
End: december 14, 2012 at 19h

Visit site(s):

Institution: Institut de Biologie Physico-Chimique (IBPC),
Address: 13 rue Pierre et Marie Curie 75005 Paris

Conduct or programme of visit:

Laboratory of Physico-Chemical Biology of Membrane Proteins
Université Paris Descartes, CNRS, UMR7099

Program of the visiting committee

08:30	Welcome to the committee (15 min)
08:45	Centering of the committee
	Preliminary meeting of the committee (closed hearing) (30 min)
	Attending: Committee members, AERES scientific delegate
	Scientific part
09:15	*Site: Bibliothèque Edmond de Rotschild RdC*
	Attending: Committee members, AERES scientific delegate, representatives of Institutions and unit members
	Presentation of AERES evaluation and of committee members
	(10 min)
09:25	Presentation of the unit project: Director (25 min + 25 min discussion)
10:15	Scientific Presentation Theme 1 (12 min + 13 min discussion) Crystallography on complexes and supercomplexes of the electron transfer chain
10:30	Break (15 min)
10:55	Scientific Presentation Theme 2 (12 min + 13 min discussion) Conformational selection of GPCR ligands upon binding to their receptors as observed by NMR
11:20	Scientific Presentation Theme 3 (12 min + 13 min discussion) From *in situ* to in cell solid state NMR
11:45	Scientific Presentation Theme 4a (11 min + 12 min discussion) Applications of amphipol technology to the study of membrane proteins
	Scientific Presentation Theme 4b (11 min + 12 min discussion) In the cauldron of *in vitro* synthesis: membrane proteins, detergents and new surfactants
	Meeting with representatives of Institutions
12:30	*(30 min discussion with committee members)*
	Attending : Committee members, AERES scientific delegate, representatives of University of Paris Descartes and of CNRS

13:00	*Lunch - buffet / discussion*
14:30	Meeting with researchers, technicians, doctoral students and post doctoral fellows
	in parallel the committee splits into three groups.
	Meeting with researchers
	Meeting with technicians
	Meeting with doctoral students and post doctoral fellows
	Attending: Committee members, AERES scientific delegate, without the team leaders, without representatives of institution and without the direction of the unit
15:00	Meeting with the unit Director
	(30 min discussion with the committee)
	Attending : Committee members, AERES scientific delegate, Unit Director
	Débriefing of the committee
15:30	Deliberation of the committee (closed hearing) *(150 min)*
	Attending : Committee members, AERES scientific delegate
18:00	*Thanks and leave of the committee*
18:15	*End*

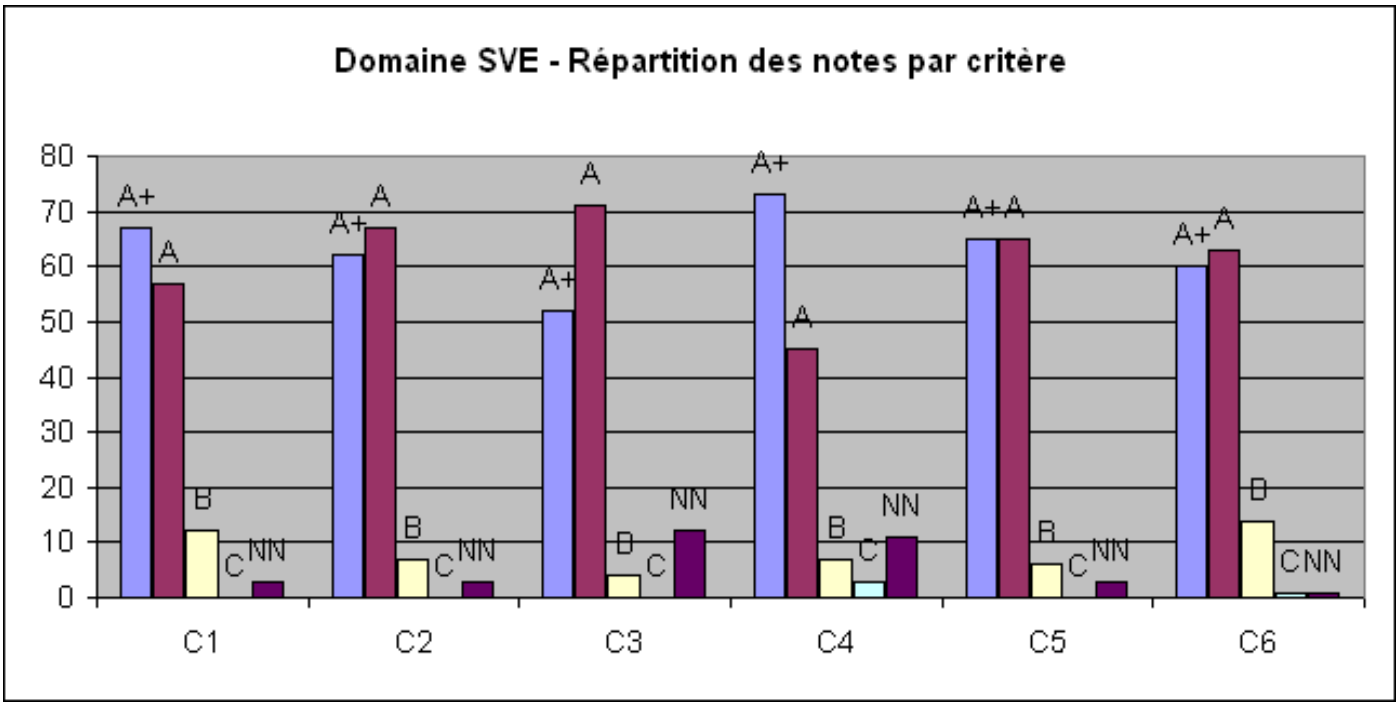
6 • Statistics by field: SVE on 10/06/2013

Notes

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

Pourcentages

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



7 • Supervising bodies' general comments

université PARIS DIDEROT PARIS 7

Le Président

P/VB/NC/YM – 2013 - 059
Paris, le 05 avril 2013

M. Pierre Glaudes
Directeur de la section des unités de l'AERES
20 rue Vivienne
75002 PARIS

S2PUR140006421 - Laboratoire de Biologie Physico-Chimique des Protéines Membranaires - LBPC-PM - 0751723R

Monsieur le Directeur,

Je tiens en premier lieu à remercier les membres du comité de visite de l'AERES pour la production du rapport sur l'unité « Physical and chemical biology of membrane proteins ».

Je me réjouis des appréciations élogieuses qui sont portées sur ce laboratoire, dont vous avez en particulier souligné l'excellente qualité des publications et la position de leader au niveau international dans le domaine des polymères amphiphiliques.

Le comité souligne que le haut niveau de recherche et le rayonnement national incontestable de l'unité, attestés par les projets contractuels qu'elle coordonne (3 ANR, 2 Labex, 2 Equipex), ont permis d'attirer des chercheur.e.s juniors et seniors pour cette unité, encore de faible taille, que l'Université soutient à la hauteur de ses moyens.

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

Vincent Berger

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