Laboratoire de chimie des métaux en biologie

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Laboratoire de Chimie et Biologie des Métaux, UMR 5249

From the

CEA

CNRS

Université Joseph Fourier

May 2010

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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

May 2010

Research Unit

Name of the research unit: Chimie et Biologie des Métaux

Requested label: UMR

N° in the case of renewal: 5249

Name of the director: M. FONTECAVE

Members of the review committee

Committee chairman:

M. P.J. DYSON, EPFL, Lausanne

Other committee members:

M. J. STILLMAN, University of Western Ontario, Canada

M. I. SCHALK, CNRS, Strasbourg

M. A. EDELMAN, Faculté de Médecine site Necker, Paris

M. J.F. MOUSCADET, CNRS, Ecole Normale Supérieure

M. J. STURGIS, University of Aix-Marseille 2

M. B. GUIGLIARELLI, University of Aix-Marseille 1,

L. CASELLA, PROFESSOR, University of Pavia

Committee members suggested by CNU, CoNRS, CSS INSERM, CSS INRA, INRIA, IRD:

M. C. POLICAR, (CONRS)

M. C. GRECK, (CNU)

Observers

AERES scientific advisor:

M. R. RÉAU

University, School and Research Organization representatives:

M. G. MASSIOT, Directeur Scientifique Adjoint, Institut de Chimie, CNRS

M. E. SAINT-AMAN, Université Joseph Fourier

MR. J.-C. CINTRAT, CEA

Report

1 • Introduction

The visit was held between 8 and 10 February 2010. The program began with presentations from the director of the unit and then his successor. This was followed by a discussion with the Laboratory Council (without the directors) and then presentations describing the performance of the unit over the evaluation period and a general presentation on the new projects. The committee also met with the main funding partners of the unit. On February 9 the evaluation committee divided into two groups, which then met with all the teams of the unit. This part included presentations, posters and discussions. The committee members were given sufficient time to ask detailed questions after each presentation and were also provided with copies of all the presentations given during the evaluation process. It should be noted that the information provided was extremely helpful to the committee and has greatly facilitated the evaluation process. February 10 was reserved exclusively for a meeting of the evaluation committee members who had held shorter private meetings on the previous two days.

The unit was created in 2007 from the amalgamation of three units, and another team subsequently joined the unit thereby forming the largest entity within the Institute of Research on Technology and Science for Life. The unit is now undergoing a major restructuring/reorganization and the details of this will be provided later in this report. The unit is located at the CEA. The research domain of the unit is concerned with the chemistry and biochemistry of metals in biology in the broadest sense, spanning fundamental science to applications and technological issues. The activities of the unit correspond to priority areas for the university, e.g. Pole 'Chemistry, Life science and Health, Bioengineering', PhD program 'Chemistry and Life science'.

The unit is managed by a Director and a Deputy-Director. They are assisted of an Administrator. There is an executive board which is composed of the team leaders. There is also an elected Council of the Laboratory. The interaction between the various bodies appears to be very good.

- 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)	8	9
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	27	29
N3: Number of other researchers (Forms 2.2 and 2.4 of the application file)	2	-
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	13,3	13
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		1
N6: Number of Ph.D. students (Form 2.7 of the application file)	16	9
N7: Number of staff members with a HDR or a similar grade	21	22

2 • Overall appreciation on the research unit

• Summary

The unit is world class with a very high international standing. The research of the unit is of a very high quality. The unit is unique in that it is highly multidisciplinary, studying the role of metals at a molecular (chemistry) level that are involved in biological processes. While many groups around the world study topics covered by this unit, none compare in terms of the size and diversity of this unit. Fundamental research and applied research are covered by the unit and it benefits from strong underlying core facilities. The unit has competences that do not exist, within the same unit, elsewhere in France. The structure of the unit has undergone a transformation and the new structure provides a greater integration of the unit activities, leading to a much better coherence and mass. Moreover, a refocusing of the research activities into highly important topics in the energy and health domains should help to meet the challenges facing society. High level research in chemistry, physical chemistry, organic chemistry, biochemistry and biophysical chemistry, cell biology is undertaken. Key collaborations allow a large range of topics to be studied, especially in terms of applied research. The interdisciplinary research at the interface of chemistry, biochemistry and biology provides a unique training environment for young researchers, many of whom have flourished within the unit. The unit has a strong management structure and clear vision.

• Strengths and opportunities

- Unique research activities at the interface of chemistry and biology focusing on the vitally important biological role of both essential and toxic metals.
- Excellent management/organization with an improved structure that should increase the dynamics of the unit.
- Excellent infrastructure with some unique competences.
- Very strong local support from the university and also from the CNRS and CEA.
- Very high quality of publications, e.g. in Science, Nat. Chem. Biol., PNAS, J. Am. Chem. Soc and Angew. Chemie.
- High international reputation and visibility.
- High success rate of funded research projects (contracts).
- Reorientation towards high priority projects in nanoscience, health and energy.

• Weaknesses and threats

- Lack of adequate laboratory space as well as appropriately located office space for the Physical Chemistry of Metals in Biology team affects scientific productivity.
- Loss of support/technical staff could reduce productivity.
- Access to instrumentation outside of the unit can be problematic.

- Recommendations to the head of the research unit

- To find a solution to the location of offices of the 'Physical Chemistry of Metals in Biology' team as urgently as possible and to obtain additional laboratory space to allow the installation of new equipment.
- To find a solution to the reduced number of technical support staff – the understaffing appears to the committee to be problematic currently and could become critical in the near future.
- Such an outstanding research unit deserves a larger audience at the Université Joseph Fourier and more of the team members should be encouraged to participate in teaching.
- To seek more funding at the European level, at least two of the team leaders are at the level of advanced ERC awards.

- Production results

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

A1: Number of lab members among permanent researchers with or without teaching duties who are active in research (recorded in N1 and N2)	38
A2: Number of lab members among permanent researchers with or without teaching duties who are active in research (recorded in N3, N4 and N5)	14
A3: Ratio of members who are active in research among staff members [A1/(N1+N2)]	100%
A4: Number of HDR granted during the past 4 years	6
A5: Number of PhD granted during the past 4 years	35
A6: Other relevant item in the field: non publishing permanent	2

3 • Specific comments

- Appreciation on the results

The unit is engaged in research at the interface of chemistry and biology and spans basic research through to applications. The underlying theme is the role of metals in biological systems. The combined activities of the unit make it unique in terms of the size and range of interconnected projects undertaken and the level of originality is high. Certain facilities, such as Mössbauer spectroscopy, allow experiments to be undertaken that can only be performed in a few labs throughout the world – only one other such facility in Europe. The research is highly relevant to many topics, including health, the environment and energy. The very high quality and impact of the research is evident from the quality and number of publications and conferences emanating from the unit (see below).

The productivity and quality of the unit is very high: 175 papers plus 40 more from members who joined after 2005. The output of publications exceeds 1 publication/researcher/year. However, the quality is extremely high: 2 Science, 2 Nature Chem. Biol., 5 Angew. Chemie, 5 Proc. Natl. Acad. Sci., USA, 4 J. Am. Chem. Soc. Members of the unit have presented results at a large number of national and international meetings and have also organized a number of scientific meetings. 28 PhD thesis have been produced during the reporting period and 18 post-docs have worked in the unit, these collaborators have a very high rate of employment or further study on leaving the unit (ca. 94%).

The unit is weighted towards fundamental research although it has strong interests in applications. Most of the applied studies are conducted with other academic research groups and also some other government funded organizations. The unit produced 2 patents during the reference period and it appears more are in the pipeline. Increasing efforts towards applied studies are planned by various teams in the next quadrennial project.

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

The director of the unit has been elected to the College de France and is a member of the French Académie des Sciences. Several members of the unit are associated with the editorial boards of international journals. Members of the unit were invited to present lectures at >60 international conferences at ca. 70 scientific centers and a considerable number of oral communications at international and national conferences. The unit has also organized 19 scientific meetings and in 2013 will host the largest international conference on metals in biology (ICBIC) with more than 1000 participants expected.

The unit is successful in recruiting high level scientists – in the last period at the postdoc and PhD levels. It is clear that the scientists are highly motivated and productive. It is less easy to judge the percentage of scientists from abroad, from the names of the post-doctorals and students it is probable that some are foreigners, but precise numbers cannot be given.

The unit has an extremely good track record in obtaining competitive funding, with 34 on-going contracts. For the last two years their contracts now exceed the recurrent funding. For ANR contracts, in 2008 the success rate was 36%, this level being considerable higher than the national average. The unit is embedded within a significant European pole of research on metals in biology, e.g. the Institute of metals in Biology of Grenoble, Integrated functions of proteins from life to nanotechnologies, NanoBio and the Grenoble institute for Cancer. Industrial partners support some of the projects within the unit.

The unit has a large number of international scientific collaborations, with the majority in Europe and the USA, but also with Canada, India and South America. The unit is also involved in numerous national scientific networks concerned with both scientific topics but also techniques.

The main way in which the unit has exploited the value in their research has been through collaborations, it should be noted that the fundamental research undertaken facilitates others working on biomedical and environment applications. The personnel of the unit also popularize science to the public with seminars in the Palais de la Découverte, Science Festival and one member publishing in 'la Recherche'.

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

The organization and management of the unit by the director have been excellent. The Director/Deputy-Director, Executive Board (team leaders) and Council of the Laboratory each play a determining role. The discussions that the committee had with the Council of the Laboratory indicate that communication is very good and that the goals and needs of the unit have been identified and discussed. The Council of the Laboratory appears to appreciate the direction of the unit. Communication of the unit in a broader sense is also very well done, as evidenced by the strong support the unit receives from the Université Joseph Fourier, and support of the CNRS and CEA.

The unit organizes many scientific events, about 4 per year, at the national and international level, which helps to provide considerable visibility. The unit is involved with the organization of weekly seminars for young scientists as well as the organization of seminars by distinguished guests. The unit also participates/organizes a biannual international scientific meeting of the Institute for Metals in biology. The organization of ICBIC-16 in 2013 will further improve the international recognition of the unit.

Just over 30% of the unit members are involved in teaching, mainly at the Université Joseph Fourier. All types of courses at all levels are provided. Practical courses, tutorials and lecture courses are given to bachelor, master and doctoral students, with the emphasis to more advanced courses. The unit contributes to the life of the school in other ways such as participation on examination committees.

- Appreciation on the project

The new structure of the unit has been carefully planned in a logical manner that will enhance the scientific aims of the unit as a whole. In the new structure there are 6 main teams (see individual reports below). One of the teams provides a proteomics platform that will benefit many of the projects in the other teams and the Mössbauer facility within one of the teams is also of critical importance to other teams in the unit. There is also a group of theoretical chemistry and modeling that supports the projects of the other teams. In addition, many other interactions/collaborations between the teams can be expected and certain shared resources help to make the scientific projects feasible. The improved structure should further enhance an already dynamic and strong unit. The new projects expand on the strengths of the unit, but at the same time, the unit has made considerable efforts to redirect its areas of expertise into highly relevant and important topics of our time, i.e. in energy, the environment and in areas of health, including neurological diseases and cancer and the effects of nanoparticles on humans. It is important to note that the strength of the unit is in studying the highly complicated role of metals in biological systems, which requires expertise in spectroscopic tools, proteomics, molecular biology, biochemistry, synthetic chemistry etc. The expertise in these areas gives the new projects a very high chance of success.

Resources are extremely well balanced in the new structure, in terms of both equipment and human resources. It should be noted that the unit increasingly relies on contract funding and has adapted very well to this new challenge. The ratio between directors of research and researchers is ideal but the level of support from technical staff is subcritical and is considerably lower than the national average (average researcher: technician in the unit in 2011 = 2.9 versus an average of 1.5 for an interdisciplinary laboratory in the CNRS). However, the unit has and is trying to improve this situation and support from the funding agencies needs to be provided. There is a transparent common budget for expensive/shared equipment and for the maintenance of such equipment. In addition, certain general consumables such as gases, solvents, enzymes etc are provided within the framework of a common budget.

A number of innovative projects have been proposed by the unit that profit from the strong competences of the unit but address topics of increasing national and international importance. The reorganization in the structure of the teams has been adopted to thoroughly address the objectives of the new projects. The originality of these projects comes, to some extent, from finding highly important topics in medicine, energy, environment etc, and basing them within the expertise of the unit with a clear focus on the role of metals. The multidisciplinary approach that has been proposed to study the projects is also original and gives the team a considerable advantage over the majority of its competitors. The diversity of the projects is also very broad but compatible with the size of the unit.

4 • Appreciation team by team

Title of the team: BIOCATALYSIS

Name of the team leader: M. Marc FONTECAVE

- 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	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	7	8
N3: Number of other researchers (Form 2.2 and 2.4 of the application file)	16	0
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	1
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	10 (4)	2
N7: Number of staff members with a HDR or a similar grade	6	7
Post Doc	12	3

- Assessment of work produced and scientific quality

The Biocat team consists of 10 staff members, including researchers and teaching researchers, all of them participating to the authorship of the publications of the group. Although there will be some significant reorganization in the entire UMR, this team will maintain the same consistency in the next quadrennial period. The scientific activity of the team focuses on the development of several parallel research lines, addressing both fundamental problems and more applied topics of modern bioinorganic chemistry, in all of which transition metal ions play a central role. The diverse research lines can be grouped into four major topics: metals and biotransformation of macromolecules (formerly iron-dependent radical enzymes), assembly of metallic sites, metals and stresses (formerly the antioxidant enzyme superoxide reductase), and metals and hydrogen. The topics are actually intermingled, with an increasing interchange of competence between the participants, also because of the strong interdisciplinarity existing in each research line. The richness of the expertise existing within the group, spanning from organometallic catalysis and synthetic coordination chemistry to molecular biology and microbiology, is unique at the European level and constitutes an important added value for the team.

The scientific results obtained by the Biocat team are outstanding, both in qualitative and quantitative terms, and are documented by a number of indicators. In the last quadrennial period the team published more than 70 original papers, a remarkable number of which are in journals of high impact factor, and with a global average impact factor above five, which poses the team at the highest international level. The research efforts have been made possible also thanks to a large number of grants and fellowships (14) that members of the team have been able to obtain from different agencies.

- Assessment of the influence, appeal and integration of the team in its environment

The outstanding scientific quality of the research carried out by the team is testified by the large number of invitations to international conferences (35), which reflects its high visibility and international recognition. The attractiveness of the team is further confirmed by the number of doctoral (10) and postdoctoral (12) students, including several foreigners, that worked in the team during the period covered by this assessment (2005-2009). The collaborations of Biocat with other teams in France, other European countries, and in the U.S.A. are also numerous and active.

- Assessment of the strategy, governance and life of the team

The reorganization that the team will undergo in the next four years appears to be fully functional to the new scientific tasks. In particular, the integration of two new research scientists with experience in synthetic chemistry and microbiology will further broaden the expertise of the team and strengthen its scientific potential. The planned redistribution of human resources meets the objective of equalizing the critical mass of research effort along the main research lines, with a better chance to render each of the subgroups competitive at the highest scientific level. Again the strong interdependence between parallel research lines constitutes an added value for the team.

- Project assessment

The projects proposed by the Biocat team extend on some of the themes successfully developed in the previous quadrennial period, with the objective to address several issues and unsolved problems, such as unraveling the complex protein machinery which controls the assembly of iron-sulfur centers, but notably introduces several innovative themes in line with the emerging requests from society. The emphasis given in the project to new perspectives in green chemistry, alternative energy sources, health, and toxicology completely responds to this growing request. The competence existing in the team, the good command in the approach to interdisciplinary research, and some preliminary but already important results recently obtained by the group and thorough management of the projects is an excellent indication that the more ambitious objectives will be achieved.

- Conclusion

The Biocat team has outstanding productivity, excellent international recognition and visibility, which makes it one of the top European research groups at the interface between chemistry and biology.

Strong points of the team are certainly the interdisciplinary expertise and the opportunity for most of the members to contribute to more than a single research line, enforcing the mutual benefits of the collaboration. In addition, the research projects have important applicative perspectives.

– Recommendations

To the group: Maintain the high level of the science and productivity, and the collaborations with the other teams in LCBM, and encourage the taking out of patents.

To the funding agencies: Provide a position for a technician (ITA) to strengthen support to the research activities.

Title of the team: BIOinorganic Catalysis and Environment (BIOCE)

Name of the team leader: M. Stéphane MENAGE

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

	Past CRBio + BHAM	Future BIOCE
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2 + 1	3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2 + 2	3
N3: Number of other researchers (Form 2.2 and 2.4 of the application file)		
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2 + 1	2 (1)
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	2,5 + 4	3
N7: Number of staff members with a HDR or a similar grade	4 + 0	1

Two researchers of the team BHAM (Biodégradation des Hydrocarbures Aromatiques et Métalloenzymes) join the team CRBio (Chimie Rédox BIOinspirée) to create the new team BIOCE.

Comment N4 : C.Falco (N4 will be 1) will retired in september 2010.

- Appreciation on the results

The research developed by both teams (this team is based on the merger of two teams) is original and the quality of the results is good. The research interests cover the fields of chemistry and biochemistry: the design of new catalysts for enantioselective oxidation and bacterial biodegradation of polycyclic aromatic hydrocarbons. The number of the publications is satisfactory and the impact factors of the journals are good. The evolution is positive and the last few papers have been published in high-level international journals. Four PhD students completed their thesis examination between 2005 and 2008.

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

The members of team have given invited conferences at international and national meetings and seminars in scientific centers. The CRBio team has been able to attract new scientists: a CNRS technician in 2006 and a CNRS researcher (CR1) in 2008. Actually, three PhD students are working in the new team BIOCE and one is co-directed with ENS Lyon. Four Post-Doctoral researchers collaborated or collaborate with the team. The ability to raise funds was confirmed by five successful proposals (ANR, CEFIPRA, Région Rhône Alpes). The team has several national and international collaborations.

- Appreciation on the strategy, management and life of the team

The merging of the two former teams (BHAM and CRBio) into a larger team is justified by the similarity in the research objectives and the gain of a good balance between the expertise in chemistry and biochemistry that should substantially increase the scientific impact of the new team. The team is well organized and managed. The members are involved in the organization of scientific meetings and certain members of the team participate actively in teaching and contribute to the organization of research at the local level. The direction of the unit (UMR 5249) will be undertaken by the team leader.

- Appreciation on the project

The scientific projects are well structured and combine the expertise of chemists and biochemists for a better understanding of dioxygen activation and for the design of bio-inspired inorganic systems. The objectives are original and clearly developed, for example, understanding the reactivity of iron metalloenzymes at the molecular level and subsequent development of new solutions for asymmetric catalysis based on such enzymes.

- Conclusion:

A new team has been created that combines chemists and biochemists. Their research interests are centered on dioxygen activation and bioinorganic systems. The team members are young and dynamic. They are well involved in the life of the research unit and in teaching at a local level.

– Strengths and opportunities

The double expertise in chemistry and biochemistry of the team will be a strength for the future and the realization of the project. Several grants were obtained to promote the development of subjects at the interface.

– Weaknesses and threats

The scientific production should be reinforced.

– Recommendations

The team should make efforts to fully integrate the two former teams to produce a cohesive research environment.

Title of the team: Physico-chemistry of metals in biology

Name of the team leader: M. Jean-Marc LATOUR

- 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	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	4
N3: Number of other researchers (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)	4,5	4,2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	1
N7: Number of staff members with a HDR or a similar grade	3	2
Post Doc	3	

Administrative staff : the 0.5 is for the secretary that was part-time in the lab (all mornings). Now, this is only 20 %, hence the 0.2

- Appreciation on the results

During the reference period (2005-2008) the team published 14 papers in very high impact factor journals (average impact factor of about 6, note that these 14 publications are those within the group, and do not take into account the publications from former members for newcomers). Their research interests cover a wide range of topics in the field of metals in biology, from the biochemistry of metalloproteins including Fe-S clusters and Zn fingers, modeling of metalloproteins with peptides (Zn(Cys)4 project), small complexes as catalysts (bimetallic complexes project), all of which are supported by a strong expertise in physico-chemical methods related to magnetochemistry (Mössbauer, EPR, magnetic measurements). This diversity is possible through the interdisciplinary nature of the group that has expertise in chemistry, biochemistry, spectroscopy and physics. Some very challenging original research projects have been funded, and have flourished, partly due to the engagement of two new young and dynamic researchers. Moreover, the Mössbauer spectroscopy unit is dedicated to studying biological systems and the competences of this facility are unique in France, and are recognized worldwide, as indicated by strong international collaborations. Three PhD students completed their thesis examination between 2005 and 2008.

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

During the reference period, the team was able to attract a new scientist and recruit a young scientist and two technicians. Members of the team gave conferences in international and national meetings, and at foreign research centres. The Mössbauer facility was reshaped with the arrival of new instruments. Their specificity for biological samples has already induced new collaborations from all over the world (France, England, Korea, Japan, Portugal). There are at most 4 comparable facilities worldwide and it is clear that the facility run by this team has a high international visibility within the community. As an additional asset, a contract with EDF brings some financial support. The team successfully raised external funding (4 grants from ANR, CEFIPRA, CIBLE).

- Appreciation on the strategy, management and life of the team

During the reference period, the team has experienced a profound reorganization in terms of staff and available machines. The development of the Mössbauer facility is a pertinent scientific strategy in the context of the unit and it will extend the possibilities of external collaborations for the team.

Researchers are involved in long-term teaching, administration and research. The efficiency of team is reduced by the separation of the laboratories/central administration from the offices and this situation urgently needs to be improved.

- Appreciation on the project

The projects are highly interesting and represent a balance between scientific individual projects and the development of the Mössbauer facility. Fundamental spectroscopic projects have been encouraged so that the facility does not become a service facility. In parallel, cutting edge projects of young researchers were have been encouraged and supported.

- Conclusion:

The team is a well-known, outstanding group that has many new highly interesting projects. The team has wisely invested in a unique Mössbauer facility dedicated towards the study of biological samples. It should be noted that there is only one other comparable laboratory in Europe. They have been able to support new emerging themes.

– Strengths and opportunities

- New challenging projects with interesting possible connections within the team and also with other teams in the unit.
- A capacity to support young researchers and their projects
- A unique Mössbauer facility in France
- A strong expertise at the frontier of biochemistry, chemistry and physical-chemistry

– Weaknesses and threats

The main threat is for the team to conduct projects in domains where the researchers of the group will not be seen as leaders, especially for all young researchers of the group.

– Recommendations

To ensure the durability of the group a solution has to be found with regard to their installation close to the Mössbauer lab and close to the rest of the unit.

Title of the team: Proteomics and cell differentiation

Name of the team leader: M. Thierry RABILLOUD

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

- Appreciation on the results

The research developed by the team is of the highest importance for applications of proteomics in different fields of biology. The team headed by a DR2 CNRS, includes 1 CR1 INSERM 2 CR CEA 1 MCU and 2 Technical staff. The current organization of the team results from a major redefinition of a former immunology laboratory. This was undertaken to promote a rational clustering, based on a methodological synergy. Two teams of this lab teamed up in 2007 to form the Proteomics and cell differentiation team. Another CR CEA is going to join this team for the next period. This team may be considered as a world leader, having developed a comprehensive set of 2D electrophoresis techniques devoted to proteomics studies. The current applications are in basic biology projects, in particular in the field of immunology, but can be extended to translational studies. The unique expertise of the team is reflected by its outstanding contribution in this domain over the last period. The scientific contributions amounted to 27 articles, 3 reviews and 5 book chapters in top-ranked peer-reviewed journals (4 Mol. Cell proteomics, 8 proteomics, 1 J. Immunol. and 1 Nature Biotech).

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

The team leader is the associate editor of the J. Proteomics and editorial board members of Mol. Cell. Proteomics, both journals being the principal publications in the field, and has also played a major role in Human Proteome Organization. Owing to its visibility, the team has developed a network of collaborations at the national level and plays a structuring role in this domain. Its members are regularly invited in national and international conferences. Since 2007, the team has secured its funding via one ANR program and a regional program.

- Appreciation on the strategy, management and life of the team

Although small, the team is remarkably organized, each member supporting one aspect of the collective work. The arrival of a new researcher who brought to the team a significant expertise in molecular immunology enhances significantly its potential to carry out projects in fundamental biology.

- Appreciation on the project

Owing to its integration into the new unit, the team has developed two, very original, new axes of research. Preliminary results obtained guarantee the feasability of the projects. The first project focuses on proteomics studies of cells subjected to a metallic stress. The second concerns the study of cytotoxic effects of metal nanoparticles in myeloid cells which are the main scavengers of such particles. These projects fit perfectly into the theme of the new unity and already involve several local collaborations. The team also has solid expertise in immunology, enabling it to develop cellular models of interest which perfectly complement those available in the host laboratory. In return, the projects have been developed to take full advantage of the expertise available in other teams especially in the field of chemistry of metals.

- Conclusion:

This is an internationally renowned team with an outstanding leader, whose arrival in the unit provides a great opportunity to open new avenues of research in the field of the impact of metals on biological systems.

– Strengths and opportunities

- A unique expertise.
- Proprietary techniques that were developed recently providing the team with a competitive advantage.
- A set of competencies encompassing proteomics methods and expertise in immunology.
- A world renowned team leader.

– Weaknesses and threats

The limited opening of the team that hired relatively few students and postodocs so far could potentially limit its ability to conduct in-depth projects in fundamental biology.

– Recommendations

The team should develop further collaborations within the unit, especially with the biology-oriented teams that could provide interesting opportunities.

The team should seek more funding and try to recruit more young PhD students and postdoctoral collaborators.

Title of the team: Amyloid fibers: from foldopathies to Nano-design

Name of the team leader: M. Vincent FORGE

- 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	3
N3: Number of other researchers (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)	2	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	2
N7: Number of staff members with a HDR or a similar grade	1	1
Post Doc	1	

V Forge has passed his HDR at the end of 2009.

- Appreciation on the results

The members of the team have been very active with 15 publications in internationally recognized journals. The articles include all the major research themes tackled by the group over the period, including amyloid formation, interactions between proteins and membranes. Particularly noteworthy are their contributions to interaction and folding studies using time resolved NMR techniques. Overall, the period has been a productive one with much good science and excellent results. Many of the groups projects have been, and are currently, funded through grants and industrial contracts – and this situation seems likely to continue in light of the group dynamism and interest in industrially relevant topics.

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

The team is young and dynamic, including young students and post-docs as well as mature researchers. The team and its members have a good visibility in the field of protein denaturation and amyloid formation. This visibility has helped them obtain several contracts, but has not yet resulted in many international invitations or collaborations.

- Appreciation on the strategy, management and life of the team

The team has very clear goals and interests that are evolving. There is a clear strategy and a subject shift in the proposed project moving away from protein-membrane interactions towards bio-technology and nano-technology using protein engineering and the group expertise in amyloid formation and protein denaturation.

- Appreciation on the project

The projects are based on the development of the teams on-goings interests in protein denaturation and amyloid formation. The subjects proposed include studies of protein denaturation, protein engineering for nano-technology and biological aspects of amyloid formation. The different subjects go well together, due to the group strength in previous studies, and share a clear technological interest.

- Conclusion:

The Amyloid fibers group has a clear strategy, a good record and is expected to have a productive future, both in terms of academic scientific articles and patents.

– Strengths and opportunities

- Clear strategy and scientific plan.
- Dynamic approach able to attract funding and students.
- Approach likely to interface well with industrial interests.

– Weaknesses and threats

Interest in "Metals in Biology" is not fundamental to their studies and so perhaps slightly subsidiary to their main interest in amyloid and protein nano- and micro-objects.

– Recommendations

Possibly reinforce the links with other groups in the unit and increase the number of international collaborations.

Title of the team: Theoretical Chemistry and Modeling

Name of the team leader: M. Serge CROUZY

- 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)	2	1
N3: Number of other researchers (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)	0	0
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	2,5	0,5
N7: Number of staff members with a HDR or a similar grade	1	1
Post Doc	1	

Y Moreau has joined the group in October 2009.

- Appreciation on the results

Between 2005 and 2008 members of the theoretical chemistry and modeling team have published 7 papers in internationally recognized journals. The articles include a mixture of those in which molecular modeling has brought insight to collaborating biologists and chemists, and more fundamental articles driven by team members aimed at the molecular modeling community. The group has had a clear capacity to attract funding not only as a partner for biological projects in need of a molecular modeling expertise but also within consortia of theoretical and computational chemists.

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

The team is well integrated in the unit and local environment with many collaborative projects. There is also a certain national visibility within the network of computational chemists. However, there is little effort to make the team particularly attractive or to generate international visibility, for example, through participation in international events.

- Appreciation on the strategy, management and life of the team

The team's position within the unit needs to be more clearly defined: is it a service or a research group, and are its scientific objectives method development or method application to biological and chemical problems? With limited resources, it is difficult to advance rapidly on both fronts although the arrival of a new young researcher brings new expertise and significantly increases the possibilities for new and interesting projects.

- Appreciation on the project

The projects presented by the group include many exciting prospects that combine the expertise of the different members of the group and interface well with several of the other teams in the unit. The combination of subjects in the proposal includes a good mixture of low risk and high risk/high reward subjects. The subjects integrate very well into the unit and allow collaboration both with the more chemical and more biological teams to answer chemically and biologically relevant questions.

- Conclusion :

The team has a good record of publications both in collaborations with other teams and on their own right, they have exciting new projects based on the combination of older and more recently acquired competence.

– Strengths and opportunities

- Good projects being developed in collaboration both with other teams in the unit, and through national collaborations.
- Possibility of developing the exciting interface chemistry-QM-MM-biology in the context of the laboratory.

– Weaknesses and threats

- Unclear position and role within unit.
- Poorly defined management of resources and personnel should be improved to avoid dissipation on multiple projects.

– Recommendations

- Define more clearly the role of this team and its relationship with the other members of the unit and clarify the scientific priorities of the group and improve local collaborations in the domain.
- Increase international visibility and improve attractiveness to students and post-docs.

Title of the team: Biologie des Métaux: BioMet Team leader

Name of the team leader: M. Jean-Marc MOULIS

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

	Past(2005-09) TRIM + CaFe	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1 + 0	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	5 + 4	6
N3: Number of other researchers (Form 2.2 and 2.4 of the application file)	0 + 1	0
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file) Here 3,5 accounted for one hiring compensating one retirement	1,5 + 0.5	2
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0 + 0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	11 + 4	3
N7: Number of staff members with a HDR or a similar grade	4 + 2	7
Post doc	3 +1	

- Appreciation on the results

The team recently formed from parts of two previous teams, namely TRIM and CaFe. The new team has a very clear focus that includes the homeostasis of metals, the role of essential trace elements and detoxification of toxic metals, in several organisms from prokaryotic to eukaryotic cells. The productivity of both of the original teams was excellent with 20 publications for TRIM and 28 for CaFe. Many of these papers have the first or last authors as members of the teams in high quality international journals. The TRIM group has produced significant and original results in the field of the iron regulating protein Fur (Mol. Cell. Proteomics) and the P-type ATPases. The CaFe group made interesting contributions concerning the TRPC channels and iron homeostasis. Eleven theses were defended in TRIM and 3 in CaFe.

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

The members of the team have presented their work in both national and international meetings (including invitations to ACS meetings, EUROBIC and ICBIC). Both teams were previously very successful in attracting students and post-doctoral fellows and in obtaining national funding. Over the last four years both teams were also successful in obtaining grants (14 for TRIM and 5 for CaFe). Various collaborations exist with foreign partners, some of them funded by grants such as PIC and PAI.

- Appreciation on the strategy, management and life of the team

The team was newly assembled from parts of TRIM and the whole of CaFe. The committee felt that in the new team there appears to be a lack of forward direction that would allow all the members of the team to be active. The group leader also pointed out some financial uncertainties after 2010, which appears to be overwhelming the planning for a future involving all members of the group contributing to their maximum potential. Overall, the committee felt that the merger, combined with an apparent declining funding situation, requires strong leadership to inspire a goal for the team and improve fundraising, which will allow the excellent research potential of the team members to be realized.

- Appreciation on the project

With respect to the future projects, the committee worries that the group is spreading itself rather too thinly over too many different projects and directions, the details provided included (i) metal homeostasis and metalloregulatory proteins in bacteria, (ii) metal ion transporters in yeast, (iii) copper and inflammation in cystic fibrosis, (iv) metal ion channels in neurons, (v) mammalian iron homeostasis and toxicity of metals in eukaryotic cells, and a transversal project (vi) interferences between nanoparticles and metal homeostasis. These projects are all very interesting, relevant and extremely competitive, however, the risk with all these projects running in parallel is to be able to make significant progress in them all. Our view is that the group would probably profit from focusing more on far fewer selected projects concerned with metal traffic and metal homeostasis. The CFTR/PrP project, which focuses more on inflammatory processes, could be developed more in collaboration with the team ProMD.

- Conclusion :

The quality of the work performed by the members of the team is very good as shown by the publication record, and especially the high quality journals for these papers, and as well the international visibility of some of the members of the team.

– Strengths and opportunities

The members of this team have developed original systems that allow them to address important issues in the field of metals in biology.

– Weaknesses and threats

While the excellent past productivity and innovative research can survive the merger it is felt that the team needs to develop a better focus on the future plans and particularly should make efforts to obtain sufficient funds to achieve their goals. This focus requires, we believe, significant involvement of each member of the group with the full support of both the group leader and the institute director. Moreover, we believe that this group has probably too many projects planned for the size of the group.

– Recommendations

The committee recommends that this group should concentrate on a smaller number of main themes which should help to increase its impact in future publications and maintain its international visibility and at the same time result in more successful funding applications. The group needs also to develop a more positive forward direction in order to motivate the group, to hire students and to obtain funding.

Laboratoire de Chimie des Métaux en Biologie

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: Amyloid Fibers: from Foldopathies to nanodesign

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: Theoretical Chemistry and modeling

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 : Biology of metals

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

Nom de l'équipe: Physical chemistry of metals in biology

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 : Proteomics, metals and differentiation

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 : Biocatalysis

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 : Bioinorganic catalysis and environnement

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

L'Administrateur Général

Monsieur Pierre GLORIEUX
Directeur de la section des Unités de recherche

AERES
20 rue Vivienne
75002 PARIS

Saclay, le 20 avril 2010

N/Réf. : DPg/AN/np/2010-103

Objet : Observations du CEA sur le rapport d'évaluation du « Laboratoire de Chimie et Biologie des Métaux (UMR 5249)

Monsieur le Directeur, Cher Pierre Glorieux,

Je remercie l'AERES pour la qualité du rapport d'évaluation et pour la pertinence des recommandations qui ont été faites sur l'activité du « Laboratoire de Chimie et Biologie des Métaux (UMR 5249).

En tant qu'Administrateur Général de l'Etablissement CEA, ce rapport dont nous partageons très largement la vision qu'il offre du laboratoire 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.

Bien cordialement

Bernard BIGOT

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PRESIDENCE

Nos Réf. LD/GG/FT 231 -10
Tél. 04 76 51 48 29 - Fax 04 76 51 43 12

Grenoble, le 30 Mars 2010,

AERES
Monsieur le Président Jean François Dhainaut

Objet : Réponse de l'Université Joseph Fourier Grenoble 1 au Rapport du Comité de Visite
Laboratoire de Chimie et Biologie des Métaux – UMR 5249 – Directeur : Marc Fontecave

Monsieur le Président, Cher Collègue,

Nous avons examiné le rapport préliminaire d'évaluation mis en ligne sur votre application le 18/03/2010 pour :
Laboratoire de Chimie et Biologie des Métaux – UMR 5249

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