Institut de Biologie Structurale

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the unit:

Institut de Biologie Structurale

University or school

CEA

CNRS

Université Grenoble 1

Mai 2010

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et de l'enseignement supérieur

Section des Unités de recherche

AERES report on the research unit

Institut de Biologie Structurale

From the

CEA

CNRS

Université Grenoble 1

Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

Mai 2010

Unit

Name of the unit: Institut de Biologie Structurale

Requested label: UMR CNRS

No. in case of renewal: 5075

Unit director : Ms. Eva PEBAY-PEYROULA

Members of the expert committee

Chairperson:

Mr. Frédéric DARDEL, Université Paris Descartes, Paris

Reviewers :

Mr. Ronald MELKI, CNRS, Gif sur Yvette

Mr. Wolfram SAENGER, Freie Universitaet, Berlin

Mr. Henning STAHLBERG, Biozentrum, Bâle

Mr. Paulo TAVARES (CNRS, Gif sur Yvette

Mr. Georges DE TITTA, University of Buffalo

Reveiwers(s) nominated by the staff evaluation committees (CNU, CoNRS, CSS INSERM ...) :

Ms. Marie-Christine AVERLANT-PETIT, ENSIC, Nancy

Mr. Pierre PLATEAU, CoNRS member

Representatives present during the visit

Délégué scientifique représentant de l'AERES :

Mr. Yves GAUDIN

Représentant(s) des établissements et organismes tutelles de l'unité :

Mr. Gilles BLOCH, CEA

Mr. Jacques NEYTON, CEA

Mr. Thierry MEINNEL, CNRS

Mr. Farid OUABDESSELAM, Université Grenoble 1

Mr. Laurent DAUDEVILLE, Université Grenoble 1

Report

1 • Introduction

- Date and execution of the visit

The site visit took place from February 8th to 10th, 2010. The experts convened on the evening of the 8th to organise the work and share impressions on the paper documents. The next two days were devoted to hearing presentations by team leaders and also to formal discussions with various staff groups (student & post-docs / permanent scientists / technical staff) and with representatives of the "tutelles". Finally, a private meeting with the director allowed her to debrief the overall visit and clarify a few points. The last day was devoted to a closed door reunion of the committee to discuss its evaluations and prepare a draft of the present report.

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

IBS is located in the "polygone" area of Grenoble, close to the european large scale instruments, ESRF and ILL. This is also very close to other CEA and CNRS labs and to EMBL outstation, but much more distant from the main Université Joseph Fourier campus, which is on the other side of town. As suggested from its name, the IBS works mainly in the field of structural biology, covering essentially all techniques within this discipline : EM, X-Ray crystallography, NMR, Small angle scattering, modelization and various other biophysical and biochemical techniques. The Institute focuses are both the methodology, with several teams being heavily involved in developing novel tools, maintaining beamlines at the nearby ILL or ESRF, and also on various biological systems, such as membranes proteins, pathogens, macromolecular assemblies, metalloproteins…

- Management team

In its proposed configuration, IBS will be organised in 15 teams grouped into 3 thematic axes. Some of the larger teams have sub-groups, led by different PIs. Currently the lab has one director (Eva Pebay-Peyroula) and a part-time deputy director who is due to retire soon.

- Staff (according to the dossier submitted to AERES):

	In the report	In the project
N1: Number of professors (see Form 2.1 of the unit's dossier)	8	9
N2: Number of EPST, (Public scientific and technological institution) or EPIC, (Public industrial and commercial institution) researchers (see Form 2.3 of the unit's dossier)	52	55
N3: Number of other professors and researchers (see Form 2.2 and 2.4 of the unit's dossier)	-	-
N4: Number of engineers, technicians and tenured administrative staff members (see Form 2.5 of the unit's dossier)	54,65	52,65
N5: Number of engineers, technicians and non-tenured administrative staff members (see Form 2.6 of the unit's dossier)	11	-
N6: Number of doctoral students (see Form 2.8 of the unit's report dossier and 2.7 of the unit's project dossier)	34	26
N7: Number of persons accredited to supervise research and similar	43	41

2 • Assessment of the unit

- Overall opinion :

The IBS uniquely combines cutting edge research in the various aspects of structural biology and is undoubtedly one of the very best French laboratories in the field. This is exemplified by the fact that a significant number of IBS PIs have strong international recognition in their field (see team assessments below), that IBS has been remarkably successful in raising competitive funds and in the past four years has published papers in most of the major international journals in their field (Nature, Science, NSMB, PNAS, Nat. Chem Biol. Nat. Nanotech, Mol Cell, Dev Cell…). As a result, the IBS has attracted high-level international scientists as new group leaders.

In addition to this cutting-edge scientific activity, IBS maintains national beamlines at ILL and ESRF and thus provides support to the entire community in the field. This provides them with major opportunities to develop both national and international collaborations.

With this new four-year contract, IBS has undergone a major internal reorganisation, which is a first step toward the move to a new building, closer to the light and neutron sources. The committee has felt that all this has been realised within what appeared to be a generally very positive atmosphere for all staff members.

- Strengths and opportunities:

IBS has managed to set-up and maintain cutting edge platforms for almost all aspects of structural biology, either within itself or in partnership with local institutions (EMBL, ILL, ESRF…). In combination with the privileged access to the beamlines, this provides IBS with a very strong and visible vantage position within the French and European landscapes. The new organisation, which is now biology-oriented rather than methodology-oriented as it was before, should foster increased interdisciplinarity and multi-technique approaches and further improve the visibility of the Institute. The current director is commended for having successfully steered this major change rather smoothly, which is not an easy task, given the large size of IBS.

- Weaknesses and threats:

The committee was not convinced by the scientific coherence or logic of a small number of the teams within the new organisation. This has nothing to do with the individual qualities of the leaders, but rather with their

grouping within disparate teams. Also several of the key figures of the Institute are due to retire in the near future, for instance in the EM group, which may be considered a fragility if not adequately anticipated.

- Recommendations for the unit director:

Given the recent changes in the French funding system, the share of recurrent funding (CEA, CNRS, University) in the IBS budget has significantly dwindled. This has limited the management leeway for fostering new scientific projects, internal collaborations (for instance, within the three research axes) or supporting junior group installation. Possibly a new internal financing system should be discussed, where full-costs are charged to ANR type grants, in order to ease the burden on the recurrent funds. Part of this could then be used to help improving internal collaboration and coherence, to support groups which go through temporary difficulties or to provide start-up funds for new projects or young scientists.

Active action to support the EM group after the retirement of the current leader should be undertaken, the close collaboration with the UVHCI (EMBL/UJF/CNRS) being a very good possibility which the committee fully endorses.

The competitivenes of IBS is strongly dependent upon the efficiency of its numerous and well-thought platforms. A very significant part of this efficiency relies on the expertise of the technical staff actually running these sophisticated equipments. A general and clear policy regarding the recognition of the contribution of the technicians and engineers in publications could be discussed within IBS. This would help to maintain the positive spirit within the institute.

The committee supports the decision of the director regarding the mass spectrometry platform. The scientist previously in charge has had a good scientific track record and has also provided support to the other teams. However, his integration within the new biology-oriented organisation of the institute appeared difficult. A solution for maintaining access to a competitive MS facility should be sought.

- Data on work produced :

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

A1: Number of *produisants* (professors and researchers whose names appear in a minimum number of "publications" over a 4-year period) listed in N1 and N2 in the project column	62
A2: Number of *produisants* among the other staff listed in N3, N4 and N5 in the project column	-
A3: Proportion of *produisants* in the unit [A1/(N1+N2)]	95,4%
Number of theses for accreditation to supervise research defended	
Number of theses defended	43
Any other data relevant for the field (please specify)	-

3 • Specific comments on the research unit:

- Appreciation on the results

Since 2005, IBS has had a sustained high-quality throughput in terms of publication, with an average of ~100 articles / annum, for a staff of 50-odd permanent scientists. These publications are of high standard, with a very high share in the best journals in their field (for 2005-2009 : 46 JACS, 37 J. Mol. Biol., 34 JBC…) but also a significant number in the top journals (19 *PNAS*, 7 *Angew. Chem.*, 3 *Nature*, 3 *Science*, 2 *NSMB*, 2 *Nature Chem. Biol.*, 1 *Nature*

Nanotech, 1 *Mol. Cell*, 1 *Dev. Cell*, with 22 out of those 39 with first or last authorship). Quite remarkably, all teams have a high quality output (see details for each team below), with a few truly outstanding, which thus makes the whole IBS a well-balanced institution with little if any weak spots in the various sub-domains of structural biology.

Another less measurable but very significant output of IBS is the support and participation to European infrastructures. Two of the groups are actually in charge of maintaining beamlines at ESRF and ILL, where they have developed new hardware, innovative robotics, and provide expert support for the structural biology community. Some of this know-how has been successfully transferred to a start-up company which is a spin-off of IBS. The NMR group is part of a national ("Très grande infrastructrure RMN") and European network facility (EuroNMR) which offers high-field NMR time and expertise to external users.

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

IBS is undoubtedly quite attractive, as several groups have joined in during the past 4 years, including two foreign group leaders (one on a CNRS ATIP grant and the other with an ANR "Chaire d'excellence senior"). 43 PhD theses were defended in the past four years and the Institute has attracted over 70 post-doc and visiting scientists during the same period.

IBS staff members have a strong national and international recognition. The director is a member of the CNRS "Conseil scientifique". One the junior staff scientists has been awarded the "Paoletti Prize" for the best young scientist of the year in France. Most PIs have been invited to international conferences, and for instance one of the group leaders has been asked to contribute an invited review in Nature and another one has chaired a Gordon conference. Several of their papers were selected for "News and Views" and "Editor's Choices" in Nature and Science.

IBS has been extremely successful at acquiring competitive funding, with no less than 41 ANR and 10 EU grants awarded between 2005 and 2009, making it one the most successful research institutes in France for ANR.

- Assessment of the strategy, governance and life of the unit:

IBS strategy is strongly based on maintaining a number of cutting-edge technology platforms that play an essential role in the overall competitiveness of the Institute. The key to their success is that these platforms are run by expert scientists, alongside competitive research. Some of these platforms are shared with other organisations on the same site (ILL, ESRF, EMBL, UVHCI), within the PSB (Partnership for Structural Biology, a very efficient move, which, by joining forces, has allowed partners to scale up equipment and be more ambitious in terms of automated, systematic approaches for producing, labelling, purifying and crystallising proteins. The setup and array of techniques available to them is, to the knowledge of this committee, the most efficient and complete in the country.

Despite this emphasis on technological platforms, this is clearly only a mean and not an end in IBS strategy. This is exemplified by the major strategic change made by the direction in reorganising groups from a methodology-based segmentation to a biological project based organisation. One should emphasize that this is a true "silent cultural revolution" within IBS. The committee strongly thinks this was indeed the right strategic move as it will allow IBS to tackle more challenging and complex problems by focusing on the biology, by fostering multidisciplinary approaches on a given issue and by gaining better international visibility and recognition in those biological areas which they have selected. For the most part, the impression of the committee is that this reorganisation is so far a success, being for the most part coherent and rather well accepted by the staff. This will however have to be consolidated and those groups that are less well structured or integrated into the mainstream "axes stratégiques" should be helped in this reorganisation process.

The overall atmosphere within the laboratory was perceived as being very good, with most staff members being aware on the high standard of equipment and funding available to them. The projected move to a new building, "IBS-2", is a cause of excitement and a driving force for most people. All staff members, including technicians, could be associated with the further phases of the IBS-2 project in order to ensure that everyone makes this new project his own.

- Project assessment:

Most aspects of the strategic project have been discussed in the above section and appear balanced well engaged. As already stated above, this is clearly the way to go. The overall scientific project organised in three scientific "axes stratégiques" and one transverse technological theme makes sense with "Immunity and

host-pathogens interaction" axis being the most focused. Efforts should be made to strengthen this axes policy by providing incentives to groups for collaborating within the same "axe stratégique". This would help building a true Institute spirit under the new organisation.

The projects of the groups are discussed individually below and are overall of very high quality and challenging, with a good balance between bold innovative approaches, broad multidisciplinary projects and safer, solid studies. Both the technical and financial feasibility of most projects is within reach of IBS capabilities.

4 • Team-by-team

Introductory remark : because of the major reshuffling of groups and staff members within IBS occuring at this time, in many cases it does not make sense or isn't possible to fill the staff tables which compare the « past » and « future » teams, as there is no such thing as a « past » team for many of the new groups. in this respect, the committee felt that the paper documents provided by IBS indeed made it rather difficult to follow some of these group reorganisation. This was very much clearer from the site visit presentations.

Team 1:Protein-GAG interactions

Team leader: Hugues LORTAT-JACOB

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		-
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		1,5
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		-
N6: Number of Ph.D. students (Form 2.7 of the application file)		2
N7: Number of staff members with a HDR or a similar grade		1

- Appreciation on the results

This group works on the study of the determinants involved in glycosaminoglycan(GAG)-protein interactions, how these regulate the cell functions and how protein-heparan sulphate interactions can be used to manipulate a biological system. The group examined the role of a particular GAG family, the heparan sulphates, in pathological conditions. Especially they focused on interactions with cytokines and HIV gp120 and they were able to develop a synthetic dodecasaccharide that show low nanomolar antiviral activity in a cell based assay. This is very interesting as its mode of action is different from that of current AIDS antivirals.

In parallel the *Protein-GAG interaction* group develops methodological aspects related to the specific needs of their ongoing projects. In particular, they have set up a screening strategy using microarrays and SPR technologies to evaluate the structural diversity of heparan sulphate and synthesized labelled them with ^{13}C and ^{15}N for structural purposes using NMR.

The group shows an excellent productivity and a high standard of publications. 28 articles where published in first rank journals (Nature Chem. Biol., PLoS Pathogens, EMBO report, PLoS One, Curr. Opin. Struc. Biol. , ...), many of them with first or last authorship from the group. Three patents were also taken on the group developments.

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

Key external and internal partnerships have been developed to broaden the projects perimeters and develop competence of the group, in particular in the field of carbohydrate chemistry, which is critical for their project.

The members of the group have been invited in international conferences and universities to give lectures, they should continue developing the international visibility. In the last four years, two theses were defended in the group and one is in progress. The group has been comforted by the recruitment of a junior researcher. The group has an excellent ability in raising money, according to the number for ANR grants (5 ANR, 1 ANRS , Lyon Biopole, Mitzutani foundation for glycoscience), hence the group might be reinforced with postdoc recruitments.

The group has been involved in local development and technology transfer with the development of the microarray screening tool. This was supported by funding from the Lyon BioPole cluster (2008/2011).

The group leader is a recognised expert in glycobiology and is invited in local and European universities for lectures on either GAG, chemokines or SPR.

- Appreciation on the project

Their main projects are to investigate the heparan sulphate side of the interactions, to characterise heparan sulphate protein complexes at a structural level and to integrate structural and functional data at the cellular level. This fits in very well with the overall IBS strategy and shows a very broad integration of techniques, from chemistry to in vivo assays. It is backed-up by strong collaborations and relies on the technological development performed by the group. Overall, the project appears well structured and very clear. This latter aspect should thus be favoured.

- Conclusion

  - Overall appreciation

This is an excellent group, well focused on glycobiology. They have a very good productivity. Their strategy is very innovative and efficient, based on multidisciplinary approaches. They were able to set up key collaborations for securing all the ressources central to their biological project (organic chemistry, MS…). The project is well-thought and clear.

  - Strengths and opportunities

The group integrates a broad variety of approaches from chemistry to in vivo studies. The development of SPR technology (plasmon resonance chip) for glycan-protein interactions screening is a unique tool giving them a clear advantage.

  - Weaknesses and threats

The potential to develop the HIV inhibitor all the way to the clinic is probably quite remote but the molecule is likely to be an interesting biological tool for understanding HIV-1 entry.

  - Recommendations

Pursue collaborations as planned with structural biology groups within IBS to gain structural insights in heparan sulphate / protein interactions, as this would lead to important and novel biological information.

Team 2: Immune response to pathogens and altered-self

Team leader: Nicole THIELENS

- Staff members (on the basis of the application file submitted to the AERES)

	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)		6
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		5,4
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)		3
N7: Number of staff members with a HDR or a similar grade		6

- Appreciation on the results

This group, which gathers 3 teams already in the Institute, performs structure-function relationship studies on the soluble innate Immune proteins involved in the clearance of pathogens and damaged host cells. Experimental approaches include biochemistry, structural biology, genetic engineering and cell biology. Members of the group are in charge of 2 platforms of the Institute.

The group shows good productivity, with 65 publications over the period, 30 of which with first or last authorship. These articles were published in very good journals (*EMBO Rep., J. Immunol., J. Biol. Chem.*,…). The productivity of team 2 (Altered-self phagocytosis: recognition and signaling, 4 publications) and team 3 (Structural biology of the cellular immune response, 6 publications) was, however, not as high as that of team 1. Five PhD theses were defended.

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

The group has a high international visibility in the field of innate Immune proteins. Staff members of the group were invited to give 13 invited lectures in international congresses. They obtained 3 grants, including 2 ANR grants. The group has well-established national and international collaborations, as judged by the number of publications with authors from external laboratories.

- Appreciation on the strategy, governance and life of the research group

The 3 teams of the group share common interests in the innate immune response. They were already collaborating (team 1 with team 2, team 2 with team 3) in the previous organization of the Institute. They seem motivated to develop common projects in the next few years. It is also worth mentioning that the group interacts with many other teams of the Institute. A rotating representation at the direction committee of the Institute has been adopted. Two members of the group are lecturers at the University of Grenoble.

- Appreciation on the project

In the next 4 years, the group plans to study (i) the molecular interplay of the soluble proteins involved in the innate immune response (team 1), (ii) the recognition of apoptotic cells by the complement proteins (teams 1 and 2),

(iii) the intracellular phagocytosis signaling pathways (team 2 and 3) and (iv) the structural bases of the T cell response (team 3).

This project is especially important because the understanding of the innate immune response may lead to the development of new therapeutic or vaccinal strategies.

The previous solid experience of the group members in the study of the innate immune proteins should allow them to continue their important contribution to the understanding of the mechanisms of the innate immune response.

- Conclusion

  - Overall appreciation

This group is a well-though association between three teams with common interests and complementary expertises. All three teams showed a convincing desire to build a true common project, athough at present, only team 2 (altered-self phagocytosis) truly interacts with the other two.

  - Strengths and opportunities

mutidisciplinary approach, with the use many different techniques.

  - Weaknesses and threats

Risk of dispersion (teams 2 and 3).

  - Recommendations

The group should continue to favour common projects.

Team 3: Bacterial pathogenesis

Team leader: Andrea DESSEN

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		-
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		-
N6: Number of Ph.D. students (Form 2.7 of the application file)		1
N7: Number of staff members with a HDR or a similar grade		1

- Appreciation on the results

The Bacterial Pathogenesis group used X-ray crystallography to study the mechanisms of bacterial resistance to beta-lactam antibiotics and of secretion of virulence factors (type II and type III secretion systems). Noteworthy contributions included the determination of PBP protein structures leading to structure-based understanding of PBPs resistance to Beta-lactams and design of non-lactam inhibitors. Another important output was the structure of the *Pseudomonas aeruginosa* virulence factor PscF bound to its chaperones PscG ans PscE. Research of the group is internationally recognized.

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

The research group is internationally recognized from its work on structural biology of bacterial PBPs and secretion systems. It is highly attractive for foreign students and post-docs. The team leader gave 10 invited Conferences, including one at a Gordon Conference, since 2005. The group has an excellent national and international network of collaborators which proved to be very effective for raising European funds to carry out research on beta-lactam resistance. It has also well established collaborations to support the work on bacterial secretion systems. Extramural funding was raised from the EU, CEA, DGA and the Region Rhone-Alpes.

The head of the group was formerly associated to the team of Membrane Proteins (LPM). She published 14 manuscripts between 2005 and 2009 (1 Nature Chem Biol, 2 PNAS, 2 Structure...). In addition to some teaching activity on X-ray crystallography, she supervised 5 PhD students and 8 post-docs in the past 4 years.

- Appreciation on the strategy, governance and life of the research group

The group is well-structured which renders it competitive for risk-taking in new structural biology research projects. This is suitable to expand the research to important molecules of other bacterial secretion systems as proposed in the research project.

- Appreciation on the project

The project builds in present research themes and expands to type IV and type VI secretion systems. The group has the necessary expertise on X-ray cristallography to carry out competitive work in this enlarged field of research. The network of collaborative groups is very well-choosen to provide the genetics, biochemistry, bacterial

cell biology and pathogenesis studies necessary to support the structural biology work and its biological implications. It is a strong project that will very likely produce novel contributions for understanding bacterial pathogenesis and antibiotic resistance.

- Conclusion

  - Overall appreciation

This is a well focussed team producing very nice results on bacterial pathogenesis. The strategies are inventive and well conducted. The group leader is young and dynamic. Overall, a very promising group.

  - Strengths and opportunities

It is a well-structured group of X-ray crystallography with an enthusiastic leader. The project themes are timely for the general field of bacteriology and infection. The structural biology work is strongly supported by a network of interdisciplinary research including in-house, national, and international groups.

  - Weaknesses and threats

At the present time, the strategy is almost entirely based on X-ray crystallography. The project could benefit from other structural approaches available within IBS.

  - Recommendations :

The group has a growing interest on secretion systems which are large macromolecular assemblies. This goal recommends more intensive interaction with electron microscopy groups that can provide EM reconstructions of such large assemblies. Partnership with industry exploiting the team structural biology information for development of new antibiotics and to control infection by bacterial pathogens could add further impact to the research.

A stronger investment in the overall structural biology of a well-chosen secretion system could be a plus for outstanding achievements.

Team 4: Structure and function of *Streptococcus pneumoniae* surface proteins

Team leader: Thierry VERNET

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		1
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 (Form 2.2 and 2.4 of the application file)		2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		3
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		0
N6: Number of Ph.D. students (Form 2.7 of the application file)		1
N7: Number of staff members with a HDR or a similar grade		3

- Appreciation on the results

The Laboratoire Ingénierie Moléculaire (LIM) (future Structure and function of Streptoccocus pneumoniae surface proteins) has an excellent expertise on the molecular analysis of S. pneumoniae resistance to antibiotics. The team uses biochemistry, bacterial genetics and structural biology to understand pneumococcal resistance to ß-lactams. The strong collaboration with the LPM group (future Bacterial pathogenesis) led to major achievements on the high resolution structure of Penicillin-binding proteins (PBPs). Combination of the structural data with site-directed mutagenesis highlighted new determinants of PBPs resistance. The role of PBPs in peptidoglycan assembly led the team to study pneumococcal cell division focusing on two membrane associated membrane complexes. The promising biochemical results provide a solid basis for future research.

A second research theme is pneumococcal surface proteins that act as virulence factors for infection of humans. A rather diverse interest in zinc homeostasis, migration through extracellular matrix and pili assembly is pursued. The group runs the gene cloning platform ROBIOMOL where they provide in collaboration with the PX Therapeutics company, a service of cloning, mutagenesis, small-scale protein production and purification services. This platform is a central element of the IBS organisation. The PX therapeutics company (50 employees) was originally incubated in the laboratory based on the group leader expertise in recombinant protein production.

The group has very good scientific productivity. Its members published 29 research papers, frequently as first and/or last authors, in well ranked journals (J Mol. Biol, J. Biol. Chem., Mol. Microbiol.). Some of their structural collaborations have also led to first rank publications (PNAS).

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

The team's research on S pneumoniae has national and international recognition. The group leader gave three invited conferences in international meetings. During the last four years, six theses have been defended and two PhD students are currently in the group. Four postdocs were recruited on CEA funds, mostly coming from France, two postdocs collaborators are currently in the group.

The LIM was very successful in raising funds, which include grants from the EU, ANR, région Rhone-Alpes and RTRA FINOVI. In particular one young researcher of the group obtained a «jeune chercheuse/jeune chercheur» ANR grant.

The LIM has a well established interdisciplinary network across Europe. Their research is presently funded through the EU INTAFAR FP6 network.

- Appreciation on the strategy, governance and life of the research group

The group organization will be maintained in the future organisation of the IBS. It is a well-structured group whose permanent members have enough distinct expertise to tackle the different themes proposed in the research project. Their activity is well-integrated at the IBS, leading to productive intra-mural collaborations, being also supported by complementary national and international collaborations. Very good record of students and post-docs training.

The only assistant professor of the group is involved in full-time teaching activities, while other members of the team participate in courses in general biology, molecular biology and biochemistry at Grenoble' University.

- Appreciation on the project

The team will carry on with its strong research on the mechanism of ß-lactam resistance in S. pneumoniae focusing on PBPs structure/function. An important part of the project involves the virtual screening and chemical synthesis of compounds with antibiotic abilities within a collaborative EU-funded project. The search for other anti-pneumococcal targets justifies the interest of the group on surface proteins of the bacterium and assembly of its cell wall. This research orientation is also relevant for studies on the host/pneumococcus interaction. One potential concern is that the number of questions raised on the molecular basis of pathogenesis might be too diverse for in-depth studies. The research activities of the group are evolving in pertinent, highly competitive, domains. Its capacity to maintain and develop intra-mural, national and international collaborations provides a strong support for competitive progress.

- Conclusion

  - Overall appreciation

The group has a high expertise on pneumococcus surface proteins and their interactions. They have a strategic view of important questions on their research field, with the long term goal for new drugs development against the pathogen. Overall, a well structured research team.

  - Strengths and opportunities

This is a solid group on pneumococcal research supported by an effective collaborative network. They take namely advantage of the strong IBS structural biology resources. The RIOBIOMOL platform is a strength of the group and a key resource for IBS.

  - Weaknesses and threats

The research directions proposed might be too broad for detailed molecular analyses.

  - Recommendations

The group has a good medium and long term vision of the developments in their field, however, increased focus on the strong topics could be beneficial. Strong collaborations with other teams (e.g. Bacterial pathogenesis) should be continued.

Team 5: Viral Infection and Cancer

Team leader: Carlo PETOSA

- Staff members (on the basis of the application file submitted to the AERES)

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)	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	4
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2,8
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	-
N6: Number of Ph.D. students (Form 2.7 of the application file)	2
N7: Number of staff members with a HDR or a similar grade	2

- Appreciation on the results

The group on Viral Infection and Cancer resulted from the recent fusion of three teams. The Virology team studies the RNA genome-attached terminal protein VpG of potato virus Y, an intrinsically disordered protein that inhibits host cell translation, and the development of the adenovirus dodecahedron as a delivery system in animal models. The Cell Biology team has a long lasting interest in different key proteins for cell mitosis and chromosome partitioning (Aurora B kinase, Eg5...). The Virus Structural Biology Group that recently joined the IBS carried out high impact studies on the epigenetic silencing of the EBV virus, lytic cycle activation and chromatin remodelling.

The Virology team published 12 papers between 2005 et 2009 (Vaccine, PloS One, J Biol Chem...). The PI is coordinator of grants from AR, NATO, ANR and Rhone Alpes.

The Cell Biology team, formerly the Cytoskeleton Proteins team, published 11 papers and filed on patent. Evidence was provided that mitotic exit requires upregulation of phosphatase(s) activity(es) in addition to Cdk1 inactivation (J. Cell Biol publication). Their research is supported by grants from ANR, ANRS and ARC.

The Virus Structural Biology Group that recently joined the IBS published 7 papers since 2006 (Nature, Mol Cell, Proteins, PloS Pathogens...). The structure of the Epstein-Barr virus transcription factor Zta is of relevance to understand the switch from latency to lytic cycle of this virus (Mol Cell publication). The discovery of the molecular mechanism of recognition of histone modifications by Brdt was a major breakthrough to understand the histone read-out code (Nature publication). The group leader has co-organized 5 EMBO courses on the structural biology of macromolecular complexes. Several installation grants (ATIP from CNRS, ANR and Rhone-Alpes) to establish independent team at the IBS.

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

The group has complementary expertises but distinct research themes. Its attractiveness and impact is thus shaped by the features and projects of its individual teams. The Virology team has long lasting European interactions. It was also effective to attract extra-mural funding. However, its appeal was limited probably due to the small size of the research group and to the uncertainty on the strategy to ensure continuation of its activity in the long-term. The Cell Biology team has undergone several changes on its researchers composition during the past 4 years mainly due to the departure of three PIs. As a result of this reorganisation the team is presently composed of 2 permanent scientists and 3 technical staff. Its know-how on mitosis combined with imaging and flow cytometry expertise renders it

attractive for collaborations (essentially national, at present) and students training. The Virus Structural Biology Group became rapidly visible due to its high impact publications, it has attracted several post-docs. A European network of collaborations is well established.

- Appreciation on the strategy, governance and life of the research group

The Viral Infection and Cancer group has complementary expertises (virology, cell biology, structural biology). Common lab seminars and interest on nucleocytoplasmic transport brings some interaction within the group. However, the different teams appear to continue essentially their previous research subjects without defining major common research themes that would provide a strong added value to their association.

- Appreciation on the project

The Cell Biology team proposes new studies on the function of HBXIP on hepatitis B infection and the Structural Biology team will renew is interest on the nucleo–cytoplasmic transport of HIV-1 regulatory proteins. These research directions will increase the focus of the group on virus infection. The risk-taking of the Structural Biology team to tackle essential steps on the human viruses EBV and HIV multiplication cycles might be highly rewarding.

The teams have the necessary expertise to carry out the research proposed successfully. A major concern is the lack of unifying projects that fully exploit the complementary expertise of the teams.

- Conclusion

– Overall appreciation

Scientifically, this group has a strong track record and has produced high quality research in various aspects of virology and cell biology. The unity and central theme of the group has however appeared somewhat artificial. It has yet to demonstrate that it will be able to identify and develop common projects.

– Strengths and opportunities

The teams of the group have complementary expertise and are clearly competent in their respective fields. The scientific productivity is good. The leader of the group recently made some major contributions to structural virology that are internationally recognized. The research projects of individual teams build on the strong points of their previous research.

– Weaknesses and threats

The lack of synergy between the research projects of the teams. The current status of two of the team leaders is uncertain : one is emeritus and another one has yet to get a tenured position.

– Recommendations

It is strongly recommended that the teams built common research themes centered on the highest impact topics of the group in order to build a sustainable research group.

Team 6: Electron Microscopy

Team leader: Jorge NAVAZA / Guy SCHOEHN

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		-
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		-
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		3
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		-
N6: Number of Ph.D. students (Form 2.7 of the application file)		1
N7: Number of staff members with a HDR or a similar grade		2

- Appreciation on the results

This group is composed of two principal investigators, which are both of outstanding productivity in their field. The leader of this group is a senior person who has made major contributions to this field, mostly in the area of method development in the form of computer algorithms. The other PI is a structural biologist with an excellent productivity from his own research and numerous collaborations.

The senior team leader has published 14 publications during the last 5 years (1 Nature, 1 EMBO J, 1 Virology, 1 JMB…). The algorithmic developments that are behind the software packages that he produced are groundbreaking and enjoy outstanding visibility in the field. The second team leader has contributed to an excellent number of high-level publications (30 in the last 5 years: 2 JBC, 2 JMB, 3 JoVir, 3 PLoS, 1 Science, 2 Structure, 4 Virology, etc.). Given their small current staff size, the productivity of this unit is outstanding.

This group performs high-level electron microscopy research. Due to the high acquisition and maintenance costs of the required instrumentation, this group is expected to not only perform its own research (and possibly method development), but also to make this technology available to collaborators. This group is doing this in an extraordinarily good manner. The majority of IBS projects appear to collaborate with the electron microscopy unit, and thereby strongly benefit from the existence of this unit.

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

This group's PIs are regular speakers at international conferences, and (co-)organizers of national and international meetings. Their visibility is outstanding. The senior team leader has published the second most cited paper in chemistry in the previous decade. Their excellent reputation and the arrival of a top-of-the-line transmission electron microscope "Polara" leaves no doubt that this group would be able to recruit top-level members also in the future. Currently, however, there is a severe lack of staff that strongly limits this group's effectiveness (see below).

This group had success in rising funding, (EU, CNRS, HFSP, ANR, Rhone-Alpes…). The younger PI also raised the funding for the new instrument (2.5 MEu)

- Appreciation on the strategy, governance and life of the research group

This group maintains an excellently organized and maintained electron microscopy facility at the IBS. However, the fact that the younger PI has two appointments at the IBS and UVHCI and runs separate EM units in the two

institutions raises some concern. Merging the two units into one central PBS electron microscopy unit, to be located in the new IBS2 building, should reduce the required floor space, facilitate instrument maintenance and user training, and eliminate duplicated support infrastructure for the machines, thereby reducing costs.

This group has made major developments to the fields of XRD and cryo-EM of icosahedral particles. Some of these developments have successfully established themselves and became some of the most cited works in the field, while others (specifically icosahedral particle image processing) are strongly underused because of high computational requirements. Nevertheless, it is generally accepted in the field that the algorithms and software from this IBS electron microscopy unit is the strongest possible approach.

- Appreciation on the project

The current plan to implement correlative light and electron microscopy (CLEM) is an excellent choice; the PIs are here following the global development. CLEM combines electron tomography with fluorescence light microscopy, and thereby enables significant insight in cell biology applications.

- Conclusion

  - Overall appreciation

Already before the arrival of the new microscope, this unit is one of France's best-known cryo-EM units. The arrival of the new top-of-the-line instrument will allow this unit to further establish itself as a national lighthouse in cryo-EM.

  - Strengths and opportunities

Even with the upcoming retirement of the senior PI, this unit is fortunate to have a top-level younger cryo-EM expert, who is likely able to maintain the reputation of this unit in the field. The new Polara instrument will solidify this unit's position at the forefront of the cryo-EM field.

  - Weaknesses and threats

This panel sees a concern in the upcoming retirement of the senior PI of this unit. The already critically small staff would lose another member. The future scientific leadership of this unit might be well resolved with the younger PI from within this unit. However, reinforcing the EM group should be a major priority of IBS.

  - Recommendations

The committee suggests the development of a plan for funding the maintenance costs of the Polara. In addition, the modernization of the available software package could be realized within a two-year project of a software developer.

Team 7: Adaptation to Extreme Conditions and large molecular assemblies

Team leader: Bruno FRANZETTI

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		-
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 (Form 2.2 and 2.4 of the application file)		1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		4
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		-
N6: Number of Ph.D. students (Form 2.7 of the application file)		2
N7: Number of staff members with a HDR or a similar grade		4

- Appreciation on the results

This group focuses on the molecular adaptation to extreme conditions (high salt, pressure and temperatures). It federates two teams : a structural biology and a biochemistry group. The teams have purified and solved the structures of a number of large extremophile protein complexes with enzymatic activities using X-ray crystallography. The group aims to understand the adaptation of cells and enzymes to extreme physico-chemical conditions. To this end it has undertaken the characterization of the cell proteolytic machinery and of the basic mechanisms of protein folding and association under extreme conditions. The latter objective might lead to the design of proteins with properties of interest for industry.

In its new form, the group generated 34 publications over the last 4 years (1 PNAS, 1 JBC, 3 Biochemistry, 1 Mol. Microbiol., 2 Angew Chem.). Two PhD theses were defended over the evaluation period.

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

The group has 5 active grants (3 ANR, one of which is coordinated by the group), one CNRS grant (coordinated by the group) and one Eurocore grant. The group established numerous and fruitful collaborations both with research groups and platforms within the institute and with French and European teams. The group also appears well integrated into the extremophiles community and is a member of the national GDR “Deep Sea” and the European network “Extremophiles Research in Europe”. The group interacts with the Ifremer for sample collections. Six contributions to international conferences were presented.

- Appreciation on the strategy, governance and life of the research group

The complementarities within the group are high and the biochemistry and structural biology competences very well suited. The group is very well integrated within the institute and the local environment with numerous interactions with internal and external (ESRF and ILL) partners.

- Appreciation on the project

The group aims to develop new methodological approaches to document protein and proteome evolution under extreme conditions (e.g. high pressure crystallography). The group is also involved in developing for the community

anomalous X-ray scattering in the presence of lanthanoids. There is a feeling that the group should develop a platform for the expression, purification, biochemical and structural characterization of the protein complexes the group studies under extreme conditions. Indeed, pressure, temperature and the ionic strength impact the folding, protein-protein interactions and activities of the macromolecules the group studies. It is therefore critical when one gets involved in characterizing the interactome, in particular multisubunit complexes such as the peptidasome, to avoid as much as possible recombinant protein and perform the studies under relevant extreme conditions. The committee has expressed both interest and doubts regarding the strategy for "resurrecting" ancestral proteins: although very appealing in principle, the multiparametric pressure of evolution on protein folds and properties could lead to difficult to analyse results.

- Conclusion

  - Overall appreciation

A research group with an original research project, at the heart of the « Limits of Life » strategic axis. Very well integrated within the French networks working on these topics.

  - Strengths and opportunities

The group has unravelled some truly unique biological systems on which they have a real edge. The high pressure crystallography work developped in the group is strong and has allowed the group to set-up numerous interesting collaborations.

  - Weaknesses and threats

The scientific output is good, but the share of publications in which the group is the lead contributor is not as high as it could be.

  - Recommendations

Build on the group strengths, i.e. the study of these truly original archeal complexes and the fine crystallography developments to improve their publication output in terms of first or last authorship. Investigate the feasibility of analysing the protein complexes and their interactions in conditions closer to their physiological environment.

Team 8: Metalloproteins

Team leader: Juan FONTECILLA

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		8
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		2,1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		-
N6: Number of Ph.D. students (Form 2.7 of the application file)		2
N7: Number of staff members with a HDR or a similar grade		4

- Appreciation on the results

This group consists of two teams. **Team I** "Heavy metal transmembrane signaling" investigates extra-cytoplasmic functions (ECF) performed by different bacterial proteins. They contain nickel and initiate responses to stress by triggering the expression of specific genes. Among the ECF system is the CnrYXH protein complex (**c**obalt and **n**ickel **r**esistance) studied by this team that is of interest for medical, environmental and biotechnological purposes.

Team II "Structure / function relationships of metalloproteins" studies enzymes containing the iron-sulfur cluster Fe_4S_4 that convert S-adenosyl-methionine to the 5'-deoxyadenosyl radical whose chemical reactions are investigated, *i. e.* the maturation of active sites of the enzymes hydrogenase and nitrogenase, among others. Of interest are also bacterial hydrogenases that require Ni or Fe or both and might be of importance in the production of the energy carrier hydrogen by sunlight when they are fused to protein subunits of photosystem I of photosynthetic bacteria like *Synechocystis*. This team studies the nickel transport across membranes in microorganisms by ABC (**A**TP **B**inding **C**assette) transporters such as the NikABCDE complex of which the structure of NikA has been determined and the nickel trafficking in the human pathogen *Heliobacter pylori.*

The mechanisms of metalloproteins and the design of artificial metalloenzymes for asymmetric catalysis are supported by theoretical studies using molecular dynamics and quantum mechanics.

The number of publications from this group is high (total of 57 over the period 2005-2009) in very good to outstanding international journals (2 papers in *Science*, 1 invited review in *Nature*, 1 in *Nature Chem. Biol.*, 8 in JACS,..). In addition, book chapters have been published, and 4 patents have been filed. 1 PhD thesis has been defended.

- Assessment of the impact, the attractiveness of the research group and of the quality of its links with international, national and local partners

The quality and stability of the partnerships of this group is excellent (cutting edge). The studies on metalloproteins are complementary and of highest quality. The research carried out by the teams is very well visible and has a high impact in biochemistry. Both PIs of this project have been invited as speakers to a number of international conferences. Their ability to recruit top-level scientists is very good, because both PIs are highly visible in France and abroad due to their excellent publications. This group is well funded by the IBS and extramural grants (6 ANR grants in 2005-2009). Both PIs collaborate nationally and internationally with several groups in Belgium, Spain and England.

- Appreciation on the project

The project has furthered our understanding of the function of metal ions in biology. The work on hydrogenases might lead to the sunlight-driven production of hydrogen to solve future energy problems, especially if hydrogenases are coupled to photosystem I. The unit is very well organized, with good flow of communication. The group's relevance of initiatives is excellent, and the teams are engaged in several national and international scientific coordinations. The PIs have described in their proposals far-reaching and visionary future research. Their project on the understanding of how complex metallic active sites are assembled is a fundamental biological question and they are one of the few groups in the world to be able to address it.

- Conclusion

  - Overall appreciation

The projects are very original, the risks are well balanced. As in the past, excellent results are expected from this group in the future.

  - Strengths and opportunities

The group is very dynamic, addresses far-reaching biological questions and has a very strong international visibility (as evidenced by an invitation to write a review in Nature in 2009). They have also developed a highly efficient set-up for producing protein and performing structural biology under anaerobic conditions.

  - Weaknesses and threats

The charismatic group leader is due to retire at the end of the next "quadriennal". Solutions for continued existence of this productive group should be thought of during this upcoming period.

  - Recommendations

Improving the convergence between the two teams would be a plus, possibly by investigating common interests and developping common tools for metalloprotein characterization.

Team 9: Synchrotron group

Team leader: Jean-Luc FERRER

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		-
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 (Form 2.2 and 2.4 of the application file)		1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		6,25
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		-
N6: Number of Ph.D. students (Form 2.7 of the application file)		1
N7: Number of staff members with a HDR or a similar grade		2

- Appreciation on the results

This is a highly productive group that underpins virtually all of the structural work at the IBS. It is composed of a team that maintains the current beamline and a research group that is developing unique technology for the beamline and in furtherance of new IBS initiatives in drug development. It has 5 active grants. It runs the beamline FIP-BM30A at the ESRF and has made important contributions to the development of robotics that have dramatically improved its ease of use and overall productivity. While some of the developments recapitulate advances elsewhere, some – notably G-Rob – is unique. The impact of the group is seen in the number and quality of structures coming from the entire IBS. Its role in local and national work of high quality is clear. Many of the crystallographers at IBS have commented that a sizable advantage they enjoy in the competitive world of structural biology is the proximity, the quality, the accessibility, and the ease of use of the beamline. The number and quality of the publications of the group as main authors are modest, the exception being the structural survey of the plant phenylpropanoids which is of the highest quality. It must be stressed that without the contributions of this group the excellent publications of the rest of IBS would be far fewer. As collaborators they appear on about 30 publications/year, in journals of high quality.

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

The group and the beamline attract users from IBS, from Grenoble, from France and from other parts of the world in large part because of its productivity. The team leader is not as visible outside of France as he could be, but that may be a consequence of the all-consuming job to keep the line productive and the users contented. The principal investigator has a solid network of partners in the biological community in and around Grenoble who clearly prefer to work at the team's beamline because of the high quality of the service it renders, and because the group leader has the capacity to make important contributions to difficult experimental challenges.

- Appreciation on the strategy, governance and life of the research group

The team is organizationally solid, as evidenced by their high productivity. The high quality of publications coming from work carried out on the beamline cannot be achieved without a strong organizational talent and good teamwork. Essentially the team members touch the scientific lives of all of the students, post-docs and researchers who come to the line; giving a high impact to the teaching efforts of the team. The team itself has two graduate students. The group juggles well the need to keep the beamline up and running while finding time for significant

technology development. Its robotics developments are challenging and have the potential to make significant improvements in the quality and quantity of diffraction work executed on the line.

- Appreciation on the project

The panel was uniformly concerned that, in what appeared to be an effort by the group to become more biologically "relevant", the projects to incorporate cell based assays and in silico screening were proposed as future directions ; these were efforts not well suited to the talents of the group and would significantly dilute the synchrotron efforts. There was little enthusiasm to see the team move in either of those directions. However, the development of crystallization plates that can be put directly into the beam, and the development of the G-Rob and other robots to aid in druggable target screening efforts, is a direction towards more biological relevance that the panel could strongly support. In addition the work on high pressure crystallography can become very important when done in the context of the « Limits of Life » work on extremophiles, and in concert with efforts on the part of computational modelers to understand more fully the energy landscape of the protein folding problem.

- Conclusion

  - Overall appreciation

The group is strong, and should continue to play to its strengths: delivery of quality beam time, development of new tools to speed data measurement and the integration of new technologies to identify lead compounds for potential drug development via in plate and on robot (G-Rob) screening of crystals.

  - Strengths and opportunities

The clear strength of the group is in providing a well operated beamline to IBS structural scientists.

  - Weaknesses and threats

The committee is concerned about a potential dilution of efforts which is risked with the proposed development of in silico identification of lead compounds and in cell-based assays.

  - Recommendations

The committee commends the group's efforts to become more biologically oriented, but urge the group to put its efforts into areas for which they already have demonstrated high competency, namely in the development of robotics for freezing crystals, getting crystallization plates in front of the X-ray beam, and in developing G-Rob further.

Team 10: NMR

Team leader: Bernhard BRUTSCHER

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		1
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 (Form 2.2 and 2.4 of the application file)		2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		2,8
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		-
N6: Number of Ph.D. students (Form 2.7 of the application file)		1
N7: Number of staff members with a HDR or a similar grade		6

- Appreciation on the results

The NMR group is one of the largest IBS groups, with 7 permanent scientists and 3 engineers. It operates a facility comprising three high field NMR spectrometers (1 x 800 MHz and 2 x 600 MHz) two of which are fitted with cryoprobes and one of which is equiped with a solid state-MAS probe. This platform has been recognised as part of the CNRS NMR '*très grande infrastructure de recherche*' and also as an EU facility (EU-NMR).

The activity of the NMR group is twofold, with a focus on methodological development and also tackling novel and challenging biological projects : very large macromolecular assemblies, viral proteins, RNA-protein complexes, bacterial cell wall. They have thus obtained extensive NMR assignments on very large proteins such as the TET archaeal protease, a 500 Kda complex, which is a real «tour-de-force» achievement. On the methodological side, they have developed a combination of original methods for ultrafast NMR (SOFAST) spectroscopy which are now being widely used in the NMR community as it is the only technique which is both rapid and sensitive.

Their scientific output in terms of publications is high-standard and steady, with 62 papers since 2005, 40 of which with senior authorship (1 NSMB, 3 PNAS, 7 JACS, 2 JBC…). Their 2005 JACS paper on the SOFAST spectroscopy has attracted 70 citations in the past four years.

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

The group has a strong visibility and success at both national and international levels. Collectively, they have been invited to give 25 talks at international conferences. One of the younger scientist has obtained the CNRS Paoletti prize and also the bronze medal in 2008. Since 2005, the NMR group has attracted 1 HFSP, 4 ANR and 1 EU FP7 grants. This has allowed them to hire a steady number of both French and foreign post-docs (5 are currently in the group).

Within the framework of the EU-NMR network, they provide national and international access to the NMR facility (20 days/year) which allows them to initiate some collaborations. They have a continued collaboration with the Weitzmann institute for fast NMR spectroscopy and with the Grenoble EMBL outstation for viral proteins.

- Appreciation on the strategy, governance and life of the research group

The NMR group operates with a rather original «democratic» yet efficient organisation, with a rotating governance and no-real sub-teams, which is unusual given the large size of the group (almost 20 persons, including post-docs, students and grant-funded technical staff). Rather, they form project-based temporary associations where

they join forces. The specificities of the scientists are varied, from theoretical aspects to biology-oriented projects. This combination is highly efficient, as the NMR methodologists are pushed forward by the needs of the biological spectroscopists, while in return, the latter benefit from the progresses made by the former.

- Appreciation on the project

The projects on transient phenomena, large macromolecular assemblies («nanomachines») and bacterial cell wall are both ambitious and interesting. They address difficult but very relevant biological questions, which also connect to the subjects of IBS groups (bacterial antibiotic resistance, macromolecule dynamics...). The miRNA project falls within a highly competitive area and appears less connected the rest. Many of these projects will however benefit from the tools they have already developed (isotope labeling strategies).

- Conclusion

  - Overall appreciation

The group is both very active and dynamic, one of the most innovative in the field, with strong synergies both internal and external.

  - Strengths and opportunities

Continued collaboration with other IBS groups is a strong point and should be developed. It would help to capitalise on methodological progresses and build a more integrated biological theme. Overall this could allow the group to make the couple of major breakthroughs required to reach the top international level.

  - Weaknesses and threats

Several of the projects are risky, either because they are very competitive (e.g. micro RNA) and/or because there are serious technical hurdles.

  - Recommendations

Pushing NMR limits both in terms of methodology and objects of study should be continued. Contingency plans should be discussed and envisioned whenever required.

Team 11: Protein dynamics and flexibility

Team leader: Martin BLACKLEDGE

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		-
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		-
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		-
N6: Number of Ph.D. students (Form 2.7 of the application file)		1
N7: Number of staff members with a HDR or a similar grade		1

- Appreciation on the results

This group has been established as spin-off of the NMR group in 2007. It is focused on studies on protein motion and flexibility, with an emphasis on intrinsically disordered proteins. They use a combination of NMR, MD simulations and other biophysical techniques. The group has only two permanent scientists, the second of whom was just recruited in 2009.

Although small, this group has been outstandingly productive, with 52 publications since 2005, 32 with corresponding authorship, including 2 PNAS, 2 Angew. Chem. and 8 JACS as senior author. The quality is constantly high, with established collaborations with NMR groups in Basel (Biozentrum), MPI Göttingen and Lyon and the SAXS group at EMBL-Hamburg, in addition to local IBS interactions.

The work of this group is highly innovative and their approach to the description of ensemble structures of disordered proteins is a major advance in the field, which uniquely combines modelisation and experimental approaches. As intrinsically disordered proteins are increasingly recognised as important cellular players, this is truly a breakthrough which opens the way to the exploration of unchartered territory.

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

This team, despite its small size, has a very strong international visibility. This can be seen from its publications, which were singled out in several «news and views» and «editor's choice» in both Nature and Science. 9 papers were also selected by the Faculty of 1000 since 2005.

The team leader has chaired a Gordon conference on biological NMR in 2006, is an editor of the Biophysical journal and has been invited 41 times at international conferences. He has also been instructor at 10 international schools and workshops (7 EMBO courses).

The group has also been efficient at securing grants and fellowships, for over 1,5 M€ since 2005 (2 ANR, 1 EU FP6, 2 EMBO Fellowships...).

- Appreciation on the strategy, governance and life of the research group

The group is small and mostly thrives on the charismatic leadership of its PI, which could be considered as a fragility. The recent recruitment of a junior scientist is good as it will secure know-how and allow to share the supervision workload.

- Appreciation on the project

The projects really focus on major current issues at the forefront of the field : protein dynamics and molecular recognition, atomic description of large disordered proteins (tau), order to disorder transitions... On the one hand, this may seem over-ambitious given the size of the group, on another hand, given its past track record, it could very well be feasible. One of the strong points of the projects is the network of international collaborations with excellent groups which will provide the complementary expertise in NMR, SAXS, computation or biochemistry. The group intends to develop its wet lab capacities, which is good, it should do so with the help of IBS know-how.

- Conclusion

  - Overall appreciation

Excellent group, working on innovative and ambitious projects, with an outstanding scientific productivity and a strong international visibility.

  - Strengths and opportunities

The strong points are the integration of both NMR, computation and other biophysical approaches, the ambition to tackle complex biological systems and the creativity of the principal investigator.

  - Weaknesses and threats

The small size of the group which is still strongly dependent on its PI

  - Recommendations

This team has strong collaborations outside the IBS, but could possibly increase its local collaboration inside the Institute, as several other groups could certainly benefit from the truly unique know-how of this team.

Team 12: Dynamics and kinetics of molecular processes

Team leader: Martin WEIK

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		7
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		-
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		-
N6: Number of Ph.D. students (Form 2.7 of the application file)		4
N7: Number of staff members with a HDR or a similar grade		4

- Appreciation on the results

This group federates 4 teams with expertise in crystallography, optical spectroscopy, fluorescent proteins properties, neutron spectroscopy and computational methods for understanding of dynamic aspects of biological macromolecules in a cellular context. Aspects such as structural protein dynamics in aging and antibiotic resistance are actively studied. Insights into structural protein dynamics are translated into the design of drugs. Protein damages by reactive oxygen species are also studied. The reactivity and dynamics of proteins at sub-angstrom resolution are documented using both experimental (neutron scattering) and theoretical (modeling and simulation) approaches. Finally, the structural dynamics of fluorescent/photosensitive proteins is documented for their use for the tracking of single molecules by super-resolution light microscopy. A number of unique highly competitive tools and facilities ranging from the open source “pdynamo” software to the high-pressure neutron scattering cell and photoactive proteins for single molecules tracking are developed within the group.

In its present form, the group generated 101 publications over the last 4 years, a significant number of which in very high impact factor journals (1 Science, 4 PNAS, 2 EMBO J). Six PhD thesis were defended over the evaluation period.

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

The group has numerous active grants (ANR, EU FP6 & FP7, DGA, CEA…) accounting for 2.3 Million €, five of which are coordinated by the group. It has established numerous and fruitful collaborations within the IBS. It also has very close interactions with the iRTSV in Grenoble and with national and international teams. The complementarities within the group are high and could further be strengthened by a dedicated use of the neutron scattering activity to document the biological models.

The group has a very good national and international visibility, with numerous invitations to international conferences (57 communications). The tools developed by all the teams within the group are critical for the institute and have major impact within the field (the “cryobench platform” for kinetic crystallography studies, molecular modeling with the freeware “pdynamo”, incoherent neutron scattering for dynamic and elastic measurements and the dynamics of fluorescent proteins and their use for single particle imaging in vivo). The neutron scattering line developed by one of the teams is unique for documenting the internal dynamics of proteins at the highest resolution. The number of PhD students reflects the visibility and attractivity of the group.

- Appreciation on the strategy, governance and life of the research group

The complementarities within the group are high. There is a feeling that the developments made on the neutron scattering line (IN13) at ILL will allow (i) the group to populate the field of sub-angstrom dynamic structural biology and (ii) the institute to make breakthroughs in the "limits of life" priority axis. This will have significant impact on the scientific production of the team running this line for the community. In contrast, while methodologically challenging, the energy-consuming project aiming at documenting the stiffness of cultured cells during apoptotic events appears of limited interest. The team heavily involved in the design and characterization of fluorescent/photosensitive proteins structural dynamics is well positioned to develop probes for tracking single molecules by super-resolution light microscopy. This provides a clear strategic advantage for the institute within this emerging field. The benefit to risk ratio of the methodology developed by this team needs being oriented toward the institute benefits. This can easily be done by establishing tight interactions with other teams studying the dynamics of cell biology processes. Collaborative work with the IBS teams investigating protein folding under extreme conditions might be also of significant interest for the design of novel, non oligomeric fluorescent proteins.

- Appreciation on the project

The integrated approach proposed by this group is cutting-edge and very well suited to characterize dynamic and kinetic aspects of molecular processes. The cryobench platform that allows X-ray diffraction, fluorescence, UV/Visible and Raman spectroscopy measurements together with neutron scattering measurements and their skills in molecular modeling and simulations should allow the characterization of molecular events at an unprecedented resolution. The translation of the group's know-how into the design of improved fluorescent/photosensitive proteins and their use to document cellular events at high-resolution light microscopy is sensible.

- Conclusion

– Overall appreciation

The complementarities within this group are perfectly suited for its objectives. The competences within the group and its size are adequate.

– Strengths and opportunities

The association of these teams into a group brings together complementary expertise and cements previous collaborations, providing an added-value to this re-organization. The group benefits from unique know-how in the structural dynamics of proteins, molecular modeling and simulation, the use of elastic incoherent neutron scattering and that of fluorescent/photosensitive proteins. The cryo-bench platform under development will undoubtably allow the group to tackle issues of high interest, establish numerous interactions within the institute and play a key role within national and European networks.

– Weaknesses and threats

The know-how in elastic incoherent neutron scattering measurements should be better focused to projects that exploit best its potential for the documentation of dynamic and kinetic molecular processes (e.g. conformational changes, dynamics and motion…).

– Recommendations

Further reinforce the transversal research between the teams of the group on their strongest biological systems. The expertise on structural dynamics of fluorescent/ photosensitive proteins could, in addition of being devoted to biological issues studied by a local laboratory (iRTSV), be further opened to internal collaborations. This would highly benefit the institute but would also require reinforcement of the team personnel.

Team 13: Membrane transporters

Team leader: Valentin GORDELIY

- Staff members (on the basis of the application file submitted to the AERES)

	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)		1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		1,3
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		2
N6: Number of Ph.D. students (Form 2.7 of the application file)		5
N7: Number of staff members with a HDR or a similar grade		2

- Appreciation on the results

This group is formed by two PIs, who are both interested in the structure and function of transmembrane proteins, and who apply similar methods.

Both groups study a number of membrane protein structures of high importance. These proteins are among the most important target proteins in pharmaceutical research, and include mitochondrial carriers, transporters, gap junctions and receptors, including GPCRs. This group is also at the forefront of membrane protein crystallization technology, a very complex but important field. They have further advanced the lipid cubic phase *in meso* crystallization method. This led to the genesis of extremely large and well-ordered (world-record setting resolution) crystals of a seven-transmembrane helix protein, which is likely to enable investigations by neutron diffraction. This would lead to a major break-through in the understanding of the mechanism of these proteins.

Both groups have a strong publication record (24 publications since 2005, excluding the articles from the team leader prior to its arrival at IBS : 1 TIBS, 1 Ann. Rev. Biochem, 1 JACS, 1 Biophys J., 2 PLoS One, 4 Biochemistry… The new team leader also has a 2006 *Nature* paper from before his arrival at IBS), the PIs are regularly invited speakers at international meetings, and have well-funded research programs, including EU FP6 and FP7, ANRS, ANR, DFG (Germany), BMBF (Germany), RMES (Russia), and CIBLE grants.

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

One PI obtained the CNRS silver medal (2005), chairs the French Membrane Protein GDR and is a member of major scientific advisory boards (e.g. ANR steering committee, CNRS, ENS-Paris, ENS-Lyon and IBISA). The team leader obtained an ANR “Chaire d’excellence sénior” 2008, the German “Outstanding Scientist” in 2006, and is co-responsible for the CEA (IBS, France) – HGF (FZJ, Germany) 5.1 specific agreement and has a second appointment as Professor at a German university. Both groups run active research programs with 7 PhD students and 1 postdoc. These PIs are well networked throughout Europe, and participate in several large funding networks (EU FP6, FP7).

- Appreciation on the strategy, governance and life of the research group

The converging research interests of the two PIs reflect in the harmonious functioning of the group. Method development to improve the efficiency and quality of membrane protein crystallization by in meso technology is progressing well, and provided world-record quality results.

- Appreciation on the project

Structure determination of membrane proteins remains a challenging method, where despite massive funding investment throughout the world, only very few labs were actually successful in obtaining high-resolution structural information on these most-important biological proteins. This IBS group is one of the most successful groups in this field, and in addition they have advanced the crystallization technology, to lead to better-ordered lipid-containing 3D crystals from less sample volume. The lack of the availability of a high-end UV light microscope to localize 3D crystals in the in meso phase is surprising. Investment into such an instrument appears reasonable, if the PIs were interested.

Extension of their work from "classic" membrane proteins to two-membrane spanning gap junctions, and planning to further expand their research focus from the molecular level to the tissue level, is a challenging and fascinating project. Given the past strong track record of these groups, this project appears feasible.

- Conclusion

  - Overall appreciation

This is a very strong group with homogeneous interests and an excellent balance between biologically oriented research, method development, application of world-record technology to important target proteins, and the inclusion of new and challenging target systems to study.

  - Strengths and opportunities

This group is combining expert knowledge in in meso membrane protein crystallization with an ideal environment (proximity to ESRF).

  - Weaknesses and threats

The « two-membrane » spanning gap-junction protein project appears daunting and in its present stage is still very sketchy.

  - Recommendations

Institute-support to fund an UV microscope might be considered

Team 14: Membrane and Pathogens

Team leader: Franck FIESCHI

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		1
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 (Form 2.2 and 2.4 of the application file)		2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		4,3
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		-
N6: Number of Ph.D. students (Form 2.7 of the application file)		3
N7: Number of staff members with a HDR or a similar grade		4

- Appreciation on the results of the group

This group consists of three teams with different yet related focuses associated to the "Membrane Proteins" strategic axis. **Team I** is engaged in the synthesis of novel detergents (surfactants and amphiphilic polymers) for the preparation of membrane proteins and their crystallization. Since this is of interest to many researchers of IBS, team I is associated with several other teams, in particular with team III of this group. In addition, team I studies structures of proteins related to virulence and human pathogenicity using X-ray crystallography, small angle neutron scattering, and electron microscopy. **Team II** is investigating the structures of membrane proteins like the neutrophilic NADPH oxidase complex and C-type lectin receptors. In addition, they are engaged in structural studies of proteins CCR5 and CXCR4 that interact with and recruit human immunodeficiency virus (HIV-1) and are consequently of major medical interest. Team II is also engaged in *in vitro* synthesis of membrane proteins and is involved in setting up the Membrane Protein Purification Platform (MP_3). **Team III** focuses on proteins that use ATP or GTP to carry out different reactions. Of interest are transporters of the ATP binding cassette (ABC) type like BmrA and YheI/YheH and the highly conserved bacterial GTPases YphC and YsxC that interact with ribosomes.

Over the period, the three teams contributed to 59 papers in international journals (1 *Nature Protoc.*, 3 *Langmuir*, 2 *Biophys. J.*, 7 *J. Biol. Chem.*, 8 *Biochemistry*…), 27 of which with first or last authorship. They also filed 1 patent. 3 theses were defended. The quality of the partnership is very good, the individual teams are complementary in their interests and work.

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

All three team leaders are supported by French grants (5 grants from ANR, 2 from ANRS, 1 from Sidaction,…) and two have in addition EU grants and industrial contracts, one has a Bill and Melinda Gates grant. All three team leaders have collaborations in France and abroad (Argentina, Spain, Italy, USA, Canada, Israel). The development of novel detergents for the purification and crystallization of membrane proteins is also of interest to other groups in the IBS as well as for academic and industrial researchers.

- Appreciation on the strategy, governance and life of the research group

The group is well organized and covers the chemical synthesis of novel detergents, their testing for membrane protein purification, biophysical studies and drug development. Their internal and external communication is well documented.

The initiatives of this group are broad, from the development of novel detergents to their application in the preparation and crystallization of different membrane proteins. The structures of drug transporters and of membrane proteins interacting with HIV-1 are of medical interest. Possible risks appear to be well-balanced.

One of the team leaders is Professor at the UJF Grenoble, one lectures to Ph.D. students on membrane transporters and one teaches at UJF Grenoble, at ENS Paris and at Toulouse, and participates in research courses at HERCULES, IMABIO, GFCC, EMBO.

- Appreciation on the project

The group has conceived a long-term scientific project from the synthesis of novel detergents to the structure analysis of different membrane proteins that are of pharmaceutical interest. The teams are well funded, their equipment is state-of-the-art. The research outlined by the group is highly original and of interest to other members of IBS that are interested in membrane proteins. The aims are ambitious but possible risks are manageable and positive results are expected.

- Conclusion

  - Overall appreciation

This is a solid and sound proposal with above average aims and expectations. The synthesis of novel detergents is both of academic and industrial importance and the elucidation of the envisaged protein structures is of pharmaceutical interest.

  - Strengths and opportunities

Complementary groups with converging interests. The common focus on using novel detergents for crystallisation/solubilisation is a plus which could benefit several other groups within the “membrane proteins” strategic axis

  - Weaknesses and threats

As very often for structural biology studies of membrane proteins, several of the projects are still quite risky and have yet to yield functional proteins and/or diffraction quality crystals.

  - Recommendations

Contingency plans should be thought of in case some of the projects fail to yield results. Possibly a refocusing on the most successful ones could improve the overall efficiency of the group.

Team 15: Channels

Team leader: Michel VIVAUDOU

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		-
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		-
N6: Number of Ph.D. students (Form 2.7 of the application file)		-
N7: Number of staff members with a HDR or a similar grade		1

- Appreciation on the results

This group, already in Grenoble, joined the IBS in 2007. Members of this group develop two major research topics: the characterization of the structure-function relationships of the ATP-sensitive potassium channel and the design of ion channel-based bioreceptors for the study of receptors.

Over the period, the group published 9 papers, 4 of which with first or last authorship of a group member. Two PhD theses were defended.

The development of a very clever idea deserves a special mention. The members of this group showed that the electrical conduction properties of the pore-forming protein Kir2.6 can be controlled by the binding of a ligand to a receptor genetically fused to Kir2.6. The proof-of-concept was established with two proteins of the GPCR (G-protein coupled receptors) family. This result, which opens very promising perspectives for the pharmaceutical screening and biodetection, led to a publication in *Nature Nanotech*. and to a patent application.

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

The result on the coupling between a channel and a receptor had a high impact, as evidenced by a `news and views` in Nature Nanotech. The team leader obtained 4 grants, including one from the EU and one from ANR. In 2009, a young scientist, recruited by the CNRS, joined the group.

- Appreciation on the strategy, governance and life of the research unit

The scientific activity of the group is well-balanced, with a good compromise between safe and risky projects and a good compromise between fundamental and biotechnological research.

- Appreciation on the project

The projects of the group include (i) molecular physiology studies on the K-ATP channels, (ii) the development of ion channel-coupled receptors and (iii) the characterization of mitochondrial transport systems, in particular by developing nanodroplet-based artificial bilayers. A longer-term objective is the crystallization of the entire SUR/Kir2.6 K-ATP channel.

The latter project is ambitious. Success would constitute an important breakthrough because the two components of the K-ATP channel belong to protein families which are crucial for human health and disease. However, the project is also risky.

The development on the coupling between receptors and channels (or transporters) is very promising, with many potential applications in fundamental research and nanotechnology.

- Conclusion

  - Overall appreciation

The group performs original research, with many potential applications.

  - Strengths and opportunities

The mutidisciplinary of the approaches is a strength and their technical expertise in techniques which are unique within IBS (e.g. patch clamp) is important for the whole Institute.

  - Weaknesses and threats

The project on the nanodroplets less convincing than the other ones, at least in its present stage

  - Recommendations

Further developments based on the exploitation of the ion channel-receptor technology are highly recommended.

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

Nom de l'équipe : PROTEIN-GAG INTERACTIONS

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

Nom de l'équipe :IMMUNE RESPONSE TO PATHOGENS AND ALTERED-SELF

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

Nom de l'équipe : BACTERIAL PATHOGENESIS

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

Nom de l'équipe : STRUCTURE AND FONCTION OF *STREPTOCOCCUS PNEUMONIAE* SURFACE PROTEINS

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

Nom de l'équipe : VIRAL INFECTION AND CANCER

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

Nom de l'équipe : ELECTRON MICROSCOPY

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

Nom de l'équipe : ADAPTATION TO EXTREMES CONDITIONS AND LARGE MOLECULAR ASSEMBLIES

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

Nom de l'équipe : SYNCHROTRON GROUP

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

Nom de l'équipe : NMR

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

Nom de l'équipe : METALLOPROTEINS

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

Nom de l'équipe : PROTEIN DYNAMICS AND FLEXIBILITY

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

Nom de l'équipe : DYNAMICS AND KINETICS OF MOLECULAR PROCESSES

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

Nom de l'équipe : MEMBRANE TRANSPORTERS

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

Nom de l'équipe : MEMBRANE AND PATHOGENS

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

Nom de l'équipe : IONIC CHANELS

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

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L'Administrateur Général

Monsieur Pierre GLORIEUX
Directeur de la section des Unités de recherche

AERES
20, rue Vivienne
75002 PARIS

Saclay, le 07 mai 2010

N/Réf. : DPg/AN/np/2010-134

Objet : Observations du CEA sur le rapport d'évaluation de l'« Institut de Biologie Structurale » (IBS)

Monsieur le Directeur,

Je remercie tout d'abord l'AERES pour la qualité du rapport d'évaluation sur l'activité de l'« Institut de Biologie Structurale » et pour la pertinence des recommandations qui ont été faites.

En tant qu'Administrateur Général de l'Etablissement CEA, ce rapport dont nous partageons très largement la vision qu'il offre de l'institut n'appelle pas de commentaires particuliers de ma part. Je puis vous assurer que je prêterai la plus grande attention à la mise en œuvre des actions qui permettront de répondre aux recommandations formulées par l'Agence.

Veuillez agréer, Monsieur le Directeur, l'expression de mes cordiales salutations.

Bernard BIGOT

Commissariat à l'énergie atomique et aux énergies alternatives
Centre de Saclay – 91191 Gif-sur-Yvette Cedex
Tél. : 33 - 1 64 50 10 00 – Fax : 33 - 1 64 50 11 86 – bernard.bigot@cea.fr

Etablissement public à caractère industriel et commercial
R.C.S. PARIS B 775 685 019

PRESIDENCE

Nos Réf. LD/GG/FT 290 -10
Tél. 04 76 51 48 29 - Fax 04 76 51 43 12

Grenoble, le 13 Avril 2010,

AERES
Monsieur le Président Jean François Dhainaut

Objet : Réponse de l'Université Joseph Fourier Grenoble 1 au Rapport du Comité de Visite
Institut de Biologie Structurale – UMR 5075 – Directrice : Eva Pebay-Peyroula

Monsieur le Président, Cher Collègue,

Nous avons examiné le rapport préliminaire d'évaluation mis en ligne sur votre application le 06/04/2010 pour :
Institut de Biologie Structurale – UMR 5075

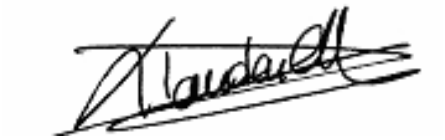
Au nom de l'établissement et de l'ensemble des membres de ce laboratoire, nous tenons à vous faire part de nos remerciements pour cette évaluation approfondie.

Nous nous associons aux observations générales formulées par le directeur de l'unité

Nous vous prions de recevoir, l'expression de nos cordiales salutations.

P/ Le Président de
l'Université Joseph Fourier Grenoble I
Farid OUABDESSELAM

P/O Le Vice-président
du Conseil Scientifique de
l'Université Joseph Fourier Grenoble I
Laurent DAUDEVILLE



PJ : Courrier du Directeur d'Unité mentionnant les erreurs factuelles à corriger avant la publication finale

Institut de Biologie Structurale Jean-Pierre Ebel

To whom it may concern

Grenoble, the 9th of april 2010

The report of the AERES visiting committee is very complete and contains a number of highly interesting remarks that will be in the near future of great help to the IBS management and to the teams. The IBS thanks all the members of the committee for this important contribution.
Several recommendations or comments mentioned in the report retained our attention, among these we would like to comment three of them in the following text.

General comments on the number of post-docs and PhD students per group

The numbers indicated in the document correspond to the personnel that will be present in January 2011 as identified from the IBS personnel file. The document sent to the AERES has been revised in September 2009 and does not take into account all the numerous grant applications already underway or currently under preparation. The numbers are therefore underestimated. The document transmitted with this letter, provides the revised figures (although incomplete because some grants are still under evaluation). The numbers in parenthesis correspond to the number of open grant applications, we estimate that 0% of them will be successful.

Remarks concerning Electron microscopy

The director of the unit is aware of the fragility of the EM team. She is also aware of the high importance of this approach in structural biology as it allows understanding the architecture of complex assemblies. Since several years, special efforts were undertaken by the IBS to attract researchers and reinforce technical support. Therefore new positions were dedicated to EM. In 2007, the IBS recruited a technician who participates in running the EM facility, and in 2009 a researcher experienced in cryoelectron tomography. In order to anticipate the retirement of J. Navaza, a young scientist was selected to apply to a CNRS position in 2009 and 2010. If successful, this application will help to pursue the developments undertaken by J. Navaza.

IBS – UMR 5075
41 rue Jules Horowitz
F-38027 Grenoble cedex 1
Tél. (33) 04 38 78 96 47
Fax (33) 04 38 78 94 84
email : non.prenom@ibs.fr

The efforts of the IBS towards EM will continue in the next years. As pointed out by the committee, the new building will allow reinforcing the already existing cooperation between the IBS and the UVHCI, bringing together several highly experienced researchers in EM.

Remarks concerning team 5

Several remarks concerning the organization of team 5 were addressed:
« The committee was not convinced by the scientific coherence or logic of a small number of the teams within the new organization. This has nothing to do with the individual qualities of the leaders, but rather with their grouping within disparate teams. » (p.5)

« [the Virology team's] appeal was limited probably due to the small size of the research group and to the uncertainty on the strategy to ensure continuation of its activity in the long-term » (p.16, bottom).

« The different teams appear to continue essentially their previous research subjects without defining major common research themes that would provide a strong added value to their association » (p.17, par.2)

« A major concern is the lack of unifying projects that fully exploit the complementary expertise of the teams » (p.17, par. 4)

Team 5 (Viral Infection and Cancer) consists of a Virology team, a Cell Biology team and a Virus Structural Biology team.
The Virology team is led by an emeritus researcher who will leave the IBS in August 2011. At that time the team will be dissolved and its activity discontinued.

The strategic merit of Team 5 thus lies entirely on the association of the Cell Biology and Virus Structural Biology teams. These two recently created teams joined forces shortly before the AERES evaluation and have not yet had time to demonstrate the value of their partnership through common publications.
However, they have defined and are actively pursuing a joint project that regards the interplay between proteins that regulate or interfere with mitosis (survivin, HBx) and proteins that mediate nuclear export (CRM1, Ran) – thereby combining the specialties of both teams. The project's multi-disciplinary nature spans structural and cell biology, and hence exploits the two teams' complementary expertise. This unifying project is ambitious in scope and likely to have a major scientific impact.

Remarks concerning team 9

As mentioned by the committee, this team has an outstanding activity in developing the FIP beam line at the ESRF for the French structural biology community. The creativity of the group is high and the quality of the developments largely acknowledged by the community. However, the committee recommends that the team focuses its efforts to domains where its expertise is the strongest and in particular warns against the development of cell-based assays. The director of the unit is aware of the strength of this team in developing highly efficient tools, but also recognizes that this level of development can only be achieved by a team which is itself implicated in structural biology research. In addition to the forefront beam line developments more “classical” structural biology studies will be pursued by the team and the cell-based assays mentioned in the presentation will be undertaken in collaboration. More efforts to create better links on scientific projects between the team and other IBS teams will be undertaken in the future years.

Best regards

Prof. Eva Pebay-Peyroula
Director Institute of Structural Biology J.P. Ebel