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

Department for the evaluation of research units

AERES report on interdisciplinary unit:

Laboratoire d'optique et Biosciences

LOB

Under the supervision of the following institutions and research bodies:

École Polytechnique

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,

- Ms Valentina EMILIANI, 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:	Laboratoire d'Optique et Biosciences
Unit acronym:	LOB
Label requested:	UMR CNRS and INSERM
Present no.:	INSERM U 696 - CNRS UMR 7645
Name of Director (2013-2014):	Mr Jean-Louis MARTIN
Name of Project Leader (2015-2019):	Mr François HACHE

Expert committee members

Chair:

Ms Valentina EMILIANI, Université Paris Descartes, CNRS

Experts:

Mr Damien GALANAUD, Université Aix-Marseille (representative of CSS INSERM)

Mr Brahim LOUNIS, Université de Bordeaux

Ms Agnès MAITRE, Université Pierre et Marie Curie, Paris (representative of CoCNRS)

Mr Marc MOREAU, CNRS

Mr James STURGIS, CNRS

Scientific delegate representing the AERES:

Mr Jacques HAIECH

Ms Sylvie MAGNIER

Representatives of the unit's supervising institutions and bodies:

Mr Pierre LEGRAIN (representative of Doctoral School n° 447 « PolyTechnique »)

Mr Patrick LE QUERE, École Polytechnique

Ms Anne ROCHAT, INSERM

Ms Pascale ROUBIN, CNRS

Ms Laurence PARMENTIER, INSERM

1 • Introduction

History and geographical location of the unit

The research unit "Laboratoire d'optique en biosciences" (LOB) has been created in 2001 by Mr Jean-Louis MARTIN with the aim to create an interdisciplinary laboratory at the interface between Physics (optics and spectroscopy) and Biology. The laboratory is organized in teams assembled on the basis of specific research axes. Each team can comprise more than a principal investigator. The same researcher can belong to different teams. The laboratory is located at École Polytechnique (Palaiseau) and administratively depends on the École Polytechnique, the INSERM and the CNRS.

Management team

The laboratory has been directed since its creation by Mr Jean-Louis MARTIN. Mr François HACHE has been elected as the director for the next 5-year contract. The management activity of the director is supported by a "Collège de direction" (CODIR) which is composed of all the researchers of the laboratory. Besides the CODIR, members of the laboratory also have regular discussions in the framework of the 'Conseil de laboratoire' and, once per year, at the "Assemblée générale".

AERES nomenclature

The laboratory is an interdiscplinary unit and falls under two AERES domains, namely the ST (Physics) and SDVE (Biology and Medicine) domains.

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent researchers from Institutions and similar positions	12	12
N3: Other permanent staff (without research duties)	13	12
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	4	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**32**	**27**

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	27	
Theses defended	19	
Postdoctoral students having spent at least 12 months in the unit*	22	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	11	12

2 • Overall assessment of the interdisciplinary unit

The LOB is an interdisciplinar laboratory is comprised of a staff of 30 people including researchers, engineers post docs and students. The research activity of the laboratory, organized in thematic teams, can count on a very broad range of complementary expertise including, nonlinear optics, optical microscopy, ultrafast spectroscopy, nanoscience, microbiology and protein dynamics. This rich and unique scientific environment has permitted to realize ambitious research projects at the interface between physics and biology. The success of the laboratory is demonstrated by a very good scientific production and the generation of several patents.

Strengths and opportunities related to the context

This research unit has reported scientific results of an excellent quality in physics, biology and at the interface between the two disciplines.

At the occasion of the visit, the experts committee could appreciate the extremely positive feedback on the working conditions within the unit given by all the unit members (researchers, technical staff, postdocs and students).

Also remarkable is the effort that the unit has demonstrated in the technological transfer of the achieved results as demonstrated by an significant generation of patents.

The Equipex project "Morphoscope2" and the new X-Bio institute represent two important opportunities for the next contract that should stimulate new important collaborations and permit increased visibility.

Weaknesses and threats related to the context

No serious threats or weaknesses have been identified. The EQUIPEX coordinated by the team is undoubtedly an opportunity to create a state of the art platform for light microscopy and to initiate new collaborations. However care must be taken to support this operation with human resources to ensure that this development does not come at the expense of creativity and innovation of the team.

Recommendations

Altough the unit has a good visibility at national and international levels, a stronger visibility at international/european level could be reached for example toward applications for ERC grants.

Care should be taken that the promotion of new technologies to a broad community of biologists will not disperse the resources of the unit in too many collaborations and/or research domains.

3 • Detailed assessments

Assessment of scientific quality and outputs

Over the past 4 years the research unit has obtained key results in a broad range of research fields. This include, for example, the screening for inhibitors of the ThyX protein with a potential as novel therapeutic agents for the treatment of Helicobacter pylorii infections or tuberculosis. The development of an impressive technical platform for ultrafast spectroscopy and its application to the investigation of ultrafast phenomena regulating protein dynamics. The synthesis on nanoscale particles for e.g. monitoring the dynamics and spatial organization of H_2O_2 signalling. The development of new microscopy configurations that will have a tremendous impact in the community of biologists. This includes an innovative multimodal (SHG-THG) microscopy technique which led to the first visualization and quantification of the early stages development of a zebrafish embryo, new optical schemes for fast and precise multicolour imaging and a robust optical system for SHG microscopy. Overall the scientific production of the laboratory has been excellent and has generated more than 130 articles on highly recognized international journals, comprising (7 biophys J, 2 PNAS , 2 Nature Methods, 1 Physical review letters, 1 Science, EMBO J).

Assessment of the unit's academic reputation and appeal

The 4 teams have a good visibility both at the national and international level. The results obtained from the thematic team 3, which place this group among the most worldwide recognized group in nonlinear microscopy, have generated about 50 invited talks in prestigious specialized conferences.

The visibility of the unit is also demonstrated by the capability of attracting foreign PhD students and outstanding visiting professors.

The research projects are all regularly financed through different funding programs mostly at national level (ANR, Région idF, RTRA triangle de la physique, CNRS). Team 3 has been recently granted with an Equipex "Morphoscope2" to set up a multiscale imaging facility at École Polytechnique that will increase the visibility of the research unit even further.

Different members of the laboratory are implicated in the coordinatiotn of scientific networks such as the axis Nanobioscience, C'nano d'Ile de France, and the axis New-contrast and in depth imaging in the framework of France Bio Imaging.

The excellent scientific carrier of the incoming director of the unit has been awarded in 2011 by the prize « Médaille d'argent du CNRS ».

Assessment of the unit's organisation and life

The laboratory is organized in thematic teams assembled on the basis of specific research axes and not on around the personnality of a scientist. This assures for each team a good critical mass and visibility, however it could also have a cost in visibility for the senior researchers (principal investigators). This is especially true in an international context where the function of team leader is having more and more a central role.

In the occasion of the different meetings organized during the visit, the experts committee could appreciate the extremely positive feedback on the working condition within the unit given by all the unit members (students, researchers, technical staff). The researchers highlighted the excellent atmosphere in the lab and feel very involved with the direction in consultations for decision-making and arbitration. The technical staff (ITA) is very well integrated in the research activity of the unit, they participate actively in the design of the experiments and share the authorship on the publications.The students and post docs have reported very good working conditions and seem well integrated in the scientific and social life of the unit. They also gave the idea of a dynamic and strongly welded group. Although the different teams have full autonomy in the organization of the internal scientific life, a significant effort is done in maintaining transversal research projects as it is demonstrated by several common publications.

Assessment of the unit's involvement in training through research

The unit members are all strongly involved in the teaching activity, mostly in M1, M2 and Erasmus courses. The incoming director is currently implicated in the creation of an interdisciplinar doctoral school in collaboration with the Université Versailles Saint-Quentin. During the 2008-2013 period, 20 students have defended their PhD.

Assessment of the strategy and the five-year plan

The 4 teams have presented research projects in line with their past activity and demonstrated that they have the financial support, man power and scientific expertise to carry out the different projects with success.

Two major events will have a major impact on the unit's life in the next five year, the Equipex project "Morphoscope2" and the new X-Bio institute.

The "Morphoscope2" project represents a unique opportunity for the thematic team "*Advanced microscopy and tissue physiology"* to explore new optical schemes for microscopy; it will also permit to increase the visibility of the whole unit and stimulate new collaborations. The new X-bio institute will attract new research teams and will considerably strengthen the interdisciplinarity of the LOB if the expertise of the new groups will be chosen to be in synergy with those existing at the LOB. These two events could help guiding the instrumental development made at the LOB toward well-defined biological questions.

4 • Team-by-team analysis

Team 1: Molecular mechanisms of microbial adaptation

Name of team leader: Mr Hannu MYLLYKALLIO

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	3 (1.9FTE)	2 (0.9FTE)
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**8**	**6**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	5	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

Team 1, "Molecular mechanism of microbial adaptation", is composed of 2 research directors, 2 assistant professors, 2 assistant engineers and 4 temporary staff (doctoral students and post-docs). The members of the team work principally on three different biological systems: thymidilate synthase X, DNA repair in Archaea and Heme based gas sensor proteins. These topics derive from the specificities and strengths of this team which are historically the genetic manipulation of Archae (very few teams in the world are able to make mutations and express proteins

heterogolously in Archae), and the fine molecular characterization of heme based sensors. These two aspects converge with the subject of thymidilate synthase X, originally derived from Archae but also present in some Eubacteria, where the team has managed to make considerable progress in describing the fine details of substrate binding and action. A more recent development of the project is the screening for inhibitors of the ThyX protein, and the application of these inhibitors as potential novel therapeutic agents for the treatment of Helicobacter pylorii infections or tuberculosis.

The project of this team has advanced very well over the evaluation period with the publication of 28 articles of which a dozen are in collaboration with team 2. Notable aspects include an investigation of ThyX structure and function with an aim to find specific inhibitors (7 articles including 2 PNAS) and a series of excellent articles on heme based gas sensor proteins (6 articles in collaboration with team 2). To these major streams are added a smaller collection of articles concerning DNA repair in Archaea and some more peripheral topics.

The project has a history of using an interdisciplinary approach, in particular a long and productive close collaboration between team 1 and team 2 on heme containing proteins. This interdisciplinarity has been and continues to be very important for the progress of the project. The production is steady and of excellent quality resulting in an international reputation for the research directors associated with the team.

Assessment of the unit's academic reputation and appeal

The team is involved in many projects, both national and european. Members of the team participate in international meetings and are visible at the international level (12 invited talks in the period 2008-2013). In particular the team has an international grant from New-Zealand as evidence of high international visibility, as well collaboration with Uganda concerning tuberculosis. Involvement in networks perhaps needs developing, especially in view of the international/european composition of the team. Contacts have however been established with the MM4TB (More medecines for Tuberculosis) consortium and this is to be encouraged.

Both research directors in the team are highly visible on the international stage and have an excellent international reputation for their associated research specificities, this is for example visible in the visits made to the team by foreign students.

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

The team has published one patent, and is involved with industrial partners for the development of inhibitors for ThyX, this would seem a reasonable track record for a fundamental science team with some projects of medical interest. The writing of an article for a general public should also be underlined as an important contribution to public awareness of biotechnology and the use of microbes.

Assessment of the unit's organisation and life

The team has many shared resources and these seem to be well used by the different members of the team. They currently have excellent accessibility to core facilities, though this will need to be maintained with the development of X-Bio.

In the local environment, the space available for the team seems adequate, though perhaps not optimal. The independence of the younger permanent members of the team needs to be encouraged, and reinforced. The team has a major role in the interdisciplinary nature of the unit, being the team with the most solid biological background. Communication with the other teams is excellent.

Assessment of the unit's involvement in training through research

The team is clearly very strongly involved in the teaching of students at the universities Paris 6 and 11, and the training of students at the lab bench. Training has been given both to students from the LOB but also visiting students from other institutes and laboratories, including foreign laboratories.

Assessment of the strategy and the five-year plan

The major thrust of the project is a continuation of the excellent research on the different proteins of interest in complete coherence with the last years. The most original, ambitious and exciting part of the project concerns the examination of NucS and DNA metabolism in living cells using a variety of microscopic techniques, though of course this comes with associated risks; however the team is ideally placed to profit from the expertise of the laboratory in advanced microscopy techniques and build on the teams expertise in the manipulation of archae. The project thus remains largely based on the competences present in the laboratory and is not over ambitious in attacking problems for which the members are not prepared.

The strategy of drug development and testing for new inhibitors of ThyX is perhaps more risky. It is not clear that the team has the experience and means necessary to be competitive in this project alone. It is thus important that they find the right partners (public and/or private) able to help the team bring lead compounds up to and through pre-clinical trials. This difficulty is of course compensated by the considerable interest that such novel antibiotics could offer to the modern pharmacopaea.

Conclusion

This team has produced excellent results, a good international visibility and is strongly involved in the development of interdisciplinary research at the LOB.

- **Strengths and opportunities:**

The strengths of the team lie in their mastery of the historical subjects, DNA replication in the Archae and Haem based gas sensors. Over recent years the team has developed considerable expertise in ThyX protein, which they discovered and this experience represents a considerable strength. The integration of a team of biologists in a laboratory dedicated to interdisciplinarity, developing new and exciting methods to attack biological questions is evidently an exceptional opportunity provided by the environment that the team has experience exploiting.

In the prospective the development of the X-Bio project represents both a considerable threat and magnificent opportunity. This arrival of new teams with the development of X-Bio could put strain on infrastructure used by the team, or alternatively expand access to important infrastructures. The team must assure that the latter occurs. Equally the arrival of new biologists as part of this program will provide the opportunity for new collaborations.

Beyond the local X-Bio project, the Paris-Saclay project clearly provides a wonderful opportunity for the different scientists associated with this development, and can only increase the international visibility and attractivity (already very good) of the team.

- **Weaknesses and threats:**

The weaknesses of the team are few and hard to identify, perhaps an over self-reliance that is exemplified by an absence from pertinent european projects, but the senior researchers of the team are aware of this and are actively seeking to fix this. Beyond the potential threat to the local environment provided by X-bio, mentioned above, no serious external threats were identified.

- **Recommendations:**

Engage actively in the X-Bio program to ensure that the arrival of new biological teams does not reduce access to core infrastructures currently not shared with other teams (cell culture, centrifuges, sequencing, etc.).

Encourage young researchers to develop and lead projects in synergy with current projects as a step to gaining scientific independence.

Find appropriate partners to help develop the ThyX inhibitor project.

Team 2: Dynamique Interne des Protéines étudiée par spectroscopie Femtoseconde

Name of team leader: Mr Marten VOS

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	5(4.3FTE)	5(4.3FTE)
N3: Other permanent staff (without research duties)	5(3.8FTE)	5(3.8FTE)
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	**12**	**10**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	7	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	4	5

• Detailed assessments

Assessment of scientific quality and outputs

The team 2 "Internal dynamic of protein" is composed by 4 research directors, 1 researcher (CR1) 5 technical engineers and 5 temporary staff (doctoral students and post doc).

The team aims to analyse protein dynamics in different biological processes (enzymatic activity, protein folding). The team has developed and uses powerful tools to study different types of biological processes. The scientific positioning of the team is the development of high quality scientific instruments, coupled with simulations of protein dynamics in the context of biology. The team has developed many collaborations with biologists within the LOB and in external laboratories, which attest of both the quality and consistency of the team scientific instrumentation and scientific recognition. The team clearly develops an interdisciplinary activity at the interface

between physics and biology, but consistency between different biological problematics could be addressed more clearly.

The team developed a platform for femto and picosecond laser sources for the study of ultrafast phenomena in biomolecules such as functional processes in proteins on time scales of the order of internal displacement in the proteins. The strength of this platform for spectroscopy lies in its numerous possibilities (Raman, absorption, fluorescence, etc.) and in particular in its ability to explore the physical phenomena on time scales covering almost 10 orders of magnitude: from femtoseconds to milliseconds. For these typical time scale, transport at the cell scale can be studied

The activity around the circular time solved dichroism is unique internationally. It will allow to observe changes in protein conformation. This powerful and highly original device has already been used to study the protein folding in water. It will take its full extent in the context of future collaborations with biologists who may use this original technique for answering questions remaining open using standard methods

The activity around the infrared spectroscopy in the femtosecond scale is at the highest international level. The team has developed new techniques for pulse shaping, frequency conversion, both powerful and original, allowing to perform the control coherent and coherent spectroscopy of proteins in the femtosecond scale. An elegant and original pump probe spectroscopy method is used to synchronize two femtosecond pulses with characteristic times ranging from the picosecond to the millisecond. This work has been the subject of several patents and industrial collaborations are underway.

Assessment of the unit's academic reputation and appeal

The team is involved in many national and international collaborations, especially with teams of biologists. The team has first-class optical instrumentation that allows to establish fruitful cooperation on various aspects of protein dynamics. Because the team is composed of physicists developing high level instrumentation and using it to solve biological problems in collaboration with several groups of biologists, it is difficult to pinpoint a specific biological focus.

The team coordinated the French network femtosecond technologies, and participated in three international programs, which demonstrates its good visibility. The director of the unit who is a team member got the silver medal of the CNRS in 2011. The team has a good international visibility as evidenced by the numerous conferences to which its members were invited and publications in international peer-reviewed journals with good level in the areas of physical chemistry, biophysics and the optics.

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

The technology transfer activity of the team is good. This transfer concerns mainly the activity of pump probe spectroscopy using shaped femtosecond pulse, which has led to the development of innovative techniques. First patent shall be transferred to the company Fast Lite. A CIFRE grant was signed. A second patent is being filed and technology transfer is underway.

Assessment of the unit's organisation and life

The team has a cooperative management that helps maintaining the coherence of the instrumentation developed between the different activities. It is strength of the team. Complementary skills (experimental / theoretical physicists and biologists) contribute to interdisciplinary and collaboration between the teams. The team fits into the interdisciplinary context of the laboratory. Several team members are heavily involved in the establishment and management of the whole laboratory (direction of the laboratory, department of physics at the École Polytechnique).

Assessment of the unit's involvement in training through research

Several team members are heavily involved in teaching courses at École Polytechnique in Master 1 and Master 2 as part of the Université Paris Saclay and in international courses (Physics for optics and NanoSciences). The team leader is currently developing an interdisciplinary graduate school "interfaces" in partnership with UVSQ.

Assessment of the strategy and the five-year plan

The team has a set of top level scientific instruments that will allow remarkable results to be gained on the dynamics of proteins. The team now plans to exploit this powerful and almost unique instrumentation to study photoinduced effects in proteins. The team is very well positioned in the interdisciplinary context of the laboratory, the École Polytechnique and Université Paris Saclay. It has developed many collaborations with biologists that have relevance both in the instrumentation developed and the biological problems studied. Interdisciplinary should be further strengthened while preserving the team potential in innovative instrumentation, and trying wherever possible to address more precisely a given biological issue.

Conclusion

- **Strengths and opportunities:**

The team has developed an original high-performance scientific instrumentation, with a strong coherence. These achievements put the team in an excellent position to strengthen interdisciplinary cooperation with biologists. The creation of X-bio is an interesting opportunity for the team for future collaboration.

- **Weaknesses and threats:**

It is important to keep the balance between excellence in scientific instrumentation and a strong opening to the biology as well as the coherence between the different activities.

The nomination of a senior member of the team as laboratory director must not destabilize the activity around the circular dichroism.

- **Recommendations:**

Continue to develop excellence in instrumentation, in the context of biological studies, in collaboration with teams of biologists.

Team 3: Microscopies avancées et Physiologie des Tissus

Name of team leader: Mr Emmanuel BEAUREPAIRE

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	6 (4.7FTE)	6 (4.7FTE)
N3: Other permanent staff (without research duties)	1 (0.3FTE)	1 (0.3FTE)
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**8**	**7**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit	8	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

Team 3 "Advanced microscopy and tissue physiology" is composed of 4 research directors, 2 researchers (CR1, CR2) 1 technical engineers and 7 temporary staff (doctoral students and post doc).

The activity of this team concerns the development of various multimodal-imaging techniques based on the use of several nonlinear optical contrasts. The team explores applications of these techniques in biology and biomedical domains.

During the last 5 years the team has realized many important innovative experimental developments, which allowed it to obtain important results. Among them, the elaboration of an innovative multimodal (SHG-THG) microscopy technique led to the first visualization and quantification of the early stages of development of the

zebrafish embryo. This constitutes a major breakthrough, which brought key information on the first cell divisions in living vertebrate embryos. The experts committee emphasizes the quality and originality of the innovative instruments conceived by the team which are based on the spectral and spatial control of the optical excitation in nonlinear microscopy. The experts committee was particularly impressed by the results obtained on tissue imaging in multiple species (such as in "Brainbow"- labelled tissues) using two-photon microscopy by wavelength mixing.

The team has shown that SHG microscopy is a valuable tool for probing collagen in biological tissues. The experts committee noted the substantive work done by the team on the understanding of the microscopic origin of the nonlinear signal in collagen structures, an important step for the quantification of collagen content in tissues. The experts committee found very interesting the introduction of the polarimetric techniques for the determination of the collagen fibrils orientation and their application to cornea imaging, opening the way to medical diagnosis. The academic production of the team is major, with 48 invited conference talks and 45 original papers published between 2008 and 2013. These article were published both in specialized and general science journals. Among the publications with the highest impact factor, one article was published in Nature Methods in 2012, 1 in Nature Methods in 2011, 1 article in Science in 2010. In the vast majority of these articles, the researchers of this team were the last and/or first authors of the paper

Concerning the THz imaging and spectroscopy, the experts committee noted the progress made towards the control of THz radiation polarization and focusing. The experts committee found interesting the result concerning the development of an attenuated total internal reflection (ATR) geometry, which leads to subwavelength axial resolution for THz micro-spectroscopy.

Assessment of the unit's academic reputation and appeal

This team has an excellent scientific production as evidenced by the number and quality of its publications as well as the number of its patents. It is internationally recognized for its expertise in nonlinear microscopy and its renown is reflected by the number of invitations to the best international conferences. It has a dense and growing collaborative network and attracts talented post-docs and young researchers, as well as visiting professors. The team is very successful in financing its activity as shown by the large number of grants obtained from public and private institutions. The expertise of the team in tissue microscopy has been recognized through the grant of an Equipex project Morphoscope2 whose aim is to set up a multiscale imaging facility at École Polytechnique. This major equipment grant will foster the development of innovative microscope techniques and offer a state of the art imaging platform for the community.

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

The integration of the team in the environment is good. Close collaboration has been developed with l'Oreal in the field of collagen imaging. These developments in understanding and imaging the structure of collagen have potentially wide applications for the cosmetic industry, and led to significant financing by l'Oreal. The investigators involved work also closely with the "Banque Française des Yeux" and the "Institut de la Vision" to apply these advanced microscopy technique in ophthalmology, both to study the structure of cornea (for grafting and to understand lesions in diabetic patients) and the structure of the retina. These projects show both the quality of the collaboration between the 2 sub units and a good understanding of the potential applications of the methods they are developing.

The team published numerous vulgarization articles and gave multiple interviews (Biofutur, Le Monde, La Recherche, pour La Science).

Assessment of the unit's organisation and life

The team is subdivided into 3 subgroups:

- technological development of third harmonic generation and non linear microscopy, under the direction of the team leader is focused mainly on the development of these technologies;

- physics and application of second harmonic generation, supervised by a senior scientist. This group is more focused on the practical application of non-linear microscopy for the imaging of collagen tissues, especially tendons and cornea;

- terahertz imaging and spectroscopy, under the direction of another senior scientist. This group is doing the most fundamental work of the 3, studying the fundamentals of the nearly unexplored field of imaging using terahertz waves.

Interactions between these 3 subgroups are unequal. Significant collaboration is present between the first two groups, particularly on the topic of corneal imaging. Collaboration between the groups of the team leader and anohter team member on technological optical developments is noticeable. However the integration of the activities of one team member is less advanced, essentially due to the very upstream character of his developments.

Assessment of the unit's involvement in training through research

The group leaders are involved in the structuration of the upcoming Université Paris Saclay. They participate in many teaching courses (mostly in M2 courses and at the École Polytechnique). During the 2008-2013 period, 10 PhDs and 8 post doctoral fellows were trained in this team, for a total of 13 PhDs and 11 post doctorants.

Assessment of the strategy and the five-year plan

In line with their achievements, the members of the team plan to explore new methodological and technological developments in nonlinear microscopy. These developments will benefit from the Equipex project "Morphoscope2" which aims at setting up state-of-the-art multiscale imaging facilities at École Polytechnique. The expertise of the team in "advanced microscopies" is the cornerstone of the project. The facility will be opened to the new biology groups joining the campus (in the X-Bio institute) and therefore will certainly result in new collaborations and synergies.

The team will continue to develop innovative multimodal nonlinear techniques and will explore the possibility to perform correlative microscopy between different modalities. The team will also use these optical techniques to tackle, in collaboration with biologists, very fundamental biological problems such as the study of the roles of fluid flows during embryonic development or the study of the differentiation and clonal structure of the developing nervous system.

Concerning THz imaging, the experts committee finds interesting the application of the attenuated total reflection imaging to study cell membrane electro-permeabilization. The experts committee also suggests that the team explores applications where THz lateral resolution does not set a severe limitation. An imaging contrast obtained under a combined THz and Optical excitations is worth exploring to be able to achieve micrometer spatial resolution of a THz spectral signature.

Conclusion

- **Strengths and opportunities:**

This team is internationally recognized for its expertise in nonlinear microscopy and has established very fruitful national and international collaborations. The excellence and international outreach of the team is reflected in its attractiveness for young talented researchers. The Equipex project constitutes an excellent opportunity for the development of a state-of-the-art imaging facility and to trigger new collaborations.

- **Weaknesses and threats:**

The team has to ensure that the many requests for collaboration do not lead to a wide dispersion of its research activities. The EQUIPEX coordinated by the team is undoubtedly an opportunity to create state-of-the-art platform for light microscopy and to initiate new collaborations. However care must be taken to support this operation in human resources to ensure that this development does not come at the expense of creativity and innovation of the team.

- **Recommendations:**

The team would gain by better integrating the THz activities.

The activity on adaptive optics should not be lost after the departure of a permanent staff scientist.

Team 4: Nanoemetteurs et Suivi de Biomolécules Individuelles

Name of team leader: Ms Antigoni ALEXANDROU

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	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.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**3**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	2	
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 *Nano imaging and cell dynamic* is composed of one Research director, one maitre de conference, one assistant engineer and 3 PhDs.

The team studies the problems of cellular dynamics and visualizes the phenomena by using rare-earth doped nano-particles. These nano-particles are designed in collaboration with chemists of the *Laboratoire de Physique de la Matière Condensée* from the École polytechnique. These particles have a great interest since they are photostable and have long life duration. The team has an important experience in single molecules tracking and has developed several outstanding tools used in numerous applications such as proteins-DNA interactions, tracking and localization of toxin receptors in clostridium, detection of ROS in vascular smooth muscles and in tumors. The ROS detection was possible since the nano-particles doped with europium have a powerful property of oxido-reduction. These particles

are very sensitive tools and have been used to follow dynamics and spatial organization of H_2O_2 signalling. In addition the team has developed a system of microfluidic channels to study red blood cells diseases.

The team has published 18 articles in journals of high quality such as Nature Nanotech, Phys Rev Lett., Biophys., J. Langmuir. The work is performed in collaboration with LOB and École polytechnique teams or laboratories of Ile de France. Above the 12 mentioned collaborations 6 have given rise to articles and 3 to a financial support.

The team Nano-imaging and cell dynamic carries out a real interdisciplinary research.

Assessment of the unit's academic reputation and appeal

The team is present in 15 national projects, in addition the team leader coordinates the axis Nanobioscience d'Ile de France and is a member of the network France Bio-imaging (call investments for the future/ infrastructure for research in biology and health coordinated by ANR). During the examined period the team has recruited one École Polytechnique Maître de Conference with an INSERM chair, one assistant engineer and has organized 3 international meetings and 3 national symposia.

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

Four patents were issued from the team's research including 2 during the examined period. A patent is in discussion with the firm Horiba Jobin Yvon concerning the amplification by nano-particles of the hydrodynamic force that acts on receptors.

One important aspect whose development is in progress concerns nano-particles with the replacement of Y^{3+} by gadolinium. This allows simultaneous measurement of ROS and high contrast in MRI imaging in small animals.

The team's results have been presented in 10 invited talks. The team is implicated in scientific animations for the general public.

Assessment of the unit's organization and life

With its expertise in tracking of single biomolecules, the team has collaborated with team 1 (Molecular mechanisms of microbial adaptation) to decipher the interaction of NucS and DNA in living cells. The team has also one common article with members of team 2 (Internal proteins dynamics).

Important collaborations exist with other laboratories of the École Polytechnique: Laboratoire de Physique de la matière condensée, Laboratoire de mécanique des solides, Laboratoire d'hydrodynamique. These collaborations have resulted in common publications and common financial supports. These collaborations play a great role in the interdisciplinary research done by the team.

Assessment of the unit's involvement in training through research

The team's members are involved in training M2, M2 Erasmus and at international level the team has hosted foreign students for the course "NSF undergraduate program".

Five students have defended their PhD and 2 post docs have participated to the projects.

Recently the team has given a scientific formation in the national workshop MiFoBio (Microscopie Fonctionnelle en Biologie).

Assessment of the strategy and the five-year plan

The team presents 6 projects which are in the continuity of previous work and based on the use of rare-earth doped nano-particles. The goal for the next five years is to increase the use of nano-particles in biology.

Various projects are listed: Study of the proteins-DNA interactions, organization of membrane dynamics, Toxin –cells interactions to understand how ingested botolinum toxin passes from the gut into the bloodstream, ROS tracking in tumor cells or in neurodegenerative diseases using Zebrafish, the investigation of sickle cell anemia and multimodal in vivo imaging. These projects will be performed either in collaboration with teams at the École Polytechnique or with laboratory in the region Ile de France. The link between the different projects is the use

of the nano-particles, but the different projects have not the same pertinence and some choices have to be made to target the more important biological projects.

Conclusion

- **Strengths and opportunities:**

The team has a strong expertise in doped rare-earth nano-particles with a solid collaboration with chemists of the "Laboratoire de Physique de la matière condensée". They are very competent in nano-particle imaging. Well-chosen collaborations have been fruitful to analyze some aspects of cellular dynamics.

The team has good publications and participates actively to the training of PhD students and post docs and has a good attractiveness for students. This team has an important activity of valorisation and is well supported financially.

- **Weaknesses and threats:**

Six different projects in collaboration are presented some with biomedical aspects. It seems that the team has no project on its own. Of course the heart of the research is the development and the exploration of the different functionalities of these nano-particles, but the different collaborations have not the same pertinence and more targeted collaborations will allow an important biomedical axis to be developed.

- **Recommendations:**

An aspect has to be encouraged, which is the optimisation of nano-particles to measure ROS with applications in some pathologies. The team have to concentrate the efforts on limited topics in order to work in depth on biological aspects. The creation of X-Bio at the École Polytechnique can provide the opportunity to recruit a collaborator more specialized in the domain of cell signalling.

5 • Conduct of the visit

Visit dates:

Start: Tuesday January 16th 2014 at 4.00 pm

End: Friday January 17th 2014 at 6.00 pm

Visit site: Laboratoire d'optique et Bioscience

Institution: École Polytechnique

Address: Aile 2, Niveau 2 (1er étage)
École Polytechnique
91128 PALAISEAU Cedex

Specific premises visited:

The laboratory and the technological platforms have been visited.

Conduct or programme of visit:

Jeudi 16 Janvier 2014

16h00-16h15	Accueil du comité d'experts	
16h15-16h30	Huis clos - Présentation de l'AERES au comité d'experts par le Délégué Scientifique de l'AERES (DS)	
16h30-19h00	Visite du laboratoire.	
Horaire:	**Groupe 1**	**Groupe 2**
16h30-17h15	Microscopies avancées et physiologie des tissus	Dynamique interne des protéines
17h15-17h45	Mécanismes moléculaires de l'adaptation microbienne	Nanoimagerie et dynamique cellulaire
17h45-18h30	Dynamique interne des protéines	Microscopies avancées et physiologie des tissus
18h30-19h00	Nanoimagerie et dynamique cellulaire	Mécanismes moléculaires de l'adaptation microbienne
19h30	Dîner	

Vendredi 17 Janvier 2014

08h30-08h45	Devant l'unité, présentation du comité d'experts et présentation de l'AERES par le DS
08h45-09h30	Présentation de l'unité, bilan et projet

Audition des équipes :

09h30-10h00	Bilan et projet équipe 1 " Mécanismes moléculaires de l'adaptation microbienne"
10h00-10h30	Pause
10h30-11h15	Bilan et projet équipe 2 " Dynamique interne des protéines"
11h15-12h00	Bilan et projet équipe 3 " Microscopie avancée et physiologie des tissus"

12h00-12h30 Bilan et projet équipe 4 "Nanoimagerie et dynamique cellulaire"

12h45-14h00 Déjeuner de travail avec les représentants des tutelles

Session rencontre avec le personnel permanent et non permanent

Le comité d'experts se répartit en trois sous-groupes

14h00-14h45 **Rencontre avec les ITA titulaires , CDD**
Auditoire : membres du comité d'experts et DS, sans les tutelles, ni la direction.
Rencontre avec les doctorants et post-doctorants et/ou CDD « chercheurs », Ingénieurs
Auditoire : membres du comité d'experts et DS, sans les tutelles, ni la direction.
Rencontre avec les chercheurs et enseignants chercheurs titulaires.
Auditoire : membres du comité d'experts et DS, sans les tutelles, ni la direction, ni les responsables d'équipes

14h45-15h15 *Rencontre avec le directeur de l'école doctorale*

15h15-15h45 Rencontre avec la direction de l'unité
Auditoire : membres du comité d'experts et DS

15h45-16h15 Pause

16h15-18h00 **Réunion du comité d'experts à huis clos**
Présence : membres du comité d'experts et DS

6 • Supervising bodies general comments

Patrick Le Quéré
Directeur adjoint de l'Enseignement et de la Recherche

Madame Nathalie Dospital
Déléguée Administrative
Section des unités
AERES
20 rue Vivienne
75002 PARIS

Objet : Evaluation AERES du LOB – UMR 7645
Référence : DAER /LL/14 – n° 111
PJ : Réponse au rapport d'évaluation du LOB - E2015-EV-0911568K-S2PUR150008334-005375-RT

Palaiseau, le 19 mai 2014

Chère Madame,

Suite à la réception du rapport d'évaluation en date du 22 avril, je vous prie de trouver ci-joint les remarques que le LOB souhaite porter à votre connaissance et les corrections factuelles qu'il souhaiterait voir prises en compte.

En tant que co-tutelle du LOB, nous n'avons pas d'autre commentaire particulier à ajouter, autre que vous prier de remercier en notre nom l'ensemble des membres du comité et son président pour le temps qu'ils ont consacré à cette évaluation.

En vous souhaitant bonne réception de la présente, je vous prie de croire, Chère Madame, à l'assurance de mes meilleures salutations.

Patrick Le Quéré
Directeur adjoint de l'Enseignement et de la Recherche

DIRECTION DE L'ENSEIGNEMENT ET DE LA RECHECHE
ÉCOLE POLYTECHNIQUE - F 91128 PALAISEAU CEDEX - T. +33 (0)1 69 33 40 01 - F. +33 (0)1 69 33 40 02

LOB

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Instituts thématiques Inserm

Institut national de la santé et de la recherche médicale

CNRS UMR 7645
Laboratoire d'Optique et Biosciences

Unité de recherche U696
Dynamique des interactions moléculaires et imagerie cellulaire

Palaiseau, le 13 mai 2014

Observations en réponse au Rapport d'évaluation AERES du LOB

Référence du rapport AERES :
–

S2PUR150008334 - LABORATOIRE D'OPTIQUE ET BIOSCIENCES - 0911568K del'unité LABORATOIRE D'OPTIQUE ET BIOSCIENCES.

L'ensemble des personnels du Laboratoire d'Optique et Biosciences (LOB) se réjouit de l'appréciation positive portée par le Comité de visite de l'AERES sur l'activité et le fonctionnement du LOB.
Nous confirmons l'analyse du Comité sur le besoin en personnel support, induit par la mise en place et le fonctionnement de la plateforme associée à l'Equipex MORPHOSCOPE porté par le LOB.

Le rapport n'appelle pas d'autres commentaires de notre part.

Jean-Louis Martin
Directeur du LOB

François Hache
Porteur du Projet (2015-2019)

Ecole Polytechnique – 91128 Palaiseau cedex
Tel : 01 69 33 50 01/02 – e-mail : jean-louis.martin@polytechnique.edu
http//www.lob.polytechnique.fr