CBS - Centre de biochimie structurale

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on interdisciplinary unit:

Centre de Biochimie Structurale

CBS

Under the supervision of the following institutions and research bodies:

Nouvelle université de Montpellier

Centre national de la recherche scientifique - CNRS

Institut national de la santé et de la recherche médicale - INSERM

January 2014

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

Department for the evaluation of research units

On behalf of AERES, pursuant to the Decree of 3 november 2006[1]*,*

- Mr. Didier HOUSSIN, president
- Mr. Pierre GLAUDES, head of the evaluation of research units department

On behalf of the expert committee,

- Mr. Yves BOURNE, chair of the committee

[1] The AERES President "signs [...], the evaluation reports, [...] countersigned for each department by the director concerned" (Article 9, paragraph 3 of the Decree n ° 2006-1334 of 3 November 2006, as amended).

Evaluation report

This report is the result of the evaluation by the experts committee, the composition of which is specified below. The assessments contained herein are the expression of an independent and collegial deliberation of the committee.

Unit name:	Centre de Biochimie Structurale
Unit acronym:	CBS
Label requested:	
Present no.:	
Name of Director (2013-2014):	Ms Catherine ROYER
Name of Project Leader (2015-2019):	Mr Christian ROUMESTAND

Expert committee member

Chair:	Mr Yves BOURNE, CNRS
Experts:	Mr Alexandre MJJ BONVIN, Utrecht University, The Netherlands
	Ms Sandrine BOSCHI, Professor (representative of CoNRS)
	Mr Marco CAPITANIO, Florene University, Italy
	Ms Anne-Catherine DOCK-BREGEON, Professor (representative of INSERM)
	Mr Oscar P. KUIPERS, Groningen University, The Netherlands
	Mr Didier MARGUET, CNRS

Scientific delegate representing the AERES:

Mr Jacques BARATTI

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

Mr Bernard GODELLE, University Montpellier 2

Mr Pierre LEGRAIN, (representative of Doctoral School)

Mr Jacques MERCIER, University Montpellier 1

Mr Jean-Claude MICHALSKI, CNRS

Ms Stéphanie POMMIER, INSERM

1 • Introduction

History and geographical location of the unit

The CBS is located on the renovated "Navacelles" INSERM site where it moved in 2005 to occupy ~2000 m2 with some additional facilities in the nearby building. Since the last renewal, the unit has performed a profound change in its organization with the creation of two departments (Structural Biology and Single Molecular Biophysics), each hosting 5 and 3 research teams, instead of 3 thematic areas. This new organization, which is driven by a recent mobility of the staff, is aimed at a better coherence and visibility as well at sharing scientific and technical culture across the two departments.

Management team

Following the departure of the former director Cathy ROYER in September 2013, Mr Christian ROUMESTAND has been appointed director of the CBS for the current term and the next period and is assisted by Mr Pierre-Emmanuel MILHIET as deputy director. A managing committee with the directors and the team leaders has been launched recently and completes the management organization.

AERES nomenclature

SVE1_LS1, SVE1_LS2, ST2 and ST4

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent researchers from Institutions and similar positions	23	22
N3: Other permanent staff (without research duties)	17	16
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	10	3 + 7 *
N6: Other contractual staff (without research duties)	6	4
TOTAL N1 to N6	57	53

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	9	9
Theses defended	11	12
Postdoctoral students having spent at least 12 months in the unit*	6	6
Number of Research Supervisor Qualifications (HDR) taken	2	3
Qualified research supervisors (with an HDR) or similar positions	11	12

2 • Overall assessment of the interdisciplinary unit

Under the leadership of former directors, the CBS has occupied a unique place with the integration of structural biology and biophysics approaches within the same lab using state-of-the-art complementary instrumentation, creating a leadership position to develop interdisciplinary projects at the forefront of integrative structural biology. This remarkable achievement was accompanied by a profound reorganization in two departments with the emergence of young teams and a novel emphasis in synthetic biology. In this context, the CBS has addressed weaknesses reported during the last AERES evaluation. The different projects can be classified into six main biological themes or research axes that bring complementary skills and can be viewed as transverse across the different teams, e.g. infectious disease, structure-function and dynamic of intrinsically disordered proteins, structure and dynamic of biological membranes, regulation of gene expression, molecular motors, synthetic biology with emphasis on in-house collaboration between teams. Besides, the CBS has to cope with the departure of a prominent scientist that largely contributed to the development of biophysics and recruitment of talented researchers. Hence, the new management team must carefully preserve the equilibrium between the two main structural biology and biophysics disciplines.

Strengths and opportunities related to the context

- Pioneering effort coupled to world-class expertise to develop strong interdisciplinary and complementary approaches in structural biology and biophysics within a same lab;
- Excellent initiatives to attract young researchers;
- Initiating timely and promising projects;
- Developing innovative technologies linked to implementation and maintenance of state-of-the-art distributed facilities.

Weaknesses and threats related to the context

- Low participation in initiatives at the European level despite individual attractiveness;
- Disparity in international leadership and visibility among research teams;
- Large redistribution of employees and reorganization of teams may not be optimal and will have to be re-evaluated internally after a few months;
- Possible decrease in teaching duties might impact local visibility for students.

Recommendations

- Attention should be made to fully consolidate and integrate the emerging teams associated to new thematic areas;
- Attention should be given to avoid a division of the unit with the organization into two departments;
- Develop a high-profile federative, interdisciplinary and cell biology-driven project across teams for high impact publications;
- Capitalize on the specific expertise in high-pressure NMR spectroscopy;
- Reinforce the staff with teaching duties;
- Ensure adequacy between permanent staff and the number of main thematic areas, especially for those lacking financial support.

3 • Detailed assessments

Assessment of scientific quality and outputs

For the 2008-2013 period, lab members have published more than 200 publications in international journals, of which about half originating in CBS (first and/or last author). 27 publications are in Journals with an IF > 7 (of which 1 PloS Biology, 2 NSMB, 2 J Cell Biol, 3 JACS, 9 PNAS, 1 EMBO J, 8 NAR, 1 Science Signaling and 2 EMBO Rep) and about 20 as internal collaborations. In addition, 6 patents were filed during this period. The CBS has a very good production. Given the stunning expertise, complementary skills and state-of-the-art technology facilities, the CBS has clearly the means to further increase the visibility of some of its research themes by focusing on integrated studies across teams in an interdisciplinary context with a potential for high-impact publications in leading journals.

Assessment of the unit's academic reputation and appeal

The CBS is the flagship of an interdisciplinary discipline at the forefront of structural biology and biophysics in the Montpellier region and belongs to the French leaders in these fields. This successful implementation of technologies has been recognized with the partnership of CBS in two major French infrastructure projects (FRISBI, FBI). CBS holds a special position in combining specific interdisciplinary competences and skills and, as such, occupies an important place in collaborative national and international networks. Local collaborations have also been emphasized and a significant number of publications (>15) results from these interactions. A total of 55 research grants were obtained by the lab members, of which 18 from the ANR, 6 from industrial collaborations, 4 from EU programs and 3 from private foundations. Moreover, the CBS has demonstrated an impressive capacity to attract and recruit staff. 1 PI has been involved in the creation of a start-up and 5 PIs benefited from highly competitive European (2 ERC starting) and French (3 ATIP-Avenir, 1 ANR Chaire excellence and 2 Region-LR) programs. A young researcher was awarded the CNRS bronze medal.

The lab has hosted 17 Postdoctoral fellows (8 being international) and 5 temporary technical staff that illustrates the very good capacity of the lab to sustain competitive scientific activity, a recommendation from the previous evaluation report.

While most PIs are regularly invited to conferences and seminars abroad and in France, attendance to international conferences as invited speakers is not uniformly distributed among teams to promote a global lab visibility. In this context, one may cite the higher visibility of the super-resolution microscopy domain.

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

The CBS ocupies a unique place in belonging to two national infrastructures with the aim to allow external users to access these advanced technologies. The CBS also promotes interactions with local start-ups and has a key role to deliver attractive educational and community-based programmes in structural biology and biophysics.

Assessment of the unit's organization and life

The laboratory life includes shared leadership, the regular meeting of consultation boards as well as regular scientific meetings for students. Meetings with the staff during the visit have highlighted the very good spirit of the lab and all the staff adheres to the restructuration and future project. Meeting with the affiliated institutions has emphasized the quite unique place of the CBS which in turn is strongly supported.

Assessment of the unit's involvement in training through research

During the past period, the CBS research staff consisted of one professor and three assistant professors ensuring their teaching duties, and the CNRS/INSERM scientists were also actively participating to teaching. All teams were active in recruiting PhD students (11 theses defended over the period and 9 PhD ongoing at the time of the visit) despite a decrease in graduate students. Overall, the CBS contributes significantly to educational activities as demonstrated by the creation of 2 Master programs. The CBS has organized several workshops, thematic schools and meetings and participates actively to the animation of the campus in training young scientists.

Assessment of the strategy and the five-year plan

The CBS wishes to develop 6 main research themes transverse to the 8 teams integrating molecular and structural biology, bioinformatics and biophysics, and consolidate its visibility by promoting local synergy. Transfer and mobility of personnel have led to reorganize the 3 research axis in two departments with 5 and 3 teams. The first theme on infectious diseases will investigate several aspects of viral transmission and will pursue on the mechanisms of *Mycobacterium tuberculosis* virulence. The second will address intrinsically disordered proteins in the context of pathologies and will be reinforced by an emerging team. The third will be dedicated to biological membranes and their components. The fourth will focus on the regulation of gene expression in the cancer context. The fifth will be dedicated to molecular motors by integrating a Labex project while a sixth theme will be initiated on the engineering of bacterial sensors by a second emerging team. While the CBS has clearly the potential to tackle this ambitious research plan, development of a strong federative project rather than too much diversity could increase its visibility. Emergence of two new teams will also demand some consideration to adapt the size and scientific objectives as opportunities still exist for some regrouping within the lab depending on the success of the teams. The strategy for the future will also consider developing new methodological approaches and reinforcing atomic force microscopy, a wish of CBS to continue implementation of integrated approaches across teams by acquiring complementary skills to address biological questions. The development of molecular and cell biology facilities to strengthen functional studies will be also considered. In this context, the demand for new space in a neighboring building to pursue a very successful attractiveness policy appears highly urgent and justified.

4 • Team-by-team analysis

Team 1 : Biomolecular Structure, Function and Dynamics by NMR

Name of team leader: Mr Christian ROUMESTAND

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	2(3)	2(3)
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	7(8)	7(8)

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	4	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	5	

• Detailed assessments

Assessment of scientific quality and outputs

Team 1 consists of 6 permanent researchers with very complementary expertise in structural biology in general, including NMR, X-ray crystallography, SAXS and biochemistry. The research is concentrated around the structural biology of infectious diseases and protein folding. They have in particular solved 15 structures of *M. Tuberculosis* (10 by NMR, 5 by X-ray), making a significant contribution to this field. This can be considered classical structural biology work. On the folding side, the team has expertise in high-pressure NMR, as one of the few labs worldwide where this particular technique is present. Using high-pressure NMR, they study various systems, reaveling their structural and energetics landscape. This is done in collaboration with other groups worldwide, among others a well known group at Johns Hopkins (Garcia-Moreno), indicating the international visibility of the team (also backup by invited lectures at international conferences). Clearly the team has a unique expertise in high-pressure NMR.

Over the last five years the team has published 35 papers, a number of which in high impact journals (PNAS, Proteins, Nature Structural & Molecular Biology, Nature). This gives an average of 7 per year, for a team of 6 researchers, which is good. One of the limitations to a higher productivity seems to be the number of post-docs and PhD students. This is however a general problem that the unit has to face.

Assessment of the team's academic reputation and appeal

The team is well known internationally and has been quite successful in raising funds with two ANR grants in the period assessed. Visibility as assessed by the number of invited lectures at international (17) and national (4) conferences is good. It is part of the French Integrated Structural Biology Infrastructure (FRISBI) and initiated the acquisition of an 800MHz NMR spectrometer in the coming years (pending a positive evaluation of FRISBI).

Next to the permanent research staff, the team counts 1 post-doc and 3 PhD students. The team leader is actively involved in teaching and developing new master programmes to attract more students to CBS.

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

The team and in particular the team leader has been successful in acquiring grants with local companies and is being supported by four contracts with large pharma industries (Sanofi-Aventis and Nosopharm). The NMR platform (IBiSa, now part of FRISBI) is offered to local, national and international users. Further a new protein production platform has been set up. The team has a clear, interdisciplinary and also unique expertise in some areas (e.g. high-pressure NMR).

Assessment of the team's involvement in training through research

With currently three PhD students, the teams clearly contribute to training through research. With the professor position of the team leader there is a clear connection with education. It seems however that the developments in the current study curricula do not prepare well students to perform research in structural biology and all associated biophysical techniques. The team (and actually the institute) has made effort to correct this by participating in and reshaping as much as possible the master programs (“Structural Biology and Drug Design” and “Molecular and Cellular Biophysics”) and is now considering also the bachelor level. This is a clear involvement in education (which is needed in order to prepare and attract students).

Assessment of the strategy and the five-year plan

The strategy for the coming years is a logical continuation of the current research topics, with structural biology of infectious diseases and protein folding using high-pressure NMR (a rather unique expertise of the CBS). All projects show a good level of interdisciplinarity and there are good collaborations in place. In particular the research lines around phospho-regulation and latency are timely and merit increased efforts. The team should also work at increasing their scientific outputs and ambition levels.

Conclusion

A well-established, complementary team of expert covering a variety of techniques in structural biology.

Strengths and opportunities:

- Unique expertise in high-pressure NMR;
- Interdisciplinary of the team;
- Good infrastructure in NMR (even better once the 800 MHz will be installed);
- Good collaboration network (both national and international levels);
- Transverse interactions with the other teams with strong impact on the unit cohesion;
- Good links with big pharmaceutical companies.

Weaknesses and threats:

- Limited number of PhD students and post-docs for the team size;
- International visibility/involvement in projects (EU);
- Relatively low number of new research lines over the years.

Recommendations:

- Look for opportunities in Horizon 2020 to increase visibility and funding;
- Phospho-regulation and latency are timely research that merit increased efforts;
- Keep working on the education/teaching components to attract mode students given the departure of a senior with teaching duties;
- Maintain and possibly increase output and ambition level.

Team 2 : Structure and Function of Highly Flexbible Proteins

Name of team leader: Mr. Pau BERNADÓ

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	5	5

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	4	

• Detailed assessments

Assessment of scientific quality and outputs

This is a young team whose PIs joined the CSB during the last three years. The research work concentrates on intrinsically disordered proteins using a combination of NMR, SAXS and computational modelling, an ideal combination to study such systems. The systems under study are various, including phosphorylation effects in various systems and the characterisation of GPCR tails. There is also an interest in developing new methodologies to study those systems.

The last two years at the CBS have been used to set-up the lab and all methods and establish collaborations on biological systems. In terms of productivity, the teams published 10 papers since 2012, which is a rather impressive output considering the short time at CSB. Prior to that, they have published 39 papers since 2008, including high ranking journals (PNAS, Nature 2012 and other Nature journals), which is demonstrating an excellent productivity. There is thus a high potential for this team to grow in the coming years. The team leader has been quite successful in raising funds with an ANR Chaires d'Excellence grant and an INSERM grant for a co-funded PhD student. In addition he also obtained an ATIP-Avenir 2011 grant (turned down in favor of the ANR grant).

The team is well visible and recognized internationally, with invited lectures at international meeting. The publication and citations records are already very good, showing a very promising growth.

Assessment of the team's academic reputation and appeal

Again, this is a young team starting at the CBS. The team leader is well recognized in his field, which is backed up at the national level by the ANR Chaire d'Excellence. Both PIs have been involved in the organization of international and national meetings.

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

There are activities and collaborations with external groups for SAXS analysis, one of the expertise area of the team. There is a good potential for valorization, also with respect to the NMR part and the GPCR project which should attract interest from industry.

Assessment of the team's involvement in training through research

The team has currently one PhD student. No other teaching activities reported at this stage.

Assessment of the strategy and the five-year plan

The three main research areas for the coming years focus in structural studies of disordered proteins or segments thereof in huntington disease and GPRCs, and methodological development in this area. These are highly medically relevant and timely topics. But there is also competition in this area. The team has a good network in place, but will have to find its "niche".

Conclusion

A young, dynamic and excellent team that recently joined the CBS with lots of potential for further growth. The research area is highly relevant and timely and expected to lead to excellent publication with a good potential for valorization

Strengths and opportunities:

- Young and highly dynamic team
- Excellent potential for growing
- Relevant and timely research topics
- Already impressive output considering the short period at CBS
- Good international network and visibility

Weaknesses and threats:

- Critical mass
- Highly competitive field

Recommendations:

- Keep getting grants to increase the group size
- Define a niche and avoid overlap with other competing groups

Team 3 : Multiscale Structural Biology

Name of team leader: Mr Patrick BRON

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	3
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	5	5

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	

• Detailed assessments

Assessment of scientific quality and outputs

There are several research projects, all well focused in the virology field and in collaboration with virologists and molecular biologists. The team solved several impressive structures, including the viral baseplates or their constituents, thus highlighting how phages inject their genome into bacteria. They also paved the way to understanding how viruses bind to their cellular receptors, and provided structural data on viral transmission. The team is now focusing its interest on pathogens with projects about HIV, influenza and chikungunya. Technically excellent, they will progress a step further, by setting-up methods for imaging at the cellular level, with the aim to bring data on how HIV spreads from cell to cell through tunneling nanotubes, or CHIKV assembly/disassembly. Of particular interest are the developments of new techniques such as the use of origami in cryoEM, or the phasing of X-ray data with negatively stained EM samples. Besides the dynamics and creativity of the persons involved, this underlines the power of the balance of expertise in this team truly devoted to multi-scale structural biology.

Assessment of the team's academic reputation and appeal

The scientific achievements of these last years (33 publications since 2008) and the high quality of the results illustrate the dynamics of this quite new team, and bode well for the future projects. The level of publication, and ranking of the team members in the author's list appears to be somewhat modest, suggesting a lack of leadership in the collaborative work. This may reflect some understatement of their input value as structural biologists, a problem frequently encountered in such multidisciplinary projects.

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

Interactions are strong with other teams of CBS, such as Team 5 in the Structural Biology Department, but also with the Biophysics Department, as with the active collaboration with Team 8 in the development of correlative EM. Involvement in the unit day-to day life is manifest with the role of one team member as CBS administrator of the informatics and webmaster. With its deep involvement in the technical platforms for EM and crystallography, Team 3 is instrumental in CBS cohesion. The links with the scientific community are strong, especially at the national/European level, as CBS is one out of the 5 centers of the French Infrastructure for Integrated Structural Biology (FRISBI), open to molecular and cell biologists from both academia and industry from France and Europe, and as such directly linked to and part of the European INSTRUCT Infrastructure. The team is locally involved in the platform IBISA, more precisely in the poles (1) Crystallography, bringing expertise in crystallization, and structure solving and (2) Electronic Microscopy. This type of activity is quite time demanding, and could outbalance the workforce of the current team.

Assessment of the team's involvement in training through research

This is a quite recent team (2008), which can now capitalize on the past efforts to setup and validate an in-house heavy instrumentation. This explains why there is only one student in the team, for the moment. However, the involvement of one team member who is teaching in the Master BioMed, should help to improve this situation in the future.

In addition, the team participates to training through research, as this constitutes the spirit of the FRISBI/INSTRUCT program.

Assessment of the strategy and the five-year plan

The future projects are focused on human pathogens such as HIV, influenza and chikungunya. The expertise in cryoEM and crystallography will be maintained at the highest level, along with the development of new methods in order to locate the viruses in the cells, and follow their functions, such as assembly or disassembly of particles at the highest resolution possible. Also the use of DNA origami presenting specific molecules is a new and promising avenue. Both the established and new focus and their expertise will help to increase the team visibility, and favour publication in more prominent positions and journals. On the whole, this is a strong project, which leans on cutting-edge technologies, and will generate new developments for the community. The project is of obvious interest for human health, with high probability to yield outstanding results.

Conclusion

Strengths and opportunities:

- Excellent expertise in electron microscopy and instrumentation;
- Well-balanced team composition with complementary expertise;
- High number of collaborations;
- Pro-active in the methodological development of hybrid methods;
- Promising new research line in virus visualization in cells.

Weaknesses and threats

- Lack of visible leadership in the collaborative projects;
- Lack of international visibility in the field;
- Small size of the team;
- Saturation of the operational microscope.

Recommendations

- Establish and ensure a stronger leadership in collaborative projects;
- Ensure funding to attract and recruit;
- Capitalize on the new promising research lines and interactions with the single molecule biophysics department;
- Invest in a routine microscope.

Team 4 : Synthetic biology

Name of team leader: Mr Jerôme BONNET

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions		
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	2	2

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions		

• Detailed assessments

Assessment of scientific quality and outputs

This team is newly formed and will focus on Synthetic Biology, making use of *Bacillus subtilis* as a chassis. The team leader has just been appointed after a stay in Drew Endy's lab, and no output for team 4 can be listed yet. The overall goal is to develop a programmable diagnostic platform for detection of biomarkers in clinical samples. The work is divided in three major parts: 1. Parts standardization and measurements for predictable gene expression in *B. subtilis*, 2. Engineering chimeric eSTK receptors and 3. Biomolecular computation for biomarker analyses. This program appears well balanced, innovative and relevant with good chances of high level publications.

Assessment of the team's involvement in training through research

Not evaluated

Assessment of the strategy and the five-year plan

The organization of the research into three main themes is promising. In the second subject there are good opportunities to collaborate within CBS e.g. with teams 1 and 5. The team will have to build further on the manpower and expertise in *Bacillus* (and perhaps other Gram-positives for expression) to obtain further funding to carry out these projects.

Conclusion

There are very good chances in this field. The work program is well-balanced. The team is uniquely positioned within CBS, giving excellent possibilities for collaborations in the structural field. The team needs to build on increasing its expertise on *B. subtilis* engineering. International grants like ERC or Horizon 2020 would be welcome, to extend the team with PhD students and postdocs.

Strengths and opportunities:

- Very promising and dynamic young group leader
- Already excellent scientific network
- Good opportunities to extend Synthetic Biology (SynBio) work in *B. subtilis*
- Embedding in CBS gives unique opportunities (most synbio is not embedded in Structural Biology Departments!)
- Opportunities to be involved in teaching SynBio internationally or locally

Weaknesses and threats:

- Continue to attract enough funding in a very competitive area
- Finding and appointment of skilled and multidisciplinary PD and PhD students is of utmost importance

Recommendations:

- Ensure good integration and support within CBS (good start already with ESTPK work)
- Seek international collaborations in synthetic biology with *B. subtilis*, but be complementary

Team 5 : Structures and screening of therapeutic and environmental targets

Name of team leader: Mr William BOURGUET and Mr Gilles LABESSE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	5	5
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3	3
N6: Other contractual staff (without research duties)	2	2
TOTAL N1 to N6	14	14

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	5	5

Detailed assessments

Assessment of scientific quality and outputs

The team is well recognized for its multidisciplinary skills, which combine chemistry, biochemistry, bioinformatics and structural biology (X-ray crystallography and NMR). During the previous period, the team obtained original and major results essentially on two main themes that are regulation of nuclear receptors and development of drug candidates by fragment-based approaches. The team has also developed innovative *in silico* tools to predict protein structure.

The scientific output of this team is excellent with 54 articles published in international journals of good quality (include NSMB, PNAS, Structure, NAR). This research topics also generated 5 patents, indicating that the conducted works are both scientifically excellent and socio-economically relevant. A significant proportion of the publications of the team were co-signed by external authors to the team or unit, reflecting the strength of collaborations. However, there appears to be an underrepresentation as last author of unit members on these publications.

Assessment of the team's academic reputation and appeal

The team has a good recognition, especially the two team leaders, with 10 participations as invited speaker. The team has been involved in the organization of one national meeting. The group has good national and international collaborations and is involved in different national and international collaborative networks (MobylNET IBISA, French Integrated Structural Biology Infrastructure (FRISBI), European ESFRI (EU-OPENSCREEN).

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

The team has demonstrated its ability to secure outside funding for most of their research at the national level, including 5 ANR grants. The research produced by the group has been valorized by 5 patents as well as two CIFRE grants with Oribase pharma. The team is also involved in the emergence of the AGV Discovery.

Assessment of the unit's involvement in training through research

One team's member participates strongly in teaching at the university, with 220 hours per year, and is co-head of the Master Biologie Structurale et Drug Design. One PI is member of the executive board of the doctoral school CBS2 and is involved in Master teaching for 10 hours per year. The team has currently 2 PhD students and 3 postdocs.

Assessment of the strategy and the five-year plan

The organization of the research into two main sub-groups, with one well-identified and well qualified PI for each, is consistent. The team plans not only to pursue their main projects but also to develop new integrated methodology for the structural characterization of ADMETox properties of chemicals, based on X-ray crystallography and structural bioinformatics. The existence, relevance and feasibility of the long-term projects are evident. The team has the manpower, the equipment, the expertise and the funding to carry out these projects. Their participation to the internal platform represents a long-standing commitment to improve local collaborations and productivity.

Conclusion

High quality work, expertise in the field, with nice methodological developments. Their interaction with the other teams is strong and they are able to secure funding for their projects.

Strengths and opportunities:

- Excellent productivity and funding;
- Complementary expertise in timely and relevant topics for drug design;
- Excellent valorization;
- Development of methodological tools well embedded at the national and European level.

Weaknesses and threats:

- Relatively low international visibility;
- Possible negative impact of the new start up activities on team productivity.

Recommendations:

- Maintain a good management of the research and valorization activities;
- Look for opportunities in Horizon 2020 and innovative medicine initiatives to increase visibility and funding.

Team 6 : Mechanisms of DNA segregation and remodeling

Name of team leader: Mr Marcelo NOLLMANN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	4
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	7	7

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	2
Theses defended		
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team aims, on one hand, at developing novel single-molecule and super-resolution techniques; on the other hand, it applies these advanced techniques for the study of the transport and remodeling of DNA in bacteria and eukaryotes.

The development of new methodological approaches that allow the visualization of single molecules in living bacteria or higher eukaryotes, together with super-resolution techniques able to resolve sub-diffraction intracellular structures, puts the group activities at the forefront of biophysics research. Single molecule and super-resolution techniques have been constantly developing during the last few decades, leading to improved spatial and temporal resolution. Such technological developments have allowed deciphering important molecular mechanisms in biology, with particular regards to molecular motors function and nucleic acids structure and interaction with transcription factors and processing enzymes. The team activity, thus, fits in a rapidly developing area at the forefront of international biophysics research.

The biophysics research deals with DNA structure and transport in bacteria, as well as higher-order chromatin structure in eukaryotic chromosomes, and how genetic material structure relates to transcription regulation in living cells. The physical mechanisms underlying gene activity and regulation are one of the key themes in current biophysics research.

The scientific output demonstrates excellent quality with publications during the last years in internationally renewed journals (NAR, Plos Biology, EMBO reports, etc).

Assessment of the team's academic reputation and appeal

The PI is well known at the international level, as demonstrated by several invited talks at international and national conferences and by his activity as reviewer for several national research agencies and scientific journals. Funded grants from the national funding agency as well as HFSO and a starting grant from ERC demonstrate the excellence of the team and the proposed research.

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

The PI is member of the France Bioimaging (FBI) Steering Committee; Labex EpigenMed and from France Bioimaging; GDR “Architecture et Dynamique Nucleaire” (ADN), and “Microscopie pour le vivant” (GDR2588); and has been involved in the organization of local workshops. The team has interactions with Andor technologies through an industrial contract and several national and international scientific collaborations.

Assessment of the team's involvement in training through research

The team has a very good involvement in training through research with two PhD students and four post-docs. The PI is also involved in the supervision of master’s students, teaching in university courses and EMBO practical courses.

Assessment of the strategy and the five-year plan

The strategy of the team for the next five years develops through five main research projects. One of these projects deals with the higher-order architecture of the eukaryotic nucleus investigated at the single molecule level. This research is funded by an ERC starting grant, which should guarantee appropriate funding and promising results. Other two research projects involve the study of the bacterial chromosome architecture and the mechanism of DNA segregation in bacteria, studied by super-resolution microscopy. The fourth research line follows and extends previous studies of the team on DNA segregation in *B. subtilis*. Finally, a fifth research line deals with technological developments aimed at developing fast 3d super-resolution imaging.

The research plan is convincing, timely and deals with actual biophysical problems investigated with advanced techniques that promise to give new insight into unsolved biological questions.

Conclusion

Strengths and opportunities:

- Outstanding young and highly dynamic team with excellent potential for growing;
- Excellent productivity and quality of scientific output;
- Relevant and timely research topics;
- Development of advanced single molecule and super-resolution techniques;
- Very good collaboration network within CBS;
- Excellent funding sources;
- Very good national and international network of collaborations and visibility.

Weaknesses and threats:

- Threats: Highly competitive field;
- No relevant weaknesses at the moment.

Recommendations:

- Maintain a good balance between the number of research lines and team size;
- Maintain a good balance between methodological development and science.

Team 7 : Angular dynamics and manipulation at the single-molecule level

Name of team leader: Mr Francesco PEDACI

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	1	3

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions		

• Detailed assessments

Assessment of scientific quality and outputs

The team just established at CBS in January 2013. The group aims at developing novel single-molecule techniques for the manipulation of rotary motors and the measurement of torque in macromolecular biological complexes.

The research follows from previous investigations by the team leader before arrival at the CBS where he developed an “optical torque wrench”, which is able to apply and measure torque on microscopic nanofabricated particles.

During his postdoc period, the scientific output of the team leader was of high quality, with publications in top-rated journals (Nature Physics, Nature Communications). The research topics are now funded by an ATIP-Avenir grant and a starting grant from ERC.

Assessment of the team's academic reputation and appeal

The PI is well known at the national and international level. He received an ATIP-Avenir grant and a starting grant from ERC, which indicates the excellence of the team leader and the proposed research.

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

The team leader has established collaborations with IEMN in Lille (France) for nanofabrication of the particles used in the angular optical tweezers, with the group of prof. Bertus Beaumont (TU Delft, The Netherlands), for molecular and cellular biology, and with Dr.Peter Galajda (Institute of Biophysics Cell Biophysics, Hungary) for motility assays in different conditions.

Assessment of the team's involvement in training through research

At present, one PhD student has been hired. Two postdocs will be hired in a near future.

Assessment of the strategy and the five-year plan

The scientific goals consist of three main research projects. 1) The development of novel technical advancements in optical manipulation, with a special focus on the application and measurement of torque. 2) The application of these novel techniques to the study of the flagelllar motor in *E. coli*. 3) The development of novel probes to expand near field scanning microscopy.

The research plan is well defined and scientifically solid. Although quite specific and focused on the development of techniques setup previously, the technological and methodological advancements might lead to developments with broad applicability and wide interest.

Conclusion

Strengths and opportunities:

- Young team leader with excellent potential for growing;
- Methodological development of innovative single molecule manipulation techniques;
- Excellent funding sources;
- Very good collaborative network.

Weaknesses and threats:

- No relevant weaknesses at the moment.

Recommendations:

- Finding and appointment of skilled and multidisciplinary PD and PhD students is of utmost importance;
- Extend the scientific outreach of the methodological development;
- Maintain a good balance between the number of research lines and team size.

Team 8 : Structure and Dynamics of Nucleoproteic and Membrane Assemblies

Name of team leader: Mr Emmanuel MARGEAT and Mr Pierre-Emmanuel MILHIET

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	4	5
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	10	10
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	18	19

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	5	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	4	4

• Detailed assessments

Assessment of scientific quality and outputs

Team 8 which will include 5 permanent researchers and 3 permanent ITAs for the next project, originates from the former team #2 "*Biophysique des molecules uniques*". The scientific accomplishments were achieved thanks to outstanding single molecule techniques developed by staff researchers (smFRET, PIE-FCCS, HS-AFM and super-resolution). Moreover, each PI is conducting its own project of research and is contributing to other projects in a collaborative effort by providing complementary expertise.

Two main themes were investigated:

The structure and dynamics of membrane components

They have investigated the structural dynamics of the extracellular domains of mGlu receptor by recording FRET at single molecular level (smFRET) in the presence of different ligands. This work was developed within the frame of collaboration at the local level for the biological model and international level for the methodological development.

In a long-standing collaboration with Eric Rubinstein at Villejuif, they have analyzed the membrane partition of tetraspanin by single molecule imaging. They have pursued this work through international collaborations by analyzing the role of tetraspanins for HIV-1 assembly and during infection.

The structure and dynamics of membrane microdomains were investigated using high-speed AFM within the frame of national and international collaborations.

The control of genetic expression in *Bacillus subtilis*

They have analyzed the repressor complexes both *in vitro* for the structural analysis (x-ray, SAXS, EM) and *in vivo* for the biological analysis (2-photons fluorescence fluctuation microscopy) in a network of internal (CBS), national and international collaborations. They have evidenced the competitive folding of anti-terminator and terminator hairpins upon anti-termination protein binding.

They have also investigated at a single bacterial level, the stochastic activity of metabolic gene promoters in order to understand the molecular bases of the transcriptional control mechanisms underlying bacterial adaptation to environmental changes (local and national collaboration).

Over the last period, the team has produced 51 publications (21 as corresponding authors, with 9 of them in high impact journals (IF>8) (4 in NAR, 2 in PNAS and one in JCB, Nat Struc Mol Biol and PlosBiol). One PI wa awarded by national (CNRS- bronze medal) and regional institutions.

Assessment of the team's academic reputation and appeal

The team has clearly established a good academic reputation in the field of biophotonics and AFM with national and international collaborations as testified by the number of articles published in collaboration. Visibility is also assessed by the number of invited lectures in international (21) and national (9) conferences.

During the last quadrennial, the team has attracted 9 students (3 from abroad) and 12 post-docs (8 from abroad). Two staff researchers (CR-CNRS & CR-INSERM) will join the team for the new quadrennial.

The team has secured their capacity to develop their scientific projects by a very efficient success in research funding (among them 11 ANR and 2 Investissement d'Avenir grants as partner of a LABEX and the France BioImaging Infrastructure) and two grants with private companies.

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

Two contracts were signed with private companies.

Dissemination of knowledge is assessed by the contribution of team members to the organization of summer schools (2), practical course (1 EMBO) and scientific congresses (5). Team members contribute to public outreach by participating to practical courses for high school teachers and by organizing regularly workshops for kids.

Assessment of the team's involvement in training through research

Staff members have contributed to supervise nine PhD students (four already got their diploma, five are still in training) and 12 post-docs (five are still present). The staff is active in teaching in Master BioMed, level 1 and 2, and in organizing national and international meetings and schools. One PI co-organized the EMBO Practical Course “Super resolution and advanced microscopies in living cell”. Due to the leave of one staff member fervently implied in the oragnization of the teaching, the team should consider to capitalize this investment on the education/teaching components by spliting the free teaching duties between the team staff members.

Assessment of the strategy and the five-year plan

Following the recent reorganization of the department of single molecule biophysics, team #8 will pursue two main scientific themes and keep their methodological developments at the state-of-the-art.

The structure and dynamics of membrane components

Within the frame of their collaborative network at local, national and international levels, they will investigate:

- the structural dynamics of two reconstituted GPCRs (mGluR, GABA in lipid nanodiscs based on the single molecule techniques mastered by the team. The dynamics of oligomerization of the receptors will be analyzed in living neurons. This project will benefit from new fluorescent labeling techniques keeping minimal the steric perturbation due to fluorophore addition.

- the role of the lateral segregation of tetraspanins during viral infection and cell migration by single molecule approaches. They aim at performing epitope mapping and topographic analysis of HIV-1 budding. Similar approaches will be performed to map HCV receptors. This project will be contingent of challenging but realistic methodological development in which AFM and super-resolution techniques will be combined on the same setup.

The control of genetic expression in Bacillus subtilis

Following up on their previous work, they will analyze the mechanism of transcription termination by investigating the activation of antiterminators at the structural level by NMR and the molecular dynamics by smFRET.

The mechanism of the Rho-dependent termination will be deciphered by combining superresolution, magnetic tweezzers and fluorescence fluctutation using fluorescent single molecule techniques in solution and on living cells.

All of these projects will capitalize on the methodological developments mastered by the department of single molecule biophysics.

Conclusion

Strengths and opportunities:

- Excellent quality of the scientific output
- A unique interdisciplinary team mastering broad expertise in single molecule imaging and AFM
- A very good balance between biology and methodology
- Good scientific network at national and international level
- Excellent funding strategy
- Very active in teaching and spreading knowledge

Weaknesses and threats:

- A broad range of biological projects might impact team visibility
- Broadness of the topics and size of the team might impact team cohesion

Recommendations:

- Identify one flagship project to unify the team or consider splitting the team
- Capitalize on the past realization to reinforce international visibility
- Maintain an involvement in educational/teaching activities to secure student attractiveness

5 • Conduct of the visit

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

Centre de Biochimie Structurale (UMR 5048 et U1054)
Universities of Montpellier 1 and 2, CNRS and INSERM
Director Christian ROUMESTAND
Program of the visiting committee

Date of the visit: January 16 & 17, 2013
Site for the visit: CBS, 29 rue de Navacelles, 34090 MONTPELLIER

January 16, 21013

08:00 **Welcome to the committee (15 min)**

1. Centering of the committee

8:15 **Preliminary meeting of the committee (closed hearing) (30 min)**
Attending: Committee members, AERES scientific delegate

2. Scientific part 1

8:45 **Presentation of AERES evaluation and of committee members** ***(J. Baratti and Y. Bourne) (10 min)***

8:55 **Presentation of the unit project: C. Roumestand + C. Royer (30 min + 30 min discussion)**
Attending: Committee members, AERES scientific delegate, representatives of Institutions and unit members

9:55 **Scientific Presentation Team 1 - C. Roumestand (20 min + 15 min discussion)**
Attending: Committee members, AERES scientific delegate, representatives of Institutions and unit members

10:30 **Scientific Presentation Team 2 - P. Bernado (15 min + 15 min discussion)**
Attending: Committee members, AERES scientific delegate, representatives of Institutions and unit members

11:00 **Scientific Presentation Team 3 - P. Bron (15 min + 15 min discussion)**
Attending: Committee members, AERES scientific delegate, representatives of Institutions and unit members

11:30 **Break (15 min)**

11:45 **Scientific Presentation Team 4 - J. Bonnet (10 min + 10 min discussion)**
Attending: Committee members, AERES scientific delegate, representatives of Institutions and unit members

12:05 **Scientific Presentation Team 5 - W. Bourguet (20 min + 15 min discussion)**

Attending: Committee members, AERES scientific delegate, representatives of Institutions and unit members

12:40 ***Lunch - buffet / discussion (90 min)***

3. Scientific part 2

14:00 **Scientific Presentation Team 6 - M. Nollmann (15 min + 15 min discussion)**
Attending: Committee members, AERES scientific delegate, representatives of Institutions and unit members

14:30 **Scientific Presentation Team 7 - F. Pedaci (10 min + 10 min discussion)**
Attending: Committee members, AERES scientific delegate, representatives of Institutions and unit members

14:50 **Scientific Presentation Team 8 - E. Margeat (20 min + 15 min discussion)**
Attending: Committee members, AERES scientific delegate, representatives of Institutions and unit members

3. Meeting with representatives of Institutions

15:25 *(30 min discussion with committee members)*
Attending : Committee members, AERES scientific delegate, representatives of Universities (Jacques MERCIER UM1, Bernard GODELLE UM2), of CNRS (Jean-Claude MICHALSKI) and of INSERM (Stéphanie POMMIER)

4. Meeting with researchers, technicians, doctoral students and post doctoral fellows

15:55 *in parallel the committee splits into three groups.*
Meeting with researchers
Meeting with technicians
Meeting doctoral students and post doctoral fellows
Attending: Committee members, AERES scientific delegate, without the leaders, representative of institution, without the direction of the unit and without team leader

16:25 **Break (15 min)**

5. Meeting with the director of the Doctoral School

16:40 *(15 min discussion)*
Attending : Committee members, AERES scientific delegate

5. Meeting with the unit Director

16:55 *(30 min discussion with the committee)*
Attending : Committee members, AERES scientific delegate

6. Debriefing of the committee

17:25 **Deliberation of the committee (closed hearing)** *(30 min)*
Attending : Committee members, AERES scientific delegate

17:55 ***Thanks and leave of the committee***
18:10 ***End***

January 17, 2013

09:00 **Welcome to the committee (15 min)**

1. Centering of the committee

9:15 Final meeting of the committee (closed hearing) (180 min)

Attending: Committee members, AERES scientific delegate

12:15 *Thanks and leave of the committee*

12:30 *End*

6 • Supervising bodies' general comments

Université Montpellier 1

AES Droit, Sc. politique Économie IPAG ISEM Médecine Odontologie Pharmacie STAPS

nouvelle université de Montpellier
un projet, une ambition

Monsieur Didier HOUSSIN
Président de l'AERES
Monsieur Pierre GLAUDES
Directeur de la section des unités de recherche
Agence d'Evaluation de la Recherche et de l'Enseignement Supérieur (AERES)
20, rue Vivienne
75002 PARIS

Montpellier, le 5 mai 2014

Référence : C. ROYER/Ch. ROUMESTAND : S2PUR150008478 – CBS – Centre de Biochimie Structurale - 04342321N

Messieurs,

Je tiens à remercier le comité de visite AERES pour la qualité de son rapport d'évaluation concernant le Centre de Biochimie Structurale dirigé par Monsieur Christian ROUMESTAND.

J'ai bien noté les remarques formulées par le comité de visite et je veillerai à ce que celles-ci soient prises en compte par le directeur de cette structure de recherche.

Vous trouverez ci-joint les commentaires du directeur de l'unité de recherche auxquels je n'ai rien à rajouter.

Je vous prie d'agréer, Messieurs, l'expression de mes salutations les plus respectueuses.

Philippe AUGE
Président
Université Montpellier 1

CENTRE DE BIOCHIMIE STRUCTURALE

CNRS UMR 5048 / INSERM U1054 / UM1 / UM2

Prof. Christian ROUMESTAND
Centre de Biochimie Structurale
UM1/INSERM UMR 1054
UM1/ CNRS UMR 5048
29 rue de Navacelles
34090 Montpellier Cedex

Tel : +33 (0)4 67 41 77 04
Fax : +33 (0)4 67 41 79 13
e-mail : christian.roumestand@cbs.cnrs.f

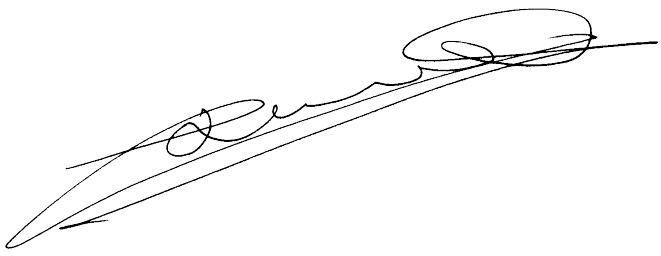
Montpellier, Le 18 Avril 2014

Dear Committee,

The CBS directors would like to acknowledge all the members of the AERES committee for their evaluation. In general, we agree with the points taken up by the AERES committee, with the notable exception of what written for Team 3 (Team Leader: Patrick Bron): in our opinion, the committee quite rightly stressed some existing weaknesses of this “young “team (started in 2010), without addressing adequately the strengths (installation of a new technology in the lab involving heavy instrumentation, found raising, involvement in master courses…). These points are developed in detail below, as well as specific comments concerning the evaluation of Team 5 and 8. We added also a small remark concerning the “introduction” chapter that concerns the whole unit.

Sincerely,

Le directeur de l’Unité 1054 / UMR 5048



Prof. Christian Roumestand

- Introduction
3. Detailed assessments.
Assessment of the unit's academic reputation and appeal, last paragraph.
"In this context, one may cite the higher visibility of the super-resolution microscopy domain".

I assume that the committee would say "advanced microscopy domain"? The "super-resolution" microscopy domain concerns essentially M. Nollmann (29 talks) in Team 6. During the period, E. Margeat and PE Milhiet also gave 16 and 42 talks respectively, on "advanced microscopies " (Atomic Force Microscopy, spFRET, Single particle tracking), which are not classified as "super-resolution".

- Team 3:
We think that a number of important points concerning the « Multi-Scale structural Biology » (MSSB) team have been either missed or not sufficiently stressed in the AERES report. With this letter, we would like to address these points in order to present a clearer view of the MSSB team activities. As a matter of fact, the team was effectively created in 2010 (and not in 2008 as stated in the AERES report) and one of its major achievements has been the establishment at the CBS of a new experimental technique, namely the cryo-electron microscopy (cryo-EM), and the setup of the corresponding technically "heavy" instrumentation.

During the year 2009, Patrick Bron has installed cryo-EM and all associated equipment dedicated to this new technology. This installation represents a financial investment of more than 1.2 M Euros shared by INSERM and CPER Languedoc-Roussillon. In this context, it is worth noting that **MSSB team started from scratch**, and that in a very short time it has been able to optimize all steps of the cryoEM single-particle analysis method, allowing us to investigate biological complexes at high resolution by **hybrid methods**. This has led to the publication of a CryoEM three-dimensional reconstruction of a biological particle with the best resolution ever obtained using data entirely collected and processed by a French laboratory.

Installation of cryo-EM at the CBS was accomplished in tight partnership with INSERM and CNRS and one major condition imposed by both funders was to open this heavy instrument to the French scientific community through platform activities. Indeed, Patrick Bron was recruited as CR1 by one of the funding institutions (INSERM), whereas CNRS recruited a research engineer for the EM platform. Surprisingly, it appears in different places in the AERES report that platform activities in cryo-EM and X-ray crystallography (the two major techniques used by MSSB team) seem deleterious for the scientific reputation of the team and for leadership recognition. Instead, we consider that opening such technologies to the national scientific community is mandatory for the realization of larger interdisciplinary projects. Often at the expense, of course, of a "good" position in the authors list when the work is published… However, we would like to point out that, since the "Multi scale structural biology" group creation in 2010, we have published 23 articles: **9 of them have an impact factor superior to 9**, in 6 of them we are either first or last author and corresponding author in 3.

Another positive point that should be mentioned is our capability **to raise funds**, as a result of our active policy in interacting with national organisms and private companies. Thus, from 2009, we have been able to raise more than 300 KE from various sources (ANR, PIR, PEPS, BUSR…). Moreover, the AERES report does not mention that we have developed a service contract with Sanofi Montpellier in partnership with INSERM Transfer.

Concerning the team's involvement in training through research, the AERES report suggests a relationship between the EM installation and the fact that we got only one PhD student over the evaluation period. The small number of PhD students is a general problem that concerns the whole structural biology community that fails to attract a sufficient number of students. This problem is probably more acute in Montpellier where the Science teaching in Biology is "historically" oriented toward Cell Biology… Nevertheless, we would like to stress that during the period of evaluation, the team hosted two post-doctoral students, one PhD student and 5 Master 2 students. In addition, a

member of the team (Stefano Trapani) is assistant professor at the University of Montpellier II and responsible of several teaching units in different master courses.

- Team 5:

We would like to bring to the attention of the AERES committee the fact that two important research themes which confer both originality and visibility to our team have not been mentioned in its report:

In 2010 Team 5 has launched an innovative research project which tackles major **public health** and **environmental** issues related to the deleterious interference of **environmental pollutants** with the endocrine system of humans and animals. More specifically, the team uses a unique combination of leading-edge structural, biophysical, bioinformatics, cell-based and in vivo technologies to better understand, and in turn better predict, how a given chemical (or a mixture of chemicals) found in our daily environment (e.g. bisphenol-A, pesticide, phthalate,…) can substitutes for natural hormones and deregulate the normal function of their intracellular receptors. Commonly referred to as endocrine disruptors, these compounds are highly suspected to produce a range of developmental, reproductive, neoplastic, or metabolic diseases. Due to its originality and international recognition, this project benefits from excellent funding [2 ANR, 2 Plan Cancer Inserm, 1 PNRPE (Programme National de Recherche sur les Perturbateurs Endocriniens) and 1 ANSES (Agence Nationale de SEcurité Sanitaire de l'alimentation, de l'environnement et du Travail)], scientific output [PNAS, EMBO R., 2 EHP (a leading journal in the field of environmental sciences), 1 Toxicol Sciences, 1 book chapter and two reviews)] and visibility (7 invited communications in national and international conferences over the 2010-2013 period). As a result we are now part of an international consortium, in charge of the structural aspects, which recently applied to the Horizon 2020 call SFS-12 through the project SFERA (Safety of Food via combined Exposure and Risk Assessment).

In tight connection with the above theme, Team 5 also engaged a long-term program related to **drug-design** by developing a novel approach combining **bio-compatible chemistry** and **in situ diffraction**. This is providing the CBS with a unique expertise in the growing and highly-competitive field of Structure-Based Drug Design. This specific position has been recognized at the national level (by selecting the CBS to develop these techniques within the infrastructure FRISBI) and it also led to the creation of the start-up AGV-discovery.

Lastly, it is mentioned in the paragraph "Assessment of scientific quality and outputs" that: "There appears to be an underrepresentation as last author of unit members on these publications." We may agree with this comment. However, it would be worth noticing that this is rather well balanced by the number of patents (5) and our significant and fruitful involvement in platform activities (development and services in both bioinformatics and X-ray crystallography). Accordingly some papers are not yet published due to pending patent applications while in the context of a platform work we favor our collaborators as last author (e.g.: 7 such publications in bioinformatics and 4 in X-ray crystallography).

- Team 8

We would like to argument that the biological topics are not as broad as pointed by the committee. We mainly addressed two main topics i) Regulation of gene expression and ii) Structure and Dynamics of Membrane Assemblies, which are both currently very active in terms of publications and funding attractiveness.

Gathering the different people of Team 8 is also based on a network of collaborations covering shared methodological developments (TIRF single molecule setup, advanced data analysis, two-photon FCCS), human resources (Caroline Clerte and Patrice Dosset - engineers) and biological topics (tetraspanins, GPCRs, transcription termination). This led to several common publications in high impact factor journals (JCB, Traffic, EMBO Reports, Molecular Microbiology, NAR, Ann NY Acad Science).

We really think that our internal collaboration within the team is a key element to maintain our ability to tackle major biological problems using the advanced biophysical methods that we develop together.