Evaluation of Research

EVALUATION REPORT ON THE UNIT

CBS - Centre de Biochimie Structurale

UNDER THE SUPERVISION OF INSTITUTIONS AND RESEARCH BODIES:

Université de Montpellier (EPE), Institut national de la santé et de la recherche médicale, Centre national de la recherche scientifique

EVALUATION CAMPAIGN 2025-2026
GROUP A

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High Council for the evaluation of research and higher education

On behalf of the committee of experts:

Eric Ennifar, Chairperson of the committee

For Hcéres :

Coralie Chevallier, President

In accordance with articles R. 114-15 and R. 114-10 8° of the Research Code, evaluation reports drawn up by the committees of experts are signed by the chairpersons of these committees and countersigned by the president of Hcéres.

To facilitate the reading of the document, the terms used in this report to designate functions, occupations or responsibilities (expert, researcher, teacher researcher, professor, lecturer, engineer, technician, director, doctoral student, etc.) are generic and gender neutral.

This report is the outcome of an evaluation by a committee of experts the composition of which is specified below. The assessments it contains are an expression of the independent and collegial deliberation of the committee. The data within it are the certified accurate data extracted from the application forms submitted by the supervising bodies on behalf of the unit.

This version of the report is public under Article R. 114-23 of the Research Code. Sections of the report considered confidential, and responses to points of attention from supervisors are not included in it.

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Mr Jean-Marc VERBARATZ, Inserm

UNIT CHARACTERISATION

- Name : Centre de biologie structurale
- Acronym: CBS
- Label and number: UMR 5048
- Number of teams: 14
- Composition of the executive team: Mr; Emmanuel Margeat, Unit Director; Ms Vanessa Delfosse, Deputy Director, in charge of building/infrastructure; Mr. Martin Cohen-Gonsaud, Deputy Director, in charge of equipment and platform

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement
SVE3 Molécules du vivant, biologie intégrative (des gènes et génomes aux systèmes), biologie cellulaire et du développement pour la science animale

THEMES OF THE UNIT

The CBS brings together structural biology, biophysics, and bioengineering to decipher how molecular structure and dynamics govern function across scales - from single molecules to cells, tissues, and organisms. It relies on a comprehensive, state-of-the-art toolkit - NMR (including high-pressure), cryo-EM, X-ray crystallography, AFM, super-resolution and single-molecule imaging/spectroscopy (e.g., smFRET), microfluidics, tightly coupled to multiscale computation to produce quantitative, predictive descriptions.
Major research themes include: (i) intrinsically disordered proteins, conformational landscapes, and phase separation; (ii) genome organization in vivo (3D chromatin folding and DNA transactions); and (iii) membrane biophysics and mechanobiology, linking chemical/mechanical signaling to cellular architecture and behavior.
A strong axis of instrumental innovation (quantitative optical microscopies, nano/micro-manipulation) enables visualization, perturbation, and measurement of living systems with unprecedented spatiotemporal resolution.
The institute also sustains a robust translational pipeline—structure-guided drug discovery and chemical biology, alongside synthetic-biology diagnostics and live bacterial therapies. Application areas span infectious disease, cancer, metabolic and neurodegenerative disorders, plant immunity, reproductive biology, and environmental health

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The Centre de Biochimie Structurale (CBS) was created in 1992 to reinforce structural biology in France, especially outside Paris. After being dispersed over multiple sites for thirteen years, the unit was unified in late 2005 on the renovated "Navacelles" site (INSERM). The CBS is headed by E. Margeat since 2024 and is housed in two buildings located on opposite sides of rue de Navacelles in Montpellier. The main site at 29 rue de Navacelles (1,839 m²) hosts ~80% of personnel and most heavy equipment (electron microscopy, NMR). The second site, on the 2nd floor of the INSERM Delegation (60 rue de Navacelles), comprises 870 m² for technical rooms, offices and a microscopy facility, plus 320 m² shared with INSERM U1058 (PCCEI). The main building will be soon expanded by adding ~1000 m² of work space.

UNIT RESEARCH ENVIRONMENT

CBS is the only interdisciplinary institute in structural biology, biophysics and bioengineering in Montpellier. CBS is embedded in the University of Montpellier BioHealth Pole, with leadership roles, and sustains a dense network of on-campus collaborations on the Arnaud de Villeneuve site (IGH, IGF, IES, PhyMedExp and CHU laboratories), complemented by cross-campus partnerships in physics (L2C), mathematics (IMAG) and chemistry (ICG, IBMM).
CBS teams are highly engaged in national and European infrastructures and consortia: FRISBI (integrated structural biology), France-BioImaging / Euro-BioImaging (advanced imaging), ChemBioFrance, and numerous GDRs/LabEx; several staff hold coordination or executive roles (e.g., IBiSA steering committee; FRISBI and FBI executive boards).
CBS maintains a strong training interface with the University of Montpellier: despite only six faculty, INSERM/CNRS researchers contribute ~150 h/year of teaching across national Master programs, with flagship local tracks in Quantitative Biology (qBio), Structural Biology & Rational Drug Design, Microscopies & Spectroscopies for Biology, and High-resolution NMR; CBS also mentors successful iGEM teams (overgraduate 2nd place, 2022). The environment is translationally active, with programs spanning kinase inhibitor development (now in clinical trials and industrial partnership with Ipsen), biomechanical biomarkers in oncology, and synthetic biology diagnostics/therapeutics in close collaboration with clinicians at Montpellier Hospital. These efforts culminated in ART-SynBio, an INSERM-recognized structure accelerating clinical translation of programmable bacterial

therapies. Overall, CBS offers a cohesive, multi-disciplinary and infrastructure-rich environment that connects discovery-driven research to training and innovation in human health.

UNIT WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maitres de conférences et assimilés	3
Directeurs de recherche et assimilés	16
Chargés de recherche et assimilés	21
Personnels d'appui à la recherche	27
Sous-total personnels permanents en activité	**70**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	24
Post-doctorants	17
Doctorants	28
Sous-total personnels non permanents en activité	**69**
Total personnels	**139**

BREAKDOWN OF THE UNIT'S PERMANENT STAFF BY EMPLOYER: IN PHYSICAL PEOPLE AS OF 31/12/2024. NON-SUPERVISING EMPLOYERS ARE GROUPED ON THE HEADING "OTHERS".

Nom de l'employeur	EC	C	PAR
AUTRES	0	2	0
CNRS	0	22	15
INSERM	0	13	10
U MONTPELLIER	6	0	2
Total personnels	**6**	**37**	**27**

GLOBAL ASSESSMENT

CBS is an excellent interdisciplinary research unit whose mission is to decipher how molecular structure and dynamics control biological function from the atomic to the cellular scale. By combining structural biology, quantitative biophysics, imaging, bioengineering and multiscale computation, CBS develops predictive and integrative approaches that place it at the forefront of modern life-science research.

During the evaluated period, CBS consolidated a highly coherent scientific policy based on advanced methodological innovation coupled to biologically and medically relevant questions. Its main scientific themes—intrinsically disordered proteins and phase separation, genome organization in vivo, membrane biophysics and mechanobiology—are fully embedded in major international research trends. These themes are supported by a remarkable instrumental environment including high-pressure NMR, cryo-EM, cryo-FIB-SEM, super-resolution and single-molecule microscopies, AFM and microfluidics, tightly interfaced with computational modelling. The strong axis in instrumental development and quantitative imaging places CBS among the leading European centers in integrative structural biology.

CBS plays a central role in the national and international ecosystem through leadership positions in infrastructures such as FRISBI and France-BioImaging, strong integration within the BioHealth pole of the University of Montpellier,

and dense collaborations with physics, chemistry, mathematics and clinical partners. The unit has demonstrated a high capacity to attract competitive funding, exceeding 6M€/year in total, mainly through ANR grants alongside with contributions from the European Research Concil (ERC), the Fondation Bettencourt Schuller, industrial partnerships, and PIA-related programs. This funding has supported the translation of methodological advances into impactful scientific output, including 54 publications in top-tier journals (PNAS, Cell, Science, Nature, EMBO Journal, eLife, Molecular Cell, Science Advances, Nature Communications), patents (i.e. patent on a novel small-molecule inhibitor of Erk2 kinase, or on a DNA-origami "Nano-winch" nanorobot), startup projects and clinical-stage developments (ART-SynBio).
The committee considers that the scientific results, visibility and attractiveness of CBS are at an excellent level. This assessment is supported by several indicators of excellence. CBS has been highly successful in securing highly competitive funding, including multiple ERC grants, major CPER investments, and substantial support from the Bettencourt Schueller Foundation—programs that are among the most selective in France and Europe. In addition, the unit demonstrates a strong capacity to attract outstanding scientists through highly competitive CNRS and CPJ (Chaires de Professeur Junior) positions, reflecting its national and international attractiveness as a leading research center. Its open-platform policy and its involvement in large collaborative projects reinforce both national leadership and international recognition. Training activities are also outstanding, with strong engagement in Master programs, iGEM mentoring and supervision of early-career scientists.
The unit's trajectory over the period is clearly positive. The change in direction, the reorganization of teams, the promotion of new research groups and the structuring of seven strategic axes for the 2026–2030 period illustrate CBS's ability to evolve, address internal difficulties and build a forward-looking project aligned with emerging fields such as AI-assisted structural biology, biomolecular dynamics and microbial systems.
Some structural weaknesses and risks remain. The sustainability of high-end infrastructures depends on continued access to competitive funding and the capacity to recruit and retain highly skilled permanent engineers, particularly in cryo-EM, IT and data science. The rapid growth of the unit calls for reinforced governance, improved coordination across teams and continued attention to gender balance and psychosocial risk prevention.
In conclusion, CBS stands out as an Excellent unit, combining scientific ambition, methodological leadership, strong institutional integration and high societal impact. Provided that the identified structural risks are adequately addressed, CBS is in a very strong position to further strengthen its role as a leading international center for integrative structural and quantitative biology.

DETAILS OF THE EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Following the previous evaluation, CBS has actively implemented most recommendations and clarified its position when it did not fully share the committee's views. In line with the call to continue investing in high-end instrumentation, the unit has significantly reinforced its technological base, notably with the acquisition of a 200 keV cryo-TEM for the PIBBS platform and a cryo-FIB-SEM co-funded with regional and national partners. In parallel, efforts have been undertaken to strengthen cryo-EM through facility reorganization, dedicated staffing and extensive training of researchers from several teams, resulting in an increasing number of cryo-EM–based publications. The recommendation to secure CBS excellence in NMR has been addressed by the recent recruitment of a young NMR expert to capitalize on the existing equipment.
The unit has also acted on recommendations concerning teaching, visibility and valorization. It has created the qBio Master program and tightening links with Montpellier University. IP scouts have visited the institute and interacted with teams, leading to several patent applications currently in progress. On the editorial side, almost all publications since 2022 now comply with the affiliation rules set by the funding bodies, particularly Montpellier University. The unit has maintained a strong and increasing budget for both teams and platforms to support its ambitions.
Regarding governance and human resources, CBS has introduced annual one-on-one meetings between each team leader and permanent researcher, providing a structured framework to discuss responsibilities, autonomy, career evolution and funding opportunities; researchers are encouraged to apply as project leaders without restriction. Dual-headed teams, initially appointed for reasons of parity, promotion of young researchers, team fusion and funding leverage, are reported by the unit to have improved distribution of duties, internal communication, mentoring and HR management, without diluting leadership or international visibility. Reappointments are explicitly non-systematic and based on scientific excellence, quality of leadership and contribution to the collective life of the unit.
On the strategic orientation of its science, CBS contests the recommendation to focus on a small set of in-house biological questions. It argues that its methodology-driven and strongly interdisciplinary model, leveraging advanced structural and biophysical tools across a broad spectrum of biological problems, is precisely what underpins its visibility and competitiveness, and that narrowing its scope would unnecessarily marginalize some teams despite the unit's excellent overall performance during the evaluation period. The unit remains open to

external scientific advice and is considering involving external researchers in strategic retreats, while expressing reservations about duplicating the role of HCERES through a formal external SAB.

B - EVALUATION AREAS

When considering the references set in the research units' evaluation guidelines, the committee will see to it that outstanding elements that relate to the strengths and weaknesses of the unit are pinpointed. Each and every assessment must be backed up with observable facts, namely from elements submitted in the portfolio. The committee assesses whether the unit's performance is consistent with its profile of activities. Information in boxes is summarily drafted based upon evaluative elements described in the subsections on the strengths and weaknesses.

EVALUATION AREA 1: THE UNIT'S SCIENTIFIC OBJECTIVES, ORGANIZATION AND RESOURCES

Assessment of the unit's scientific objectives, organization and resources

CBS has consistent and ambitious scientific objectives aligned with the expertise of its teams and research environment. Its organization into teams and shared platforms is well suited to these goals. The unit benefits from adequate human and financial resources and from high-level technical infrastructures managed by highly qualified support staff. Overall, facilities and skills support the research effectively, and management practices comply with institutional rules on safety, environment, data protection and scientific materials.

Context-related strengths and opportunities

CBS benefits from a strong and coherent scientific identity, positioned at the interface between structural biology, biophysics, imaging and integrative biology. Its scientific objectives are ambitious yet realistic, and fully aligned with national and international priorities in life sciences. The unit's organization into complementary research teams and shared technological platforms provides a flexible and efficient framework for carrying out interdisciplinary projects and translating methodological advances into biological discoveries. This structure also enables CBS to position itself as a key actor within the local and national ecosystem, notably through its integration into infrastructures such as FRISBI and its partnerships with CNRS, INSERM and Montpellier University.
The unit's capacity to attract and manage external funding is a major strength, allowing sustained investments in high-end equipment and recruitment of qualified technical staff. The ongoing renewal of its infrastructures (such as the cryo-EM and biophysics platforms) creates strong opportunities for scientific leadership and innovation. CBS's visibility also benefits from its open platform policy, which promotes collaboration with both academic and industrial partners, enhancing technology transfer and valorization prospects.
On the human side, CBS offers an attractive working environment. The unit fully supports scientific integrity and open science principles. Despite a significant delay in terms of gender balance at the end of the previous mandate, substantial progress has been achieved in recent years.
Altogether, the combination of advanced infrastructures, skilled personnel, solid institutional partnerships and an interdisciplinary scientific strategy positions CBS to take advantage of future opportunities, consolidate its position in integrative structural biology, and further increase its international impact.

Context-related weaknesses and risks for the four references above

Maintaining the current standard of high-end instrumentation requires continuous financial commitment and renewal plans, which depend on competitive funding and institutional support, despite an increasingly challenging economic climate.
Recruiting and retaining permanent technical staff with the required expertise remains difficult, especially in highly specialized domains such as cryo-EM, biophysics and computational analysis. This may affect the balance between service and research activities if not adequately anticipated.
The unit's interdisciplinary structure, while a strength, also requires careful coordination to maintain coherence across diverse scientific themes and to ensure that all teams benefit equally from shared infrastructures. Further efforts are still required to improve gender balance within the unit, and, importantly, the governance will need to address more proactively the reduction of psychosocial risks, which remain a point of attention within the unit.
The unit's management, characterized by an informal and unstructured approach, while in accordance within the previous mandate context, is no longer suitable given its current size. There is a need to implement more

structured and formalized procedures, particularly in areas such as team renewal and re-orientation, recruitment of permanent staff and psychosocial risk assessment.
Overall, the main risks for CBS are linked to sustaining its level of excellence under growing operational constraints (financial, technical and human) while preserving the flexibility and interdisciplinary dynamics that underpin its success.

EVALUATION AREA 2: THE UNIT'S SCIENTIFIC RESULTS, IMPACT AND ATTRACTIVENESS

Assessment of the unit's scientific results, impact and attractiveness

The unit has produced a large number of high-impact publications in leading journals, reflecting the excellence and diversity of its research activities in structural biology, biophysics, imaging and integrative biology. The unit also plays an active role in the coordination and management of its scientific community through leadership in research networks, participation in large collaborative projects and organization of scientific events. CBS maintains a strong attractiveness for students and collaborators, supported by its state-of-the-art facilities and stimulating scientific environment.

Context-related strengths and opportunities

CBS benefits from a strong and coherent scientific identity that combines methodological innovation with biological relevance. Its recognized expertise in structural, biophysical and integrative biology provides a powerful basis for addressing fundamental and applied questions across molecular and cellular scales. The unit's strategy, combining high-quality research, interdisciplinarity and advanced instrumentation, creates opportunities to maintain scientific leadership and attract high-level collaborations at both national and international levels.
The quality and diversity of CBS's scientific production reflect a mature research environment where rigor, creativity and risk-taking coexist. The unit's technological platforms and its involvement in large-scale infrastructures such as FRISBI, FranceBioImaging and regional initiatives ensure access to cutting-edge methods. CBS's active participation in academic networks and its remarkable ability to attract external funding reinforce its capacity to develop emerging themes and support early-career researchers. The unit's commitment to data sharing and sustainable research practices is well aligned with institutional and European priorities.
Altogether, CBS offers major opportunities to consolidate its position as a leading international center for integrative structural biology and interdisciplinary life sciences research.

Context-related weaknesses and risks

The sustainability of CBS's state-of-the-art infrastructures represents a structural vulnerability. Continuous investment is needed to keep up with rapidly evolving technologies, particularly in cryo-EM, biophysics and computational biology. Such investments depend heavily on competitive external funding and on the ability of the unit to retain or attract skilled technical personnel. Recruiting and stabilizing highly qualified engineers and permanent support staff remain difficult in the current institutional context, posing a risk to the long-term operation and performance of the platforms.
The unit's interdisciplinary organization, while one of its greatest strengths, also carries potential risks of fragmentation if communication and coordination across teams are not maintained. Ensuring that all teams benefit equally from shared infrastructures and that emerging topics are sufficiently supported requires ongoing strategic oversight.
Finally, the implementation of open science, data management and sustainable research policies (although well integrated at CBS) imposes growing technical and administrative demands. Without adequate institutional support, these obligations could increase the burden on researchers and support staff. Overall, the main risks for CBS concern the maintenance of its high level of excellence under increasing operational, financial and human constraints, while preserving its flexibility, collaborative culture and capacity for innovation.

EVALUATION AREA 3: INCLUSION OF RESEARCH ACTIVITIES IN SOCIETY

Assessment of the inclusion of the unit's research activities in society

CBS maintains strong, structured interactions with industrial, clinical, agricultural and biotech partners, leading to vaccines, anticancer molecules, startup projects and patents. Its platforms provide high-level services through numerous contracts. At the same time, CBS runs sustained outreach, school programs and public debate activities, positioning the unit as an active and responsible contributor to society.

Context-related strengths and opportunities

CBS operates in a favourable environment for interactions with the economic, clinical and biotech sectors. Its positioning in structural biology, biophysics and molecular medicine naturally supports collaborations with companies and hospitals, and fits well within the rich Montpellier ecosystem. This context facilitates industrial contracts, CIFRE fellowships and public–private partnerships, and offers strong opportunities for technology transfer and translational research.
Several research programs are directly aligned with major societal challenges, such as sustainable agriculture, food security and cancer therapy. Projects on plant immunity, biocontrol strategies, and innovative anticancer molecules, as well as the development of vaccines and biohybrid therapies, illustrate the continuity between fundamental research and high-level technologies, with patents, startup projects and industrial agreements as concrete outcomes.
CBS's advanced platforms in NMR, cryo-EM and biophysics reinforce its attractiveness for external partners seeking high-level expertise and services, strengthening its role as a regional and national reference center for structural and biophysical analysis.
On the societal side, the unit has built a strong culture of outreach and public engagement, with long-standing participation in the Fête de la Science, regular school activities, mentoring programs for gender equity, and contributions to public debates and media.

Context-related weaknesses and risks

The strong involvement of CBS in industrial collaborations, services and valorization creates a high workload for researchers, engineers and administrative staff, with a risk of limiting time and energy for exploratory or high-risk academic research. Maintaining this level of partnership activity will require stable support for technology transfer (patents, maturation, regulatory aspects) and continuous investment in platforms and dedicated personnel.
Outreach and public engagement rely largely on voluntary efforts, which may be difficult to maintain in the long term under increasing scientific and administrative constraints. In addition, the growing complexity of rules on IP, open science and ethics entails extra administrative burden and the need for continuous training and dedicated support.

ANALYSIS OF THE UNIT'S TRAJECTORY

Over the current contract, CBS has shown a strong ability to preserve its scientific coherence. The change of direction in 2022 was validated by a clear vote of permanent staff and the non-renewal or reorientation of problematic teams was the chosen unit's strategy to address internal difficulties. The promotion of the ATIP-Avenir group to full team status and the creation of a new computational design team demonstrate proactive renewal of leadership and themes.

The 2026–2030 scientific strategy is reasonably ambitious and coherent, structured around seven strategic research axes that extend the unit's historical strengths while integrating emerging areas. The focus on integrative structural biology, AI and computational design, biomolecular dynamics, mechanobiology, microbial systems and environmental exposures places CBS in competitive international fields. The new organization (11 teams contributing to several axes) is designed to favour interdisciplinarity.

The project is supported by a strong financial base, with significant and diversified external funding already secured for the next period, and by major infrastructural prospects, including a new 1,000 m² building with BSL-2 and chemistry labs, and the installation of the ART SynBio. These developments offer important opportunities for cellular structural biology, synthetic biology and translational research.

The main structural risk concerns support staff. Retirements among IT and technical personnel, combined with increased needs for data storage, GPU computing and cryo-EM/cryo-FIB processing, make reinforced recruitment at these levels critical. Without additional permanent engineers, the ambitious program in AI and integrative structural biology may be constrained by infrastructure bottlenecks. Risks also concern teaching capacity linked to upcoming retirements in key Master programs.

Overall, the trajectory of CBS is clearly positive and forward-looking: the unit has capitalized on its strengths, implemented necessary organizational changes and built a scientifically exciting and coherent five-year project, well aligned with national and international priorities.

RECOMMENDATIONS TO THE UNIT

RECOMMENDATIONS REGARDING THE EVALUATION AREA 1: SCIENTIFIC OBJECTIVES, ORGANIZATION AND RESOURCES OF THE UNIT

Ensure long-term support for technical staff and infrastructure to sustain the unit's objectives and maintain operational excellence. Securing permanent technical positions and stable funding for equipment renewal will be essential to preserve the unit's technological edge. Considering the growing needs of several teams and the difficulty in recruiting and retaining technical staff, the unit may benefit from increased sharing of technical personnel across teams and platforms. It also appears important to clarify to all staff the framework and criteria used to assess the relevance of creating new teams.
Students and postdocs also reported a lack of access to quiet, dedicated spaces for writing. Providing such environments through better space allocation or shared writing rooms would improve productivity and well-being, particularly for early-career researchers.
In addition, the physical separation between the two buildings hosting the unit was identified as a structural limitation that may hinder interactions and access to shared facilities. Improving physical connectivity or optimizing space distribution could strengthen scientific cohesion.
Finally, in view of the strong increase in the unit's size over recent years, an evolution of the governance model is recommended. While informal governance may have been appropriate in the past, the current dimension of CBS calls for more structured procedures, potentially including the establishment of a Scientific Advisory Board.

RECOMMENDATIONS REGARDING THE EVALUATION AREA 2: THE UNIT'S SCIENTIFIC RESULTS, IMPACT AND ATTRACTIVENESS

Maintain and further structure the support for interdisciplinary research areas by promoting projects at the interface of structural biology, cell biology and quantitative biophysics. Encourage cross-team initiatives around shared high-end technologies (cryo-EM, NMR, biophysics and advanced imaging platforms) in order to further promote high-impact publications and strengthen the unit's visibility. Continuity and maintenance of the cryo-EM expertise is a key strategic priority for the upcoming contract. This is essential to maintain the unit's strong reputation in the field and to fully exploit, internally and externally, the recently acquired equipment. Further reinforce the attractiveness of the unit through targeted recruitment of young scientists, support for international collaborations, and improved access to core facilities for external users. These actions will consolidate CBS scientific excellence while increasing its national and international impact.

RECOMMENDATIONS REGARDING EVALUATION AREA 3: INCLUSION OF RESEARCH ACTIVITIES IN SOCIETY

Continue to encourage and consolidate the visibility of CBS research towards society through coordinated actions in science communication and public outreach, including participation in national and local science events. Further promote interactions with industrial and clinical partners to facilitate knowledge transfer and research valorization. Maintain strong involvement in training activities for students, engineers and teachers, as well as participation of CBS members in expert committees and public debates related to health, environment and biotechnology, in order to reinforce the societal impact and attractiveness of the unit.

TEAM-BY-TEAM OR THEME ANALYSIS

Team 1 : Dynamic Structure and Function of Biomolecules by NMR

Name of the supervisor: Mr. Christian Roumestand/Ms Nathalie Declerck

THEMES OF THE TEAM

The team's primary objective is to describe the structure and dynamics of biomolecules and complexes to understand their function. The team uses an integrative approach to structural biology, focusing on advanced nuclear magnetic resonance (NMR) techniques and complementing these with X-ray crystallography, cryo-electron microscopy, fluorescence methods, and a wide range of biophysical techniques.
This work is organised around three key areas: the structural basis of plant immunity; the use of high-pressure NMR to study protein folding; and the development of vaccines against parasites (babesiosis).
The team's expertise in NMR is shared with the wider community through its platform activities, generating multiple internal and external collaborations, including industrial contracts.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Recommendations were largely taken into account

-attract PIs using NMR as a key technique: the recruitment of a CNRS CRCN who will join the team in November 2025 ensured that the expertise in NMR will remain strong within the Unit, despite several retirement of experts in the field anticipated in the next period.

-combine the specific methodological developments of the group with the specific questions of structural biology: The high-pressure methodology will be transferred to the platform activities, with a focus of the new team on a fully renewed biology programme.

-strengthen doctoral and postdoctoral training: Training has continued with one PhD defended, with publication as first author and another still ongoing. Two postdocs joined the team during this period. This arguably is still a low level of effort in terms of training. The team acknowledges that this is difficult to attract PhD candidates in biophysics locally.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**7**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	3
Post-doctorants	2
Doctorants	1
Sous-total personnels non permanents en activité	**6**
Total personnels	**13**

EVALUATION OF THE TEAM

Overall assessment of the team

The portfolio combines fundamental structural work and methodological developments in high-pressure NMR with very good to excellent scientific output.
The team has updated its project and maintained its expertise by recruiting new PIs. It has funded its main project in plant immunity and developed a network of collaborations, demonstrating excellent attractiveness.
The team has carried out excellent activities in the wider community, such as producing a recombinant vaccine against bovine babesiosis, collaborating with industry, teaching at university and promoting science to younger students.

Context-related strengths and opportunities

The team 's main research project focuses on plant immunity. It occupies a strategic position in the Montpellier ecosystem of plant biology and immunology. The team is studying the MAX family of pathogen effectors (PLoS Pathogens, 2024) and the NLR family of immune receptors, which are activated by avirulence factors to develop plant resistance. Proof of concept for designing improved immune receptors has been provided (Nature Communications, 2022), and the team is now conducting structural studies of NLR complexes with two different avirulence factors (ANR RePairs), as well as functional assays in plants. The team's research (19 publications as main authors) has been published in very good journals with a solid reputation (e.g. Structure, the Journal of Structural Biology, Scientific Reports) to excellent journals with a broader appeal such as PLOS Pathogens and Nature Communications.

The team has produced 38 publications and two BioRxiv articles, including 21 collaborative projects within the CBS and at national and international levels. Twelve of these are the result of collaborative projects conducted by the NMR platform. These collaborations have led to publications in Nature Communications, Communications Biology (2), PNAS.

One of the two PhD students has published as first author and defended her thesis; the other is ongoing. Two postdocs joined the team during this period. The team also hosted eight Master's students (M1 and M2).

The team has partnered on three ANR and one ERC projects (€915k) that cover the topic of plant immunity and are coordinated by INRAE teams. Two grants from MITI were also obtained. A helium recycling system has been installed to ensure the long-term sustainability of the NMR platform.

The team's research project on plant immunity has an obvious societal impact in terms of reducing the use of pesticides against major rice pathogens, thereby promoting sustainable agriculture. The vaccine and diagnostic activities provide concrete examples of translational impact. Collaborative interactions with industry and the Austrian government have been very productive and are a substantial source of diversified funding. NMR service activities provided €37,000. One collaborative project with Roche (€20,000) took advantage of the team's expertise in high-pressure NMR to evaluate the stability of therapeutic antibodies in these extreme conditions.

The team is involved in teaching and other related activities at UM, including in direct relation to their research activities in various Master's programmes. A new licence in bio-production is anticipated.

The team has been very active in promoting science among young people by communicating in schools, participating in the DECLIC and Apprentice Researchers initiatives, and welcoming secondary school interns. The team has also coordinated events during the 'Fête de la Science'. One of the team members is also a member of the "Femme et Science" association.

Context-related weaknesses and risks

Only 1 thesis defended and one on-going during the period is relatively low. The difficulty of attracting PhD students in biophysics in Montpellier remains a limiting factor.

Almost 10 articles are published in journals known for their fast-track process, which can diminish the reputation of the published research, regardless of its quality.

Most of the funding is as partners. Funding has sometimes been more fragile on some axes.

The main weaknesses are linked to generational turnover and resource constraints. Anticipated retirements create a risk for the continuity of both the plant immunity axis and the high-pressure NMR expertise, and the team itself states that the future of plant immunity research depends on dedicated recruitments.
Finally, the heavy involvement in platform activities, although a strength for the unit, can weigh on the capacity of PIs to concentrate on their own high-visibility projects if the distribution of tasks and technical support is not carefully managed.

ANALYSIS OF THE TEAM'S TRAJECTORY

The planned trajectory for the next period is organised around the unifying theme "Structural basis of host–pathogen interactions by NMR". Under a new leadership, the team proposes to concentrate more explicitly on NLR immune receptors (in plants and, increasingly, in human systems), on chaperone-mediated activation, and on the design and characterisation of vaccines and diagnostics in this context. Building on the team's previous expertise in immunity, the new project has a broader focus than just plants and is more in line with the one-health approach. A new theme that brings together new PIs is the study of the function of Hsp90 in activating clients (including NLRs).

The former leader of the Plant Immunity Project retired in March 2024. Three additional researchers are set to follow suit during the next period. It is a pity that this successful project, in terms of funding, publications, societal impact, links to INRAE, etc., risks coming to an end. The team is taking action by supporting an application for a permanent researcher position to ensure continuity, which seems to be a priority.

The NMR expertise appears to be in a good position for the future, given the CNRS's recruitment of a CRCN with expertise in bio-NMR and, more broadly, integrative structural biology. The NMR platform should also be able to maintain its recognised expertise in high-pressure NMR independently, thanks to its highly qualified staff (IRs).

The team project will diversify towards human health, which is a sensible choice given INSERM's supervision of the laboratory, but it could also lead to increased competition. The researcher will investigate NLR immune receptors involved in the inflammatory response, building on previous experience with plant Nod-Like Receptors.

The newly recruited CRCN (2024) will be joined by another early-stage researcher (a CRCN from INSERM) through internal mobility. This researcher has benefited from an ATIP-AVENIR position within TEAM 5 during the current period and has demonstrated his ability to secure additional funding through university programmes such as MUSE & ExposUM.

Taken together, the expertise gathered should extend far beyond NMR, with the integration of cryo-EM and mammalian cell culture offering a chance at integrative approaches. This aligns with the unit's future acquisition of a high-performance microscope.

The steps taken in vaccine development are also of interest and complement the fundamental programme well, as they are oriented towards commercial development. However, they may also be successful in providing basic results that can be used more generally to develop antibodies for vaccines.

If all these transitions are well managed, the team is in a good position to consolidate its role as a central structural biology actor within CBS and to maintain a strong impact on both academic and translational fronts.

RECOMMENDATIONS TO THE TEAM

As a risk, rather than a weakness, the balance between platform activities, of the service contract type and research needs to be carefully balance to preserve research time. The status and support of the NMR platform, including technical posts, should be strengthened in order to protect PI time for scientific leadership and project development.

Contact with the University activities need to be maintained, as teacher-researcher are retiring. Strengthening doctoral and postdoctoral recruitment remains essential; joint projects with plant biology and immunology groups and the emphasis on high-profile topics such as NLRs, vaccines and diagnostics could be used to attract candidates.

Take great care in integrating the pre-existing team strengths and newly acquired competencies. The transition of leadership and the integration of new PIs should be carefully prepared, with explicit definition of roles and scientific priorities to avoid fragmentation.

The team should, together with the unit's leadership, secure a clear recruitment and succession plan for plant immunity, so that these distinctive strengths are not diluted by retirements.

Finally, the team is encouraged to continue and extend its translational and outreach activities, which are a distinctive asset of CBS, particularly in the context of renewal of its leadership.

Team 2: Structure and Function of Highly Flexible Proteins

Name of the supervisor: Mr. Pau Bernado/ Ms Nathalie Sibille

THEMES OF THE TEAM

The team leads an integrated approach between advanced computational tools, biophysics (SAXS and NMR) and chemical biology strategies, including site-specific isotopic labelling and tailored protein engineering. The team addresses highly flexible systems, with low complexity regions and/or post-translational modifications. The Team studies their structures/functions in signalling, gene regulation, aggregation and phase separation. Its core aim is to connect conformational ensembles and dynamics of such proteins with their biological roles, notably in cancer, metabolic disorders and neurodegenerative diseases.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous HCERES report had encouraged the team to improve funding, to ensure that both co-leaders obtained HDR, to keep a strong focus on biologically relevant questions, and to fully exploit the individual labelling strategy, possibly extending it to other chemical modifications.
According to the self-evaluation, these points have been addressed.
Both group leaders now hold HDR and occupy senior research positions.
The team has obtained substantial funding, including an ERC Consolidator Grant, ANR support, Labex and LabMUSE projects, and European programmes.
The scientific portfolio has become more focused on clinically relevant questions, especially repeat-associated diseases and GPCR phosphorylation. The individual labelling strategy has been deployed in
several new collaborations, and new chemical biology tools have been developed to incorporate non-natural amino acids and specific labels, allowing high-resolution studies of disordered regions and transient interactions.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	**4**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	1
Post-doctorants	1
Doctorants	1
Sous-total personnels non permanents en activité	**3**
Total personnels	**7**

EVALUATION OF THE TEAM

Overall assessment of the team

The team's scientific work combines methodological originality with clearly defined biological questions. Recognized for its integrated approach to intrinsically disordered proteins and low-complexity regions, the team shares its methodology with the scientific community. The team has obtained competitive European funding and has a strong network of international collaborators. Overall, the committee considers the team to be excellent.

Context-related strengths and opportunities

The team studies intrinsically disordered proteins (IDPs) and domains using a variety of experimental methods, such as SAXS and NMR, in conjunction with chemical biology and modelling tools. The team addresses biological mechanistic questions related to the dynamic properties of the system, such as the formation of liquid-liquid phase separation. The team also investigates cell signalling mediated by ID domains, as seen in GPCRs. Its research also has a strong methodological programme. This includes computational approaches to building ensembles for IDPs and the introduction of isotopically labelled amino acids, for example with 19F to study Huntingtin (Nature Structural & Molecular Biology) or with alanine (ACS Chemical Biology). Conceptually coherent, the projects focus on two major biological areas: the structural basis of diseases associated with homorepeats and low-complexity regions, and the conformational and functional effects of phosphorylation patterns (particularly GRK-mediated phosphorylation of GPCRs). The team thus sits at the interface of structural biology, chemical biology, and signalling research in an internationally highly competitive field.

The team has produced 14 publications as first/last corresponding authors, in journal very well-regarded in the field such as structure (3), J Mol Biol (2), ACS Chem Biol, with highlights in renown journal such as Nature Struct. Mol. Biol, Sci. Adv. and JACS. Additional collaborative work leads to a total of 61 publications (including 2 BioRXiv), published in J Mol Biol, Nat Comm, Nucleic Acids Research, J Med Chem, Nature Structural and Molecular Biology, PNAS, Nature Chemical Biology, etc. A collaborative project with Team 5 on the regulation of nuclear receptors by intrinsically disordered co-regulators lead to 2 publications (Structure, JMolBiol).

Research project was funded by 3 newly acquired ANR (and one already granted for the next period) and one on-going, including two as coordinators. IDEX/I-Site initiative granted 3 PhD fellowships and one PoC grant. Partnership within EU projects lead to mobility and training (MSCA staff exchange and RISE), such as short incoming mobilities of PhDs from Argentina (3). An ERC consolidator grant (2015-2022) overlapped the period. This project aimed at developing chemical biology tools to study proteins with low complexity regions, such as huntingtin.

One HDR was obtained during the period. Three PhD students defended their thesis (two will join in 2025), two of them co-supervised and located in other laboratories (for computational projects). In addition, 8 Post-doc joined projects encompassing the period.

The team contributed to training in EMBO courses and the French RENAFOBIS. Team researchers were invited to conferences and seminars, including international ones, and participated to various conference organization through scientific and organization committees.

The team manages the NMR and biophysical platform at the CBS

Context-related weaknesses and risks

The team is composed of 2 researchers and two support personnel as permanent staff.
As a small team, it relies on short-term contracts to pursue its scientific programme, which makes it highly dependent on funding. For example, the end of a large ERC grant can result in significant fluctuations in team size. This raises questions about the capacity to sustain all areas of research with sufficient personnel. Securing and renewing funding for core projects is a constant challenge in such a competitive field. Consolidating highly technical expertise in chemical biology and kinase production is another issue: without explicit measures, there is a risk of losing these skills.

The two PIs are the only researchers in the team and do not agree on a shared vision for the project or its management. The future structure and leadership of Team 2 are therefore not clearly defined, suggesting a possible reconfiguration in the next contract and making the topic of sustaining the project with critical mass even more relevant.

There is limited in-house expertise in cell biology and in vivo experiments, which restricts the scope to which structural and dynamic findings can be validated functionally and published in biology-oriented journals. The team has no strong interactions with biology laboratories to extend its research into a larger context. The team's valorisation activity is low, but this is obviously limited by the team's size.

The relationship with university teaching activities seems rather limited, which could affect the ability to attract promising students to the team project.

ANALYSIS OF THE TEAM'S TRAJECTORY

The scientific trajectory of the team is clearly promising. It builds on strong methodological foundations and on biologically meaningful questions. The international momentum on IDPs, phase separation, signalling by disordered regions and PTMs offers an excellent context.

The first part of the trajectory concerns continuation of the project on GPCR regulation. The local concentration of GPCR experts provides natural opportunities for fruitful collaborations and it can be exploited for many receptors (e.g. ANR AudioGPCR). Other projects are collaborative, based on already explored system such as the molecular mechanisms associated with Ki-67 function, a cell proliferation marker or new projects, to investigate the transcription factor STOP in plants. Although the NMR sub-projects have in common the study of signal transduction and regulatory processes by IDP conformational changes and/or PTMs, characterized by NMR, they lack a clear thematic focus. This poses the risk of dispersion and loss of visibility, as well as a strong reliance on collaborative work.

In the second part, the team will continue its integrated efforts to characterize low complexity regions of IDPs, combining chemical biology, biophysics and computation. In particular, it will focus on polyQ and polyA streches that are involved in several diseases. Interestingly, a project concerns transcription factor in plants and would be complemented by in planta experiments. Computational approaches will try to obtain general principles governing the structure of low complexity regions, leveraging experimental data, mainly acquire by NMR and specific labelling. A methodological project concerns the generation of IDP ensemble using massive compilation of data from alphafold database and from SAXS/SASDB coupled to an AI algorithm to gain a predictive power. The team is well positioned to leverage this recent and increasing progresses using computational generative models and it could lead to synthetic biology approaches that would be very well exploited within the laboratory.
Chemical biology approaches will continue to be developed to improve SANS measurements by incorporation of amino-acid specific deuteration, using cell-free synthesis and the use of gold-nanoclusters, already funded by an ANR.

However, the institutional trajectory is more uncertain. The decrease in staff size after major grants, combined with the lack of clarity about Team 2 as a single entity, raises the possibility of structural reorganisation. There is a risk that, if not carefully managed, this could fragment the expertise built up over the years and weaken the group's visibility. Conversely, if the reconfiguration is used as an opportunity to stabilise leadership, clarify axes and secure resources, the team's trajectory could be strengthened.

RECOMMENDATIONS TO THE TEAM

The structure and leadership of the team needs to be defined in close coordination with the unit's direction.

On the scientific side, the group should continue to capitalise on its methodological strengths while systematically embedding its projects in collaborations that provide strong cellular and in vivo validation, in order to compensate for the limited in-house biology and to increase visibility in disease-oriented journals. Although the NMR sub-projects (part 1) have in common the study of signal transduction and regulatory processes by IDP conformational changes and/or PTMs, characterized by NMR, they lack a clear thematic focus. This poses the risk of dispersion and loss of visibility, as well as a strong reliance on collaborative work. The GPCR project seems to be strong in terms of perspectives and integration.

Efforts to secure long-term funding for each major axis should build on the ERC and ANR track record and on the high biomedical relevance of the topics.

The team should also put in place explicit measures to conserve and transmit its chemical biology and kinase-production know-how, for instance through shared platforms, cross-training and documentation.

Finally, a more targeted strategy to attract PhD students and postdocs, including co-supervision with cell biology or clinical groups and clear communication on the international profile of the projects, would be beneficial to rebuild a critical mass.

Team 3 : Multi-Scale Structural Biology

Name of the supervisor: Mr. Patrick Bron

THEMES OF THE TEAM

As the team did not include its report in the unit's evaluation dossier, the aspects listed below cannot be assessed.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

N.A.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	0
Post-doctorants	0
Doctorants	0
Sous-total personnels non permanents en activité	**0**
Total personnels	**5**

EVALUATION OF THE TEAM

Overall assessment of the team

N.A.

Context-related strengths and opportunities

N.A.

Context-related weaknesses and risks

N.A.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team will not be renewed in its current composition. Therefore, the team's trajectory will not be addressed in the present report.

RECOMMENDATIONS TO THE TEAM

N.A.

Team 4 : Workshop on Structural Biology, Chemistry, and Informatics

Name of the supervisor: Mr. Gilles Labesse/ Ms Corinne Lionne

THEMES OF THE TEAM

Team 4 (ABCIS) develops an integrated structure-based drug design programme at the interface of structural biology, bioinformatics, chemoinformatics and medicinal chemistry. The main scientific focus is the detailed characterization of therapeutic targets and their ligands in order to guide rational design of small molecules. The team combines X-ray crystallography, biophysical assays and time-resolved enzymology with virtual screening, docking and comparative modelling, as well as micro-synthesis of focused series of compounds.
The thematic portfolio covers kinase inhibitors in oncology (including ERK inhibitors that have led to a start-up and a clinical programme), anti-infective projects on bacterial and parasitic targets, and collaborative work on nuclear receptors and other signalling proteins. ABCIS also develops and maintains several widely used computational tools and servers, and plays a key role in national infrastructures (FRISBI, ChemBioFrance), acting both as a research group and as an enabling platform for the unit and external users.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous HCERES report underlined the quality and complementarity of ABCIS, but pointed to the risk linked to a small team dispersing its efforts across too many projects. It recommended a clearer scientific focus and stronger leadership on a limited number of flagship projects.
The self-evaluation and current activity show that this recommendation has been taken into account. ABCIS has kept a similar number of projects but has raised their impact, with recent high-profile publications, successful translational outcomes and reinforced international collaborations. The team has also increased its critical mass by attracting additional researchers and anticipating new permanent recruitments. The balance between platform service and in-house research remains demanding, but the team has clearly structured a core of high-impact projects around which its activity is now organized.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**9**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	2
Post-doctorants	1
Doctorants	2
Sous-total personnels non permanents en activité	**5**
Total personnels	**14**

EVALUATION OF THE TEAM

Overall assessment of the team

ABCIS is a small but highly influential team that plays a central role in the structure-based and chemoinformatics dimension of the unit. It delivers excellent to outstanding scientific outputs well above what would be expected from its size, with an outstanding track record in translational drug discovery and in methodological developments. The dual identity of research team and national platform is managed with professionalism and contributes significantly to the excellent visibility of the unit at national and international level.

Context-related strengths and opportunities

The main strengths are the unique positioning at the interface of structural biology, computation and medicinal chemistry, the strong integration in national infrastructures, and the demonstrated ability to convert fundamental work into translatable projects, including patents, industrial partnerships and a clinical candidate. The planned reinforcement of human resources and the emergence of AI-based protein and ligand design, combined with cryo-EM developments in the unit, offer clear opportunities for ABCIS to consolidate its leading role in structure-based design and to drive new high-profile interdisciplinary projects.

Context-related weaknesses and risks

The main risks are related to the persistent tension between service activities and scientific leadership, and to the vulnerability associated with a still limited number of permanent staff. The breadth of the project portfolio, spanning oncology, infectious diseases and method development, may again challenge prioritization if new projects are added without strict selection. In addition, translational projects remain partly dependent on industrial interest and competitive funding, which can fluctuate.

ANALYSIS OF THE TEAM'S TRAJECTORY

The trajectory proposed for the next period is coherent with past achievements. ABCIS plans to consolidate its drug discovery pipelines on selected targets, further exploit cryo-EM and fragment-based approaches, and develop ambitious AI-assisted design of proteins and allosteric switches, validated experimentally through biophysical and cell-free systems. At the same time, the team will maintain its platform role and its open computational resources, which feed numerous collaborations inside and outside the unit.
If human resources are effectively strengthened and project prioritization remains strict, the team is well positioned to maintain and even increase its contribution to high-impact publications, translational outputs and national service.

RECOMMENDATIONS TO THE TEAM

It is recommended that ABCIS continue to clearly identify a small number of flagship scientific axes on which it leads conceptually and in publications, while keeping other activities explicitly framed as support or collaborative contributions. The team should work closely with unit management to secure long-term technical support for platform duties, so that principal investigators can devote sufficient time to scientific leadership and grant writing. ABCIS should also fully exploit the opportunities offered by AI, cryo-EM and national infrastructures to position itself as a reference group in integrative structure-based design, and to further strengthen its role in training PhD students and postdocs in these cross-cutting skills.

Team 5 : Nuclear Receptors, Integrators of Endogenous and Environmental Signals

Name of the supervisor: Mr. William Bourguet/ Ms Albane Lemaire

THEMES OF THE TEAM

Team 5 studies ligand-dependent nuclear receptors as central integrators of endogenous signals and of pharmaceutical and environmental chemicals. Its work spans from atomic resolution structures to in vivo models, with strong emphasis on transcriptional regulation, endocrine physiology, drug metabolism and endocrine disruption.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous HCERES report encouraged the team to maintain a high publication standard in line with its strong funding, to attract PhD students and disseminate results, to strengthen multidisciplinary approaches from molecules to in vivo models, and to develop the EDMon server with a clear public-health perspective, while balancing high-risk and more secure projects.
Since then, Team 5 has produced numerous high-quality publications, including structural and mechanistic studies in leading journals and invited reviews. It has advanced therapeutic projects (PXR PROTAC, optimised B-Raf inhibitors) and has substantially developed the environmental axis, notably on endocrine disruption and mixtures. EDMon and related resources have been expanded and integrated in national and European initiatives on the exposome. The team is clearly active in training and in international consortia, and appears to have implemented the previous recommendations in a satisfactory way.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	4
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**6**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	3
Post-doctorants	2
Doctorants	3
Sous-total personnels non permanents en activité	**8**
Total personnels	**14**

EVALUATION OF THE TEAM

Overall assessment of the team

Team 5 is internationally recognized for its work in nuclear receptor structural biology and environmental endocrinology. The team combines mechanistic excellence with strong translational and societal relevance. The team is one of the pillars of the unit's scientific identity and external visibility. The committee finds the overall assessment of the team to be excellent.

Context-related strengths and opportunities

The scientific activity can be grouped into four main themes: structural mechanisms of gene regulation by nuclear receptors (RAR/RXR, TRa and others); innovative therapeutic strategies based on nuclear receptors, with a major focus on PXR and drug resistance; nuclear receptors and the AHR as targets for environmental contaminants and endocrine disruptors, with particular attention to mixture ("cocktail") effects; and the development of computational tools such as the EDMon server to screen and predict the interaction of chemicals with these receptors. The future project frames these themes under the broader concept of "Nuclear Receptors and the Exposome".

The team publishes in respected journals in the field of structural biology, such as J. Mol. Biol and in journals with a broader appeal, such as PNAS or Nat. Comm. The team has supervised 3 PhD students on the period, and welcome 4 post-docs. PIs were invited to conferences, including a Gordon conference. The team has demonstrated a strong ability to fund its project, showing the attractivity of its scientific project, with 7 ANR including 3 as coordinators and 1 INCA. The team was also partner in two EU projects.
Notably, two patents were published on the period showing the team commitment to economical outcomes of its research. The team has made significant efforts to communicate its results to a broad public, by participating to multiple events e.g. Café & Vidéo du CNRS or a Conference at Collège de France.

The team's main strengths are its multidisciplinarity, its capacity to link high-resolution structures to complex physiological and toxicological outcomes, and its leadership in endocrine disruption and exposome research. It benefits from a rich network of national and European collaborations and participates in major consortia. The integration of an ATIP-Avenir sub-team on AHR, and the synergy with Teams 4 and 6 on design and modelling, create opportunities to reinforce both the therapeutic and environmental dimensions of the programme and to further influence science–policy discussions.

Context-related weaknesses and risks

The breadth and complexity of the thematic portfolio, which ranges from classical nuclear receptor biology to exposome-scale mixture effects and platform-like activities, may overextend the team if human resources do not keep pace. There is a certain dependence on external consortia and large programmes for the environmental axis, which could be a vulnerability in case of strategic shifts. Finally, the diversity of topics and sub-teams requires careful internal governance to ensure balanced visibility and career development for all researchers.

ANALYSIS OF THE TEAM'S TRAJECTORY

The trajectory towards a unified "Nuclear Receptors and the Exposome" framework is scientifically sound and timely. It capitalises on the team's historical strengths in nuclear receptor biology and incorporates emerging needs in environmental health and regulatory science. The project foresees deeper structural and mechanistic work on receptors and co-regulators, a more systematic exploration of mixture effects using both experimental and computational approaches, and the consolidation of EDMon and related tools.
If appropriately supported in terms of staff and infrastructure, the team is well positioned to remain a leading actor in nuclear receptor research and to play a prominent role in European efforts on the exposome, with impact on both therapeutics and public health.

RECOMMENDATIONS TO THE TEAM

It is recommended that Team 5 explicitly prioritise a limited number of flagship axes within the exposome framework and organise its internal structure accordingly, making leadership and responsibilities transparent. Long-term sustainability of EDMon and other computational resources should be secured through dedicated technical positions and institutional support. The team should continue to use its visibility to attract and train young researchers, while maintaining a balanced portfolio that includes both high-risk/high-gain projects and robust, mechanistically driven lines, ensuring continuity of high-quality outputs and funding.

Team 6 : Biomolecular Modeling

Name of the supervisor: Mr. Alessandro Barducci

THEMES OF THE TEAM

The team develops computational and theoretical methods to analyse complex biological systems, combining simulations, non-equilibrium statistical physics, bioinformatics, and integrative biology with experimental collaborations and using data from atomic to cellular scales. Main themes include modelling biomolecular condensates, chaperone dynamics, and molecular mechanisms in complex systems (HSP70-driven amyloid disaggregation, TET2, HIV-like particle release). The next project will model RNA in cytoplasmic architecture across scales, advance condensate modelling, explore cell physiology through computational and data-driven approaches.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team implemented the recommendations outlined in the previous report by maintaining and reinforcing a robust scientific output. They also grew in size, with plans to welcome a new Maître de Conférences (MdC) in 2026. Funding successes further strengthened the team, enabling the addition of five postdoctoral researchers and six PhD students. Additionally, they made progress in enhancing their engagement with the non-academic sector although they acknowledge their need for improvement in this aspect.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	**2**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	0
Post-doctorants	2
Doctorants	6
Sous-total personnels non permanents en activité	**8**
Total personnels	**9**

EVALUATION OF THE TEAM

Overall assessment of the team

The team meets the highest standards of quality, with results that are excellent to outstanding. The team is well integrated within CBS and UM, with solid training and outreach activities. The team benefits from a strong collaborative network and new experimental capacity that further enhance its strategic importance and future potential.

Context-related strengths and opportunities

The team shows a strong record of scientific excellence, productivity, and leadership, making it a key contributor to the unit and an attractive partner for future strategic development. Its active collaborations across France and Europe (Switzerland, Italy) further enhance its visibility and impact. The team displays a clear commitment to strengthening its experimental dimension, with a first successful setup already achieved and a well-defined plan for further expansion.

The team is highly productive with strong expertise evidenced by high-impact publications, extensive invitations (19), active scientific leadership (organization of 3 CECAM conferences and 50 webinars, and a strong network of collaborations). The excellent funding (10 national and European grants, €1.8 M). and excellent training activity, with several postdocs, PhD and M1-2 students supervised, demonstrate the attractivity of the team.

Its research program is structured around two major axes.

Biomolecular condensates. These dynamic, membraneless compartments are essential for cellular organization. To uncover the molecular principles governing their formation and regulation, the team employs a multiscale simulation strategy. they developed fragment-based atomistic MD approaches to reveal sequence-specific determinants of protein and protein/RNA condensation and demonstrated condensate-induced reshaping of RNA structures. Coarse-grained models further elucidated the effects of phosphorylation on IDP phase behavior, while liquid-state theory and simplified domain-level models explained condensate thermodynamics and SUMOylation-driven assembly. Ongoing work integrates simulations with experiments to quantitatively dissect condensate regulation through energy-dependent processes.

Quantitative cell physiology. This second axis aims at identifying universal principles governing cellular growth, adaptation, and stress response. Using theoretical modeling, statistical physics, and complementary experiments, they investigate the coupling between gene expression, metabolism, and growth. Building on a translation modeling framework they developed, they revealed how protein degradation shapes ribosome allocation and growth under nutrient limitation and extended this to ribosome recycling via ribophagy. Recent work further integrates mRNA and ribosome dynamics within generalized growth laws. Supported by new in-house experimental capabilities, they are now validating their models by quantifying bacterial physiology under controlled perturbations.

The team is deeply embedded within the CBS, operating at the crossroads of physics, biology, and quantitative modeling. Its combined theoretical, computational, and emerging experimental approach fosters deep connections with groups in experimental biophysics, structural biology, and bioengineering. The development of in-house experimental tools now enables direct validation of modeling. Collaborations—such as the co-supervised FRM-funded PhD with team 8 on single-cell ribosome allocation and growth dynamics using time-lapse microscopy—illustrate this integration. The unit should continue to support these initiatives and reinforce the team's central role in internal collaborative efforts. The arrival of a new MCF in computational structural biology will broaden the scientific scope and further strengthen ties with experimental teams.

Context-related weaknesses and risks

Sustaining long-term technical expertise represents a potential vulnerability. The recruitment of a research engineer (IR) would be essential to ensure the continuity of software development and to provide permanent technical support.

As with many research teams (substantially comprising non-permanent members), reliance on short-term contracts and the competitive nature of external funding pose challenges for maintaining stability (know-how leaving with the end of the contracts) and continuity.

While focused on two main areas, the number of research topics may dilute the visibility of the team.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team presents a clear and coherent scientific trajectory, building on its recognized expertise in multiscale modeling of biomolecular condensates and quantitative cell physiology (see above). It promises:
1. to consolidate and extend these strengths through an integrated modeling framework addressing the role of RNA in cytoplasmic organization across scales. This effort will combine atomistic and coarse-grained simulations with analytical, non-equilibrium models of translation and resource allocation, in close synergy with experimental partners (ETH Zurich, CBS). These developments aim to uncover the physical principles linking cytoplasmic architecture to translational control.

2. to advance the frontier of biomolecular condensate simulations, developing new coarse-grained and hybrid methods to explore condensate organization, metastability, and regulation by active, energy-dependent

processes. These models will be applied to biological systems of increasing complexity and to synthetic biology applications, including the design of programmable intracellular compartments in collaboration with CRI/CQSB Paris and future local partners.

3. to ensure strong conceptual integration and continuity in its quantitative physiology program. Ongoing and planned projects extend translation modeling from bacteria to plants, addressing stress responses and growth regulation in collaboration with IBMP Strasbourg. Emerging research on single-cell variability and the biophysical role of intracellular ionic environments promises to connect molecular modeling with physiological observables.

Overall, the team's trajectory combines methodological innovation, strong collaborative networks, and increasing experimental integration. This positions it to make substantial contributions to understanding the physical principles of cellular organization and to expand its influence at the interface of theoretical, computational, and experimental biology.

RECOMMENDATIONS TO THE TEAM

The team's integration of large-scale biological data highlights the need to consider emerging AI technologies, particularly deep learning, which are likely to transform the kind of modeling approaches developed by the team in the near future. Strengthening expertise in this area would enhance the team's competitiveness.

The strong synergy between modeling and experimentation consolidates its role as a key contributor to CBS's quantitative biology strategy, this can be reinforced by taking a leading role within internal collaborations.

The team should continue along its path of outstanding scientific excellence.

It is worth noting that the team is currently highly gender unbalanced; increased attention to the recruitment of female PhD students, postdoctoral researchers and permanent researchers would be beneficial.

To ensure long-term continuity of technical expertise, planning of technical knowledge transfer and shared documentation should be considered. Pursuit of European funding and reinforcing translational activity will secure long-term funding.

Finally, focusing and deepening on the two main research areas, in particular in view of the expected growth, will strengthen the already remarkable visibility of the team and the impact of the research outcomes.

Team 7: Mechanism of DNA Segregation and Remodeling

Name of the supervisor: Mr. Marcelo Nollmann

THEMES OF THE TEAM

The Chromatin Biophysics team investigates the spatial and temporal properties of chromatin using primarily biophysical approaches. The team develops and applies high-resolution imaging technologies, spatial multi-omics, and computational modeling to understand dynamic transcriptional regulation. The team's research is subdivided into three main themes: 1) developing single-cell and associated single-molecule imaging tools to probe chromatin biology; (2) uncovering regulatory mechanisms that define and sustain cell-type identity, and (3) investigating how specialized cells collaborate to enhance organism function. The team's research spans four a range of model systems including mammalian cells lines and mouse models, human tissue samples, *Drosophila* and bacterial biofilms.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous committee urged the team to maintain its strong trajectory, clarify long-term needs to remain globally competitive, reinforce bioinformatics/AI capacity, and develop outreach and economic/transfer activities. The current plan demonstrates substantial alignment with these recommendations.
Scientifically, the team has consolidated a clear, ambitious strategy centered on spatial multi-omics, advanced imaging, and mechanistic chromatin biology in well-chosen model systems and disease contexts, confirming its capacity to compete with leading international groups. Participation and leadership within major initiatives such as PEPR Cell-ID indicate careful evaluation of required means and successful access to high-level resources and networks.
The trajectory explicitly embeds computational modeling and machine learning (e.g. chromatin motif discovery, integrated spatial analyses), signaling a concrete response to calls for strengthened bioinformatics/AI. The strong open-science commitments (public code, OSF repositories, systematic preprints) position the team well for technology dissemination and future transfer. While explicit economic partnerships and structured public outreach remain less detailed, the emphasis on open tools, national platforms, and disease-relevant applications provides a solid foundation to further address these points.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	4
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**8**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	2
Post-doctorants	1
Doctorants	3
Sous-total personnels non permanents en activité	**5**
Total personnels	**13**

EVALUATION OF THE TEAM

Overall assessment of the team

The team demonstrates outstanding international leadership in spatial genomics and quantitative imaging, combining technological innovation with biological insight. Its integrated expertise, strong publication record, and commitment to open science make it an important consortium in 3D chromatin research. Continued focus, computational reinforcement, and talent development will further consolidate its exceptional impact and sustainability.

Context-related strengths and opportunities

The group demonstrates exceptional scientific productivity and originality, combining conceptual innovation with a rare breadth of technical expertise. It stands at the forefront of *spatial genomics* and *single-cell chromatin biology*, uniquely integrating custom optical engineering, automated fluidics, molecular probe synthesis, and high-dimensional data analysis. The development of Hi-M, a pioneering 3D chromatin-tracing platform, and its continued open-source evolution exemplify the lab's commitment to methodological excellence, reproducibility, and global accessibility. These innovations position the team as the leading European laboratory in this field, with clear international recognition alongside top US groups.

Scientific output during 2019–2024 is remarkable: 34 peer-reviewed publications, including 22 as corresponding author and 16 in top-tier journals, reflecting both productivity and intellectual leadership. High citation rates (>3600) confirm strong scientific impact. The group's work spans molecular to organismal scales, applying custom-built imaging systems to dissect enhancer–promoter interactions, chromatin topology, and transcriptional regulation in *Drosophila*, mammalian cells, and bacterial models. This integrative strategy—covering both fundamental physics of chromatin structure and applied biological questions—creates a powerful interdisciplinary signature.

The team also excels in training and mentoring, with numerous PhD and postdoc alumni progressing to competitive academic or industrial positions. The laboratory's commitment to open science, reproducible research, and public engagement further enhances its societal relevance. It has contributed major analytical resources—software for image acquisition, segmentation, and 3D reconstruction—released under open licenses and adopted by external groups worldwide. In addition, its funding portfolio is exemplary (> 5 M€ from ERC, ANR, foundations, and regional programs), ensuring long-term sustainability and infrastructure development. The team's leadership within major national and European networks (e.g., Cell-ID PEPR, FranceBioImaging, IBISA) amplifies its influence and fosters strong collaborative synergies. Overall, this is a cohesive, visionary, and internationally visible group that integrates physics, biology, and computation in a truly transformative way.

Context-related weaknesses and risks

While the scope and ambition of the program are clear strengths, they also pose challenges. The portfolio spans numerous technological axes (Hi-M, fluidics, AI-based imaging, biofilm analysis) and biological systems (*Drosophila*, bacteria, mammalian cells), creating a risk of strategic dispersion. Without careful prioritization, this diversity may dilute impact on a few flagship scientific questions, and strain the team's limited human resources. Facility management responsibilities (MARS) and external collaborations, though valuable, may further diffuse focus and time from hypothesis-driven research.

Another structural vulnerability is the dependency on a small number of senior technical experts for custom instrumentation and computational pipelines. Sustaining this expertise requires ongoing succession planning, documentation, and cross-training to ensure long-term resilience. The team has acknowledged past limitations in bioinformatics capacity, and while retraining of personnel is underway, there remains a shortfall relative to the complexity of multi-omic and image-based datasets being generated. Expanding internal computational strength—through dedicated hires or structured partnerships—would enable deeper analysis and integration of spatial genomics data.

Recruitment also presents a continuing constraint: few locally trained students possess the interdisciplinary profile required for advanced microscopy and quantitative image analysis. This may limit the pipeline of future researchers unless mitigated by new joint training initiatives with physics and quantitative biology master programs, or by hosting dedicated workshops to attract skilled students.

Finally, maintaining a competitive edge amid intense international competition (Harvard, Caltech, Stanford) will require a clear strategic emphasis on the lab's unique strengths—custom optical design, open-source innovation, and integrated modeling—rather than dispersing efforts across too many collaborations. Strengthening internal focus, consolidating computational expertise, and formalizing knowledge transfer mechanisms will be essential to preserve momentum and leadership in this fast-evolving field.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team's research trajectory is clearly forward-looking, building upon its established expertise in single-molecule and spatial genomics to expand toward integrated multi-omic and physiological questions. Across all four projects, there is a coherent thematic evolution—from developing imaging platforms (Hi-M, Light-Sheet Hi-M, ccMERFISH) to applying them in biologically and clinically relevant contexts, including chromatin regulation, diabetes, memory formation, and bacterial multicellularity. This progression reflects a mature and strategically diversified portfolio, translating technological excellence into fundamental discoveries of high biomedical and societal impact.

Project 1 extends the group's core strength in chromatin tracing to address enhancer–promoter communication in disease-relevant systems. Its integration of imaging, transcriptomics, and perturbation experiments across cellular and tissue models positions the team at the forefront of functional spatial genomics. The inclusion of metabolic disease models and partnerships with leaders in β-cell biology and computational systems biology ensure both biological depth and translational potential.

Project 2 demonstrates a natural evolution toward *spatial multi-omics*, uniting transcriptomic, epigenomic, and proteomic readouts in situ. The development of Light-Sheet Hi-M (LS-HiM) for volumetric imaging and the coupling of Hi-M to histone mark detection represent high-risk, high-reward technological goals that could redefine the field. The project also strengthens collaboration within the national PEPR Cell-ID consortium, ensuring sustained funding and interdisciplinary synergy with complementary experts in imaging, modeling, and oncology.

Project 3 illustrates intellectual diversification toward neuroepigenetics, leveraging the team's established tools to probe enhancer function during memory formation. This demonstrates scientific agility—translating chromatin imaging principles to neuronal function—and is supported by strong collaborations with behavioral and sequencing specialists. The planned ERC resubmission indicates resilience and ambition to secure independent international recognition.

Project 4 extends the lab's biophysical roots into microbial collective behavior, uniting single-cell imaging, transcriptional profiling, and modeling to understand multicellularity in *Myxococcus xanthus*. The approach is original and methodologically robust, benefiting from longstanding collaborations and aligning with national strategic priorities (Cell-ID, ANR programs).

Overall, the trajectory is one of *steady upward momentum*: from pioneering technology to integrative biology and disease modeling. The group's growing participation in large-scale networks and continued methodological innovation underline a sustained capacity for leadership. Its explicit commitments to open science, equity, and data transparency reinforce its credibility and ensure that its outputs will continue to set international standards in spatial and quantitative biology.

RECOMMENDATIONS TO THE TEAM

The team's trajectory is strong and ambitious; the next phase should focus on *strategic consolidation*. Prioritizing a small number of flagship biological questions—such as enhancer-promoter regulation in disease and chromatin remodeling in cell fate transitions—will maximize impact and maintain coherence across projects. Continued investment in computational and bioinformatics capacity is essential to fully exploit the complex spatial multi-omic datasets now being generated. Recruiting or partnering with quantitative analysts and data scientists should be a short-term priority.

The team should also formalize succession planning to safeguard technical expertise in custom microscopy and software development. Establishing shared documentation, training pipelines, and cross-team workshops will help sustain innovation and resilience. Finally, continued visibility in major international consortia, coupled with careful management of workload and personnel balance, will ensure that this outstanding group maintains its pioneering role as a European reference in spatial genomics and quantitative imaging.

Team 8 : Cell-Scale Physics

Name of the supervisor: Mr. Francesco Pedaci et Ms Manouk Abkarian

THEMES OF THE TEAM

The team *Physics and Mechanics of Biological Systems (PhysMechBio)* explores the physical principles underlying biological function across scales—from molecular to organismal. Its main themes include: (1) *Hemophysics*, investigating the rheology and biomechanics of blood; (2) *Bacterial flagellar motor dynamics and electrophysiology*, studying the structure–function relationships of the flagellar motor; (3) *Biofilm initiation*, examining physical mechanisms driving bacterial community formation; and (4) *Aerosol transmission*, revealing the physics of saliva aerosolization and respiratory pathogen spread.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has fully addressed the recommendations made in the previous evaluation. Concerns about low researcher numbers and funding dependency were mitigated through strategic recruitment—two engineers, three postdocs, six PhD students, and several master's students joined the group, supported by over €5M in new funding from national and international grants. The team now has a robust, sustainable structure with 4 permanent researchers (1 IR recruited during the last 2 years) and 13 non-permanent members. Increased participation in master's-level teaching has boosted visibility and attractiveness to students, with all PIs actively contributing to academic programs in Montpellier and abroad. While industrial partnerships remain limited, collaborations with medical institutions (CHU Montpellier, CHU Nîmes) now complement existing academic networks. The team also refined its scientific strategy: rather than a single, narrow focus, it has developed a *collaborative, multi-axis framework* leveraging complementary expertise in physics, engineering, and biology. This unified but diverse model has strengthened cohesion (with around half of the leading published work as inter-team collaborations), enabled new experimental setups, and enhanced cross-project synergies, effectively responding to the call for a clear, shared vision.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**4**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	3
Post-doctorants	3
Doctorants	3
Sous-total personnels non permanents en activité	**9**
Total personnels	**13**

EVALUATION OF THE TEAM

Overall assessment of the team

PhysMechBio is a highly dynamic and internationally visible team operating at the interface of physics and biology. Its interdisciplinary program combines world-class experimental biophysics, soft-matter physics, and microbiology to address fundamental biological questions with societal relevance—from bacterial flagellar motor dynamics to airborne disease transmission. The team has demonstrated excellent scientific leadership, outstanding and sustained funding, and successful renewal through recruitment and collaboration. It stands as a model of integrative, high-impact quantitative biophysics.

Context-related strengths and opportunities

The team's greatest strength lies in its *interdisciplinary depth and technical mastery*. It unites physicists, engineers, and biologists within a cohesive environment where advanced microscopy, microfluidics, holography, and rheology are applied to understand the physics of living systems. The resulting synergy produces insights of both fundamental and applied importance—linking mechanics, structure, and dynamics across systems as diverse as bacterial motors, red blood cells, and bioaerosols.
Scientific excellence and innovation:
Research on the *bacterial flagellar motor* has yielded pioneering discoveries on stator dynamics, mechanosensitivity, and proton motive force distribution, consolidating the team as a reference in molecular motor biophysics. The *hemophysics* program defines a new subfield, integrating fluid mechanics and biology to describe blood as a living material. Meanwhile, the *aerosol transmission* studies provided a globally visible contribution during the COVID-19 pandemic, offering the first quantitative links between saliva rheology, phonation, and aerosol generation. The group's pioneering work directly informed public understanding and mitigation strategies, also leading to educational and outreach publications.
Collaborations and visibility:
The team enjoys an extensive international network—spanning Europe, the Americas, and Asia—ensuring cross-fertilization of ideas and sustained visibility. Frequent invited talks by all the permanent researchers, leadership in organizing workshops, and editorial responsibilities confirm its standing in the global biophysic's community. Its connection to the LabEx NUMEV and other institutional initiatives provides privileged access to world-class facilities.
Funding and training capacity:
The group's funding base is outstanding (>€5M secured), supporting numerous PhDs and postdocs. Training is deeply embedded in its culture, with considerable teaching hours, shared supervision, open-science practices, and early exposure of trainees to international collaboration. This fosters career development and ensures a steady influx of new expertise.
Societal engagement and opportunities:
The team's work is inherently relevant to health and environmental challenges—blood disorders, infection control, and airborne transmission—and it leverages this relevance through educational publications, strong outreach, media engagement, and artistic collaborations. Opportunities ahead include expanding hemophysics and bioaerosol formation toward clinical applications, developing predictive models for biofilm formation and pathogen spread, and applying its physical methodologies to medical diagnostics, public health strategies and microphysiological systems.

Context-related weaknesses and risks

The team's diversity of projects, while intellectually rich, presents risks of strategic dilution if resources are spread too thinly across four major research axes. Each line of investigation—flagellar motor dynamics, hemophysics, biofilm initiation, and aerosol transmission—is highly ambitious in scope and technically demanding. Sustaining focus and coherence will require prioritization, maintained technical cross-breading and careful workload management, especially as the group grows.
Dependence on specialized expertise:
Much of the team's experimental edge depends on a small number of highly skilled personnel in microscopy, microfluidics, and soft-matter engineering. Without robust succession planning and structured technical documentation, turnover or temporary absences could affect productivity.
Biological depth and recruitment challenges:
While the physics and engineering capacity is world-class, molecular and cellular biology expertise remains underrepresented. Reliance on temporary staff for molecular biology work limits continuity, and the absence of a permanent biologist poses a long-term risk. Recruiting and integrating a CNRS-level microbiologist—as planned—would greatly reinforce biological depth.
Sustainability and funding:
Although current funding is strong, maintaining such a high level of resource acquisition will be challenging, particularly given the competitive landscape and the technical costs of maintaining advanced optical infrastructure. Long-term sustainability may depend on diversifying funding streams, including industrial partnerships and translational grants.

Organizational and coordination risks:
The collaborative framework across multiple PIs is productive but demands constant coordination. As the team expands, maintaining a unified strategic vision and effective communication will be essential to prevent fragmentation. Increased administrative load linked to managing numerous grants, trainees, and outreach activities could further strain leadership bandwidth.
In sum, while PhysMechBio's technical and intellectual capital is outstanding, the main risks relate to overextension, topic diversification, the need for permanent biological expertise, and the maintenance of stable funding and management structures.

ANALYSIS OF THE TEAM'S TRAJECTORY

The trajectory of PhysMechBio is clearly upward, marked by scientific consolidation, expansion, and diversification. Building on deep foundations in micro- and nanomechanics, the group has evolved into a multiscale biophysics team integrating cellular, molecular, and environmental systems. Over the next five years, four interlinked research axes define its direction: hemophysics, flagellar motor biophysics, biofilm initiation, and aerosol transmission.
The hemophysics program continues to expand the field that the team itself helped define, blending fluid mechanics, cell biomechanics, and physiology to characterize blood flow in health and disease. The work is unique in its quantitative rigor and cross-scale modeling, promising contributions both to fundamental biophysics and to biomedical applications.
The bacterial flagellar motor research, supported by HFSP and ANR funding, exemplifies continuity with innovation—moving from E. coli to more complex bacterial species, exploring energy transduction and electrophysiology through real-time optical probing. This direction reinforces the team's global leadership in the biophysics of bacterial molecular motors and extends it to the emerging frontier of bacterial bioenergetics.
The biofilm initiation project opens a novel line of inquiry—using physics-based tools to address microbial community formation and collective behavior. This integrates optical imaging, holography, and fluid dynamics to reveal early biofilm nucleation, with implications for infection control and environmental microbiology.
Finally, the aerosol transmission research, inspired by pandemic-era challenges, exemplifies the team's capacity to pivot toward high-impact societal topics while maintaining scientific depth. By combining soft-matter physics, rheology, and aerosol science, the group is defining a new interdisciplinary domain at the interface of fluid mechanics and infectious disease.
This integrated, multi-axis trajectory showcases the team's exceptional versatility, creativity, and technical reach. The planned recruitment of a microbiologist will strengthen biological integration, and sustained collaboration with medical and virological partners will increase translational relevance. The trajectory is both ambitious and feasible, grounded in secured funding, established collaborations, and a proven ability to innovate at the interface of disciplines.

RECOMMENDATIONS TO THE TEAM

The team should prioritize, consolidation and focus—maintaining its hallmark interdisciplinarity while ensuring each research axis reaches critical mass and visibility. Recruitment of a permanent microbiology or molecular biology expert is essential to complement its physical expertise and sustain long-term biological depth. Strengthening computational modeling and quantitative data analysis capacity would also enhance integration across themes. Leveraging and building upon the CBS's cutting-edge technological infrastructure may amplify the impact of scientific outcomes.
To secure resilience, the group should formalize mentorship, documentation, and cross-training mechanisms to preserve technical knowledge. Continued engagement with society, medical partners and potential industrial collaborations could diversify funding and broaden impact. Consulting with the CBS technology transfer office may help in this aspect. Pursuit of international and national funding should be maintained, while encouraging and guiding future recruitments. Finally, defining 1–2 flagship research questions linking its axes—for example, how physical forces shape biological organization across scales or how molecular to organism dynamics regulate biological function—will reinforce strategic coherence and international leadership.

Team 9: Structure and Dynamics of Membrane Assemblies

Name of the supervisor: MESSRS. Emmanuel Margeat/Mr. Pierre-Emmanuel Milhiet

THEMES OF THE TEAM

The team explores the physical and molecular principles governing the remodeling, organization and the chemical and mechanical transduction of signals in eukaryotic membranes. Its core themes include: plasma membrane organization and signaling (tetraspanins, GPCRs), nuclear pore complex structure and assembly, biomolecular condensates and phase separation. To address these topics, the team develops nanotechnological and correlative approaches (DNA origami, AFM–fluorescence, NMR, and smFRET). By combining physics, chemistry, and cell biology, the team develops state-of-the-art tools to elucidate how membranes remodel, sense mechanical stress, and transmit biochemical information in living cells.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has implemented most of the recommendations in the previous report, maintaining its world-class technological innovation while strengthening the biological focus. It successfully developed new methods—fluorescence-based sensors, correlative AFM/confocal and AFM/X-ray setups, and advanced DNA origami tools—to address mechanobiological and structural questions of major biomedical relevance. While biological questions remain slightly dispersed and importantly led by external collaboration, this refocusing toward cancer tissue mechanics, nuclear envelope remodeling, and membrane signaling has translated into a stronger publication record, including several high-impact original articles (*Nat Comm*, *Sc Adv*, *JACS*, *ACS Nano*) as leading authors.
The team achieved significant consolidation: six permanent researchers with complementary expertise in physics, chemistry, biochemistry, and cell biology, supported by four specialized engineers, provide a uniquely stable multidisciplinary environment. The recruitment of a new INSERM researcher and the successful graduation of five PhD students further strengthened sustainability. Robust funding (17 ANR grants, international programs, industrial partnerships) ensures continuity and capacity to recruit. In addition, an application to European funding has been submitted and received excellent evaluation. Overall, the team has effectively balanced technological leadership with enhanced biological relevance, as previously advised.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	4
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**9**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	3
Post-doctorants	3
Doctorants	3
Sous-total personnels non permanents en activité	**9**
Total personnels	**18**

EVALUATION OF THE TEAM

Overall assessment of the team

This is a highly innovative, internationally visible team that combines pioneering methodological development with rigorous biological inquiry. It is a recognized leader in membrane biophysics, nanotechnology, and correlative imaging, producing both conceptual advances and enabling technologies. Its multidisciplinary structure, good training environment, and collaborative openness underpin consistent excellence. Strategic consolidation around membrane protein dynamics and the new focus on mechanobiology ensures continued leadership in quantitative membrane biophysics.

Context-related strengths and opportunities

The team's foremost strength is its integration of advanced microscopies and nanotechnology to investigate membrane organization and mechanotransduction across scales. Its expertise encompasses AFM, super-resolution microscopy, smFRET, NMR, DNA nanotechnology, and protein engineering, creating one of Europe's most versatile environments for structural and dynamic analysis of membranes.
The group's discoveries on tetraspanin-mediated membrane remodeling, GPCR conformational dynamics, and nuclear pore plasticity illustrate depth and originality. By combining single-molecule spectroscopy with mechanical and structural methods, they bridge dynamic and mechanistic understanding of complex membrane systems. Their results—spanning cell migration, signaling specificity, and mechanosensitive transcription—have reshaped views of membrane protein-based signaling.
The team is a recognized driver of instrumental and methodological innovation. Achievements include DNA-PAINT and AFM–confocal integration, XRF-AFM at synchrotron facilities, and DNA origami nanomachines capable of exerting pN forces on living cells. These advances expand experimental frontiers and are shared widely through the PIBBS platform, FranceBioImaging, and EuroBioImaging, amplifying national and international influence.
The team is embedded in academic and industrial collaborative networks (Sanofi-Pasteur, CC&C), translating basic discoveries into biomedical applications, like vaccine adjuvant design and tissue mechanics profiling. It co-publishes extensively within CBS (1/3 publications) and maintains partnerships across Europe, USA, and Japan. Its funding portfolio is continuous and stable, mainly based on numerous, relatively small, national grants (~€4 M, 17 ANRs and NSF-linked). The involvement in attracting funding for large equipment (cryo-EM/FIB and confocal-FLIM-smFRET/AFM) reflects consistent competitiveness and diversity. Importantly, three of the team members are or have been importantly implicated in collective activities, being directly involved in the management of the CBS or of the pole UM BioHealth.
While the mentored PhDs is relatively limited for the number of permanent researchers, training is good in term of activities, with structured mentoring, international exposure, and leadership in the qBio program. Team members organize major events (EBSA, ESAB, Les Houches) and serve on editorial boards, reinforcing global presence. Outreach, gender-equity initiatives and sustainable research practices enhance societal impact.
Opportunities ahead include expanding into cell and tissue mechanobiology, exploiting the synergy between DNA nanotechnology and force spectroscopy by maintaining the collaboration with the new team 11, and leveraging CBS's cryo-EM and cryo-FIB developments for integrative structural analysis. The team is optimally positioned to lead in integrative dynamic structural biology and mechanosensitive membrane signaling.

Context-related weaknesses and risks

While the team's breadth is a defining asset, it also presents risks of thematic dispersion. Multiple independent projects—membrane signaling, nuclear pores, condensates, DNA nanotechnology—each require distinct expertise and resources, potentially fragmenting effort and diluting strategic focus. The expansion towards mechanobiology (at both membrane and tissue levels) may allow a coherent line across projects and represents a promising opportunity, while at the same time adds a new dimension for which the team is not yet recognized. Moreover, it may partially overlap with other CBS teams, already established experts in the field. Maintaining coherence around a few flagship biological questions will be essential to maximize impact. The development of new experimental techniques may become a weakness rather than a strength if too diversified. In this context, while the incorporation of a cryoEM expert is a great new asset, it may fragment the technological visibility of the team.
Human-resource challenges persist. Five agents working on DNA nanotechnology (1 CRCN, 1 PhD student and 3 postdocs) will leave the team to create the new team 11. Their departure may have an important impact for the team, not only in terms of personnel but also on expertise and productivity. Despite a strong permanent core, some technical and computational tasks rely heavily on individual specialists. The departure or reassignment of such key personnel could slow progress. Strengthening programming, AI-based data analysis, and simulation capacities is needed to complement experimental sophistication and reinforce quantitative analyses. Recruiting a dedicated computational biophysicist or data engineer would fill this gap.

The physical separation of personnel and instruments across two CBS buildings may hinder daily integration and collaborative fluidity, especially for students and cross-project exchanges. A clearer coordination structure and shared project management tools would help sustain coherence.
Three senior researchers carry substantial administrative responsibilities (unit leadership, platform coordination), potentially constraining scientific output and mentorship capacity. Ensuring effective delegation and succession planning for these roles will help preserve research momentum.
Finally, the diversity of technological platforms entails significant maintenance and financial costs. Sustaining this infrastructure beyond current funding cycles will require proactive strategic planning—particularly as some major ANR and platform grants approach completion. Establishing industrial service contracts or shared-infrastructure schemes could support long-term viability.
Overall, these are challenges of *success and growth*, not structural weakness. Addressing them through targeted hires, project consolidation, and resource optimization will safeguard the team's leadership and ensure continuity of excellence.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team's trajectory over the 2019–2024 period has been marked by strategic consolidation, innovation, and expansion. Building on its legacy in membrane biophysics, it has transitioned toward a truly integrative mechanobiology program that connects molecular structure, mechanical function, and cell physiology, through the important development of new correlative setups.
The research on plasma membrane signaling evolved from molecular characterization to physiological relevance, linking tetraspanin function to cancer metastasis and membrane tension control. Simultaneously, work on GPCRs reached a new level of mechanistic precision, uniting NMR, cryo-EM, and smFRET approaches to reveal conformational intermediates and allosteric regulation. These studies position the team at the forefront of quantitative receptor biology.
The nuclear pore complex program exemplifies continuity and maturation, progressing from structural visualization to dynamic assembly and mechanical adaptation during nucleo-cytoplasmic transport. The introduction of AFM–super-resolution correlative imaging opened unprecedented views of pore plasticity and basket dynamics.
Parallel developments in biomolecular condensates and DNA origami nanomechanics have created two powerful new lines of investigation that integrate seamlessly into the team's overarching theme: the physical principles of membrane and macromolecular organization. The ability to design DNA nanomachines applying piconewton forces on individual proteins of living cells represents a major conceptual and technological leap, enabling direct testing of mechanotransduction hypotheses.
The team's trajectory also shows institutional and leadership evolution. It has nurtured new permanent researchers, obtained various HDR (5/7), and assumed national and international roles in biophysical societies and imaging infrastructures. Moreover, team members are at the front of the CBS management. This leadership ensures sustainability and broad influence.
Looking ahead, the group's excellent trajectory logically extends toward cell and tissue mechanobiology, leveraging expertise in force sensing, imaging, and nanoscale manipulation. Integration with cryo-EM and computational modeling will enable correlative, multi-scale understanding of membrane-associated complexes. This direction aligns with global trends in mechanistic structural biology and places the team at the cutting edge of European quantitative biophysics.
In summary, the team has evolved from a technological powerhouse into a mature, balanced, and visionary unit driving mechanistic discoveries of high biological relevance.

RECOMMENDATIONS TO THE TEAM

The team should continue to consolidate around a few high-impact biological themes—notably membrane protein mechanobiology, GPCR signaling, membrane-biocondenstates interplay and nuclear envelope remodeling—while maintaining its technological innovation. Focusing on some of the successfully developed approaches may allow the team to deepen into the applications, leading the higher impact outcomes. Strengthening computational and AI-based modeling will be critical for integrating diverse datasets and quantitative analysis.
Strategically, the group should reinforce project coherence and internal communication, perhaps through thematic clusters or co-supervised cross-axes projects. Recruitment of an expert in computational biophysics or data science would complement existing strengths.
The team should continue collaborating with other CBS teams. Particularly with the new team 11 bringing experimental tools and expertise in membrane biophysics.
To ensure sustainability, a plan for technical knowledge transfer, shared documentation, and staff succession—especially for platform management—should be implemented. Continued pursuit of European funding (ERC, HE) and targeted translational partnerships will secure long-term growth. By focusing on coherence, digital integration, and visibility, the team can further strengthen its leader position in membrane biophysics.

Team 10 : Synthetic Biology

Name of the supervisor: MESSRS. Jerome Bonnet/Martin Cohen Gonsaud

THEMES OF THE TEAM

The team focuses on engineering smart biological systems to address key challenges in healthcare.
• Synthetic biology technology development: creation of synthetic sensing systems, genetic logic circuits, and cellular nanoshielding platforms.
• Medical diagnostics: design of bacterial and cell-free biosensors for sensitive and adaptable detection.
• Bacterial therapeutics: development of engineered strains targeting cancer, inflammatory bowel disease, and psychiatric disorders.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team has effectively addressed previous HCERES recommendations, securing sustained funding, developing new research directions and exploited the biomedical applicability of their research. The two PIs have reinforced their collaboration through joint publications (about half) and a shared ANR-funded project on engineered receptors.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	**7**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	5
Post-doctorants	2
Doctorants	5
Sous-total personnels non permanents en activité	**12**
Total personnels	**19**

EVALUATION OF THE TEAM

Overall assessment of the team

A highly innovative and productive team with strong strategic vision, leading in synthetic biology for affordable diagnostics and therapies. Its strengths in cell-free engineering, de novo protein design, and protein interaction analysis accelerate the development of programmable biological systems. Positioned at the microbiome–health interface, it exploits microbial metabolites for diagnosis and therapeutic intervention.
Beyond its academic excellence, the team demonstrates an outstanding commitment to non-academic activities, notably in innovation, technology transfer, and translational development. In this context, the establishment and development of the ART represent a particularly remarkable achievement, significantly enhancing the team's visibility, impact, and translational potential. This integrated scientific and translational approach places the team among the top groups in France and Europe.

Context-related strengths and opportunities

The team stands out for its strong expertise in engineering biosensors, genetic logic systems, and cell-free technologies, supported by a solid and enlarged base of permanent researchers and engineers. Its interdisciplinary composition and extensive collaborations enable it to address complex challenges at the interface of biology, nanotechnology, and medicine. Close ties with clinicians provide a clear translational advantage, positioning the team uniquely to bridge fundamental research and clinical applications. Sustained funding, a growing patent portfolio, and the recent creation of the INSERM Technological Research Accelerator (ART - promoting the dissemination of synthetic biology tools to academic, clinical, and industrial partners through collaborations, training, and spinoff creation) reflect both institutional recognition and long-term strategic potential. With its leadership role in France and rising visibility in Europe, the team is well placed to translate its innovations from bench to patient and market, also supported by the PoC projects for spinoff and startup creation.

Among strengths, a clear scientific identity, strong external funding (4.25 M€), PhD supervision capacity and effective interdisciplinary collaborations bridging modeling, molecular engineering, and medicine. The expansion into bacterial therapeutics is timely and promising, supported by robust preclinical and technological developments.

Context-related weaknesses and risks

The team's rapid growth (expanding from 7 to 21 members during the evaluation period) and ambitious research program come with challenges. High operational costs demand sustained external funding, and the number of publications should increase to match the enlarged staff and expanding research lines, many of which are still maturing. International visibility could also be strengthened through greater participation in global conferences and networks. Externally, the team faces strong competition from leading groups in the US and China, as well as regulatory and societal hurdles surrounding the clinical translation of GMO-based technologies.

Managing a large, multidisciplinary team will require careful attention to governance, training, and strategic planning. In a broader context of uncertain funding for synthetic biology, maintaining long-term stability will depend on continued scientific excellence, diversification of resources, and proactive engagement with regulatory and policy frameworks. The currently uneven distribution of funding across permanent researchers represents a risk.

Areas for attention include maintaining balance between exploratory research and translational focus, ensuring sustainable mentoring structures as the team grows, and strategically integrating AI and data-driven methods to enhance future modeling and design efforts.

ANALYSIS OF THE TEAM'S TRAJECTORY

Over the next five years, the team plans to consolidate its position as a leader in synthetic biology–driven diagnostics and bacterial therapeutics, supported by the infrastructure and visibility offered by the INSERM Technological Research Accelerator (ART). The program is structured around three coherent and synergistic research axes: microbial biosensors for medical diagnostics, programmable bacterial therapies, and de novo design of sensing domains.

The first axis builds directly on the team's established expertise in microbial and cell-free biosensors, now moving toward clinical translation. The focus on scaling up the modular CadC receptor platform and developing gut-metabolite biosensors demonstrates both technological maturity and translational potential. Incorporation of

new researcher and strong clinical collaborations further strengthen this trajectory, positioning the team at the interface between synthetic biology and precision medicine.

The second axis, centered on bacterial therapeutics, represents a successful expansion of the team's capabilities from diagnostics to therapy. The integration of sensing modules with secretion and bio-containment systems reflects a sophisticated engineering approach, aiming to deliver context-dependent, localized treatments. The inclusion of biohybrids—smart polymer-encapsulated bacteria— and combination with ultrasound imaging or radiofrequency-based tools illustrates forward-thinking innovation at the intersection of synthetic biology, nanotechnology, and bioengineering, with significant promise for cancer and inflammatory disease applications.

The third axis, focused on de novo protein and switch design, is particularly ambitious and visionary. It aims to address a major bottleneck in biosensor and therapeutic development—the limited repertoire of natural sensing domains—by combining AI-assisted protein design, cell-free functional screening, and structural biology. This line of research could yield transformative outcomes, though it will require careful management of computational, experimental, and training resources.

Overall, the team's five-year trajectory is strategically sound and scientifically excellent. It integrates high-risk/high-reward objectives with applied translational research, builds on a proven record of innovation, and leverages strong collaborations across academia, clinics, and industry. The program demonstrates coherence, scalability, and a clear vision for impact from molecular design to patient application.

The team exhibits excellent momentum and high international competitiveness, with strong potential for continued leadership in synthetic biology and bioengineering.

RECOMMENDATIONS TO THE TEAM

· The planned expansion into multiple advanced fronts (clinical biosensors, therapeutic bacteria, de novo protein design) is exciting but resource-intensive. Prioritizing milestones and defining success criteria for each axis will ensure sustained progress without dilution of effort.
· Strengthen AI and computational expertise to support de novo design and data integration.
· Given the team's proximity to clinical applications, early engagement with regulatory experts and translational partners (e.g., startups, incubators, clinical consortia) will be essential for managing intellectual property, biosafety, and eventual commercialization of bacterial-based products.
· Enhance international visibility through leading roles in consortia and high-impact publications.
· With continued growth and diversification, clear internal leadership roles, homogenized funding and mentoring frameworks for young researchers will be critical to sustaining productivity and cohesion across projects.
· The ART provides a powerful vehicle for technology dissemination and industry partnerships. Systematic integration of ART resources into training, IP valorization, and cross-disciplinary collaborations could maximize its long-term institutional and societal impact.
· Addressing GMO regulation and ethical considerations early will streamline future processes.
· Sustained efforts to secure EU funding and expanding translational activities will ensure long-term funding

Team 11: (ATIP-Avenir): Chromosome Structure and Control of Homologous Recombination in Meiosis

Name of the supervisor: Mr. Thomas Robert

THEMES OF THE TEAM

The team investigates the molecular and structural mechanisms underlying homologous recombination (HR), chromosome pairing and organization during meiosis. Its objective is to elucidate how DNA double-strand break (DSB) repair pathways, crossover control, 3D chromatin organization and chromosome dynamics interact to ensure genome integrity and faithful gamete formation by an integrative approach. Combining molecular biology, biochemistry, genome editing, cell imaging, structural biology and biophysics, the team characterizes, in mice, the molecular mechanisms of DSB formation, new pro-crossover proteins and new factors controlling the Synaptonemal Complex formation, then link them with HR and meiotic chromosome organization.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The team was started as ATIP-Avenir in 2018 and hosted within CBS. The 2021 HCERES evaluation did not make any specific recommendations.
However, the previous committee highlighted the risk of using crystallography and cryo-EM approaches to better characterize the structure of complexes, given to their high potential flexibility. Nevertheless, the team has published structures using X-ray crystallography. Cryo-EM remains one of the approaches considered by the team for its future projects.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	**2**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	1
Post-doctorants	1
Doctorants	1
Sous-total personnels non permanents en activité	**3**
Total personnels	**5**

EVALUATION OF THE TEAM

Overall assessment of the team

The team is very good to excellent at the national level with emerging international visibility, showing strong conceptual innovation and rapid maturation since its creation in 2018. The team built a solid reputation for originality and technical mastery in the study of chromosome structure and recombination. Its integration into CBS has been strategic, providing access to advanced microscopy and protein biophysics expertise, boosting both productivity and methodological diversity.

Context-related strengths and opportunities

The team displays a high thematic originality focus on structural aspects of meiotic recombination, bridging genome dynamics and biophysics.
The team has good to very good scientific production and visibility, considering the relatively recent creation of the team (2018) which had to manage its installation and start its dynamic. Since 2020, the team has published 3 original articles of high-quality and completeness *(2 with leading role)*: *Nucleic Acids Res*, *Nat Comm*, *and Elife (2020)*, fruits of internal collaborations with Team 5 or with the IGH unit (Montpellier) and a review (2024). Two publications are first-authored by a PhD student and a post-doc supervised by the PI, revealing good mentoring skills. The openness to collaboration, in particular in the context of the CBS, is a strength.
The team is involved in various Master's teachings and training at Montpellier and Paris Universities, although limited to ~10h/year. The mentoring activity is very good with one co-supervised PhD, one ongoing PhD, one postdoc and several master students.
The team's visibility at the national and international level is very good to excellent, with 3 invited contributions at national conferences and talks at renowned international conferences on meiosis, like Gordon conference and EMBO workshop. The team attractiveness is revealed by the incorporation of a new permanent researcher.
The team presents strong ties at the local, national and international levels, with collaborations with teams from CBS, MPI and UC-Davis.
The team has obtained substantial and diverse funding since 2021 (9 grants). As PI, 689k€ from ANR, FRM, Ligue contre le Cancer, UM or CNRS programs, showing its strong capacity to attract funding. As partner, 752k€ in collaboration with IGH groups from ANR and ANR Chaire d'Excellence, consolidating local network. Three of their grants (929k€) will extend over the period 2025-2030, ensuring funding for the team's various projects for the coming years.
The team presents excellent integration and contribution to society, being very active in CBS seminars, scientific animation and mentoring programs for young researchers or future scientists (CAMPAS) and national level (French Genetic Society Council member). The team has also coordinated 3 conferences and is asked to participate in scientific evaluation activities (juries, committees reviewing). The team promotes science to the general public and high school students (interns, Science fair). Team members are also involved in the quality of the working conditions to promote gender equality, and prevent harassment situations and risks.
Integration CBS as the new Team 3 will provide access to shared technical staff and new recruitment opportunities, enhancing the team's dynamism, sustainability, and visibility. This integration will also enable expansion into comparative meiosis across model organisms and the incorporation of cryo-EM or biophysical modeling for chromosome axis analysis.

Context-related weaknesses and risks

With five people at the moment, the team has limited critical mass, limiting the throughput and independence of large-scale studies. This could result in a high workload for the two permanent principal investigators, who manage both supervision, experiments, teaching and application to funding for projects. The team's funding is limited to relatively small but continuous national grants, which no European projects. While the team may also appear dependent on collaborations for some advanced methodologies (cryo-EM, advanced imaging and advanced modeling), the CBS provides the optimal environment for that. The above points could present a moderate structural risk, but mitigated by a strong collaborative network and support from the CBS.

ANALYSIS OF THE TEAM'S TRAJECTORY

The team, initially housed within the CBS, is now fully integrated administratively and scientifically. It will form the future Team 3, consolidating the team in the field of structural biology while bringing new skills and expertise, particularly in murine genetics and genomics, and establishing strong internal collaborations.
The team, founded in 2018, has demonstrated a fast and coherent trajectory toward maturity. Its publication level, funding success, and strong collaboration network demonstrate scientific consolidation beyond the typical scope of ATIP-Avenir projects and also indicate high potential for long-term scientific leadership. For the 2025–2030 period, the trajectory of the future team 3 is realistic, and marks a strategic consolidation phase. The scientific plan is structured around the understanding of the molecular mechanisms that control chromosome segregation during the first division of meiosis in mouse model, with three complementary objectives.

Objective 1 will decipher the molecular activity involved in meiotic DSB formation: Molecular regulation of homologous recombination initiation to understand the mechanisms that control genetic stability during gametes formation. To this end, the team plans to investigate the mode of action of different meiotic recombination proteins (TopoVIL complex). Objective 2 will determine the mouse meiotic pro-crossover activity by characterizing new pro-crossover proteins (HEIP1 and its interactors). Objective 3 will study the structural reorganization of the meiotic chromosome by characterizing new proteins required for the formation of the synaptonemal complex and the link with homologous recombination. (SMC-Condensin complex).
To carry out its projects, the team plans to rely on a multidimensional approach based on murine genetics, structural biology, genomics and new spatial genomics, cytology and super-resolution imaging. Publication of ongoing efforts towards the completion of these objectives will reinforce this working plan. In addition to the two permanent researchers, the team is currently complemented by one post-Doc, one contract research engineer and one PhD student whose defense will be at the end of 2026. The proposed project plans to recruit at least two new PhD-students and one engineer. In addition, the team will consolidate its existing collaborations but also develop new ones (CBS-Team 7 and IGH). Integration into CBS as Team 3 ensure also access to key resources (additional expertise, engineers and shared facilities and infrastructure) while maintaining focus on a fundamental biological question of high relevance.
The team is now well established at CBS and benefits from the skills and infrastructure of CBS, while in return bringing solid expertise and scientific enrichment. With its stable and reinforced funding situation, strong publication dynamics and the pursuit of a consistent and clear scientific project, it shows a promising trajectory.

RECOMMENDATIONS TO THE TEAM

Regarding the team's size and the high international competition in the team's research areas, there is a moderate risk to maintaining high level publications. This risk can be mitigated by reinforcing the strong collaborative network and support from the CBS. The team should receive support to recruit permanent staff to help laboratory management. The team should pursue competitive long-term funding (ANR, ERC) to ensure independence and maintain dynamism and visibility. The application to EU funding is particularly encouraged given the good recent scientific results.
Reinforced teaching will allow attracting new doctoral students. Further participation at international conferences, networks and schools would enhance international visibility and help in the recruitment of talented postdocs and PhD students.
While preserving its identity in genetics and molecular biology, and its focus on the mechanistic study of meiotic recombination, the team could further develop collaborations in structural modeling and strengthen its technical expertise in imaging (especially super-resolution) and quantitative modeling by leveraging the shared resources of CBS and MRI. The team may consider exploiting this rich environment and its advances to develop links with clinical research, therapeutic innovation and patenting. In this context, the team would benefit from contacting the CBS technology transfer office to further the valorisation of the scientific outcomes.

Team 12 : (ATIP-Avenir): Synthetic and Functional Genomics

Name of the supervisor: Mr. Guillaume Cambray

THEMES OF THE TEAM

The team studies how genetic variation shapes biological function and evolution by experimentally linking genotypes to phenotypes. Through large-scale DNA synthesis, high-throughput mutational scanning, and deep sequencing, it quantifies how specific mutations affect molecular and organismal traits. Combining synthetic biology, bioinformatics, and machine learning, the team develops predictive models of sequence–function relationships. Applications span viral genomics, microbial translation, and biosensor design, with long-term goals of rationally engineering biological systems for biotechnology and biocontrol.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous committee highlighted the risk of thematic dispersion and the importance of focus and funding continuity. Despite the challenge of operating as a new ATIP-Avenir team with a single permanent researcher, the team effectively built a coherent research identity in synthetic, functional, and evolutionary genomics. To sustain activity and secure funding, multiple interrelated projects were developed—on viral genome dissection, translation efficiency, biosensors, and Wolbachia plasmid engineering—each grounded in the same high-throughput genotype–phenotype framework.
This diversification enabled continuous operation and strong collaborative integration, particularly with Teams 6 and 10 at CBS, while producing several high-quality datasets and publications (*Nature Communications*, *ACS Synthetic Biology*, *ISME Communications*). The team leader successfully obtained multiple grants, supervised PhDs, defended an HDR, and built industrial partnerships (e.g. Protera, Takeda). Although resource constraints slowed analysis and publication, these outcomes demonstrate clear progress, resilience, and fulfillment of the prior recommendation to balance innovation with focus and deliverables.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	**1**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels non permanents d'appui à la recherche	0
Post-doctorants	0
Doctorants	0
Sous-total personnels non permanents en activité	**0**
Total personnels	**1**

EVALUATION OF THE TEAM

Overall assessment of the team

This is a young but highly original and ambitious team positioned at the forefront of synthetic and functional genomics. By uniting experimental mutational scanning with computational modeling, it generates uniquely structured datasets linking DNA sequence to phenotype. Despite limited staffing, it has established a strong scientific identity, impactful collaborations, and industrial partnerships. Its approaches—quantitative, scalable, and predictive—exemplify the next generation of integrative biology. It is noted that this team will close and so there is not scope for securing its long-term success.

Context-related strengths and opportunities

The team's primary strength lies in its unique integration of synthetic DNA engineering, high-throughput screening, and data-driven modeling. This combination enables experimental quantification of vast genotype–phenotype landscapes with precision and reproducibility unmatched in most biological systems.

Scientific excellence and originality

The deep mutational scanning of the *Junonia coenia* densovirus genome represents a pioneering step toward complete functional mapping of viral genomes. The discovery that hosts polymerase fidelity decreases during infection—providing the first evidence of an evolved phenotypic mutation mechanism—is conceptually groundbreaking. Together, these results redefine our understanding of viral adaptability and inform rational biocontrol design.

In the translation efficiency program, the team's multi-organism studies (bacteria, yeast) and innovative experimental designs—linking structural RNA features to translational output—advance core questions in molecular evolution and gene regulation. Integration with machine learning approaches has yielded both methodological insights (transfer learning trade-offs) and practical tools (predictive translation models now used by biotech partners).

Technological innovation and cost efficiency

The team's ability to design and synthesize hundreds of thousands of sequences at low cost establishes a rare experimental capacity in Europe. Custom-built bioinformatics pipelines and statistical modeling frameworks ensure rigorous data interpretation. These assets provide competitive leverage for national and industrial collaborations.

Collaborations and societal relevance

Partnerships with Protera, Takeda, and Toulouse White Biotech demonstrate strong translational relevance. The viral genomics program has potential applications in sustainable pest control and insect health, while microbial translation studies directly impact industrial biotechnology and synthetic gene design.

Training and integration

The team's participation in the qBio master and mentorship of iGEM teams highlight its educational commitment. It has trained postdocs, engineers, and PhDs in cutting-edge techniques bridging biology, computation, and design, thus contributing to the next generation of interdisciplinary scientists.

Opportunities ahead include applying the high-throughput genotype–phenotype framework to other compact genomes (e.g. bacteriophages or RNA viruses), extending AI-based modeling to protein-level phenotypes, and developing synthetic biology tools for non-model microorganisms. These directions align well with emerging priorities in functional genomics, synthetic evolution, and computational biology.

Context-related weaknesses and risks

The team's structural fragility is its main limitation. With only one permanent researcher, long-term sustainability has remained precarious. Despite the leader's outstanding productivity, the combination of scientific, administrative, supervisory, and technical responsibilities is unsustainable and risks burnout. Recruiting additional permanent or long-term researchers would be imperative to stabilize progress were this team to continue, but it is noted that there is no plan to continue this team.

Personnel turnover has likely caused disruptions. The necessity of training temporary staff from scratch, followed by their departure at contract end, results in periodic loss of expertise and delayed project completion. Moreover, the highly specialized skill set required—combining experimental molecular biology, computational analysis, and data science—makes recruitment challenging.

Funding structure and research cycles are mismatched. The team's projects require long development phases before yielding publishable outputs, which clashes with short-term grant expectations. This structural mismatch limits competitiveness for traditional calls and hinders continuity. Efforts to secure European-level funding (ERC) were unsuccessful, despite scientific merit, due to institutional constraints following the end of the ATIP-Avenir scheme.

Scientific risks include overextension across too many subtopics. Although thematically unified by methodology, the simultaneous pursuit of viral, bacterial, and yeast systems may stretch resources too thin to achieve full analytical depth. Greater focus on one or two flagship applications would maximize visibility and yield high-impact outcomes.
Integration across CBS has been partly limited by disciplinary distance—high-throughput synthetic biology being difficult to merge with microscopy or structural biology workflows. This isolation, largely institutional rather than conceptual, may limit collaborative growth unless addressed.
Finally, institutional inflexibility poses an existential risk: discontinuation of the INRAE–CNRS joint hosting may have jeopardized the team's continuity despite strong performance. The team's main vulnerabilities stem not from scientific weakness but from systemic and logistical constraints: insufficient permanent staffing, project longevity versus funding timelines, and institutional rigidity.

ANALYSIS OF THE TEAM'S TRAJECTORY

It is noted that this Team will close and so there is no analysis of the Team's trajectory.

RECOMMENDATIONS TO THE TEAM

Although this Team will not continue as a standalone entity, its experience offers valuable lessons for the wider institute. The group demonstrated how high-throughput experimental design, large-scale DNA synthesis, and machine-learning analysis can transform biological research when strategically integrated. The remaining Teams at the institute could build on these achievements by embedding systematic, data-rich, and computationally informed approaches into their own projects:
- Encourage cross-team adoption of high-throughput genotype-phenotype screening to strengthen links between molecular, cellular, and structural studies.
- Develop shared computational and data-science resources to support large-scale analysis and predictive modeling across disciplines.
- Apply the team's lessons on balancing ambition with focus, ensuring that methodological innovation remains tightly aligned with clear biological questions.
- When creating new or interdisciplinary teams, ensure early structural support—including permanent staff and long-term funding—to maintain expertise and continuity.
- Foster continued collaboration with industrial and international partners initiated by this Team, especially in synthetic biology, virology, and machine learning–driven biotechnology.
- By integrating these principles, the remaining Teams can potentially preserve and extend the innovative legacy established by this group while ensuring more stable and sustainable development.

Team 13 : (ATIP-Avenir): Structure and Function of the Aryl Hydrocarbon Receptor

Name of the supervisor: Mr. Jakub Gruszczyk

THEMES OF THE TEAM

The ATIP-Avenir project led by Jakub Gruszczyk focuses on the structural and mechanistic understanding of the Aryl Hydrocarbon Receptor (AHR), a key sensor of environmental pollutants and endogenous metabolites. The core theme is the analysis, by cryo-EM and complementary methods, of the cytosolic AHR complex with Hsp90 and XAP2, and of its activation by specific ligands such as benzo[a]pyrene and related compounds.
This work is embedded in Team 5's Theme 3 on nuclear receptors and AHR as targets for environmental contaminants and strongly connected to European exposome programmes. It constitutes a structural toxicology line that bridges high-resolution structural biology, molecular dynamics and environmental health questions.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous evaluation did not address this ATIP-Avenir team specifically, as it was not yet established.

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

N/A

EVALUATION OF THE TEAM

Overall assessment of the team

Within a short time, this ATIP-Avenir project has produced a first-author Nature Communications paper on the agonist-bound AHR cytosolic complex and a follow-up JMB article on AHR activation by benzo[a]pyrene, clearly demonstrating scientific excellence and originality. The group has established itself as a reference in AHR structural biology and is well integrated into Team 5 and into European exposome consortia.

Context-related strengths and opportunities

The main strengths are the high scientific quality and novelty of the structural results, the strong integration in CBS (with close links to modelling and design teams), and the alignment with societal and regulatory priorities in environmental health. Participation in large national and European programmes offers opportunities for further funding and visibility, as well as for recruitment of young researchers.

Context-related weaknesses and risks

The group remains small and depends on time-limited ATIP-Avenir funding. Its long-term positioning (independent team, sub-team, or other configuration) is not yet fully stabilised and should be clarified. There is also a strong dependence on access to cryo-EM infrastructure and advanced computation, which requires sustained institutional support. Finally, beyond the current high-impact publications, the continuity of PI-level funding will be crucial to maintain momentum and growth.

ANALYSIS OF THE TEAM'S TRAJECTORY

The trajectory is clearly ascending. Starting from the ATIP-Avenir award and integration into Team 5, the group has rapidly delivered flagship publications and taken co-leadership of the environmental contaminants theme. The planned extensions to additional ligands, co-regulators and nuclear AHR complexes, as well as closer integration with predictive toxicology tools, are logical and promising developments. The main issue for the coming years is not scientific coherence but institutional stabilisation and sustainable growth.

RECOMMENDATIONS TO THE TEAM

It is recommended that the unit and CBS management work with the PI to define a clear post-ATIP trajectory, including the question of independent team status and associated resources. The PI should continue to consolidate his scientific independence through lead-author publications and competitive grants (national and European). Strengthening the group with PhD students, postdocs and dedicated technical support will be important to reach critical mass. Finally, the team should continue to exploit synergies with modelling and toxicology resources in the unit to translate structural insights on AHR into predictive tools and to maximise impact in the context of exposome research.

Team 14 : Computational BioMatter Design

Name of the supervisor: MESSRS. Gaëtan Bellot and Alexis Courbet (ATIP-AVENIR Laureate)

THEMES OF THE TEAM

The team engineers DNA origami, de novo proteins, and hybrid DNA–protein architectures to create programmable molecular machines and protocell-like systems. Using AI-driven design, high-throughput screening, and cryo-EM validation, they aim to build a synthetic cellular platform where DNA provides structural logic and proteins provide functional operations. Applications focus on targeted nanomedicine (e.g. HER2 and PDAC therapies), synthetic vaccines, and bioorthogonal protocells, positioning the team at the interface of nanotechnology, synthetic biology, and precision medicine.

CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

NA

TEAM WORKFORCE: IN PHYSICAL PEOPLE AS OF 31/12/2024

N/A

EVALUATION OF THE TEAM

Overall assessment of the team

A highly promising and excellent, strategically designed new team operating at the cutting edge of AI-guided molecular engineering. The combination of DNA origami, de novo protein design, and hybrid nanostructures for functional nanomedicine and protocell-like systems is original, ambitious, and well aligned with institutional priorities reflecting an excellent level of scientific creativity and strategic positioning. Strong technical resources, prior patent success, and clear integration into the Synthetic Biology department support feasibility. The main challenge is to convert this excellent and bold vision into concrete, high-impact demonstrators while consolidating internal cohesion.

Context-related strengths and opportunities

The group is pursuing highly timely research.

The team articulates a clear and differentiating goal: to build programmable molecular systems where DNA origami provides structural logic and de novo proteins deliver tailored functions, ultimately converging toward synthetic cell-like entities. This positions them beyond incremental nanostructure design into an architectural framework for molecular operating systems, highly visible internationally.

Few groups combine genuine excellence in both domains. The integration of ENSnano-driven DNA origami (including isothermal assembly and complex curved architectures) with cutting-edge generative AI protein design creates a rare and powerful toolbox. This enables, the rational design of non-intuitive, algorithmically defined architectures, the fine control over functional modules (binding, catalysis, signaling), the one-pot assembly of hybrid complexes at physiological conditions, crucial for biological compatibility.

The strategy to couple genetic algorithms, neural networks, and high-throughput feedback to optimize self-assembly tackles a central bottleneck in multimeric nanostructures: defects, kinetic traps, and poor scalability. Embedding AI/ML at the core of design/validation creates strong leverage for innovation and funding (AI, digital biology, Horizon Europe).

Access to 120/200 kV cryo-EM with direct detectors, dedicated TEM expertise, and HPC resources enables rapid design–build–test cycles and structural proof at atomic or near-atomic resolution—critical for credibility in de novo design. This infrastructure, combined with in-house software, supports leadership in method development and community platforms.

Applications targeting HER2+ breast cancer and pancreatic ductal adenocarcinoma, as well as drug delivery, synthetic vaccines, and diagnostic nanodevices, directly address medical priorities. DNA/protein-based nanostructures offer biocompatibility and sustainability advantages over inorganic nanoparticles, aligning with green nanotechnology agendas and industrial interest.

The team is tightly connected to internal leaders (SynBio ART, synthetic circuits, biophysics) and leverages international links from prestigious postdoctoral experiences. Prior patenting (origami nanorobot) demonstrates a track record in valorization. These connections create multiple opportunities for joint projects, IP, and high-profile publications.

Overall, the team has the ingredients to become a reference group in AI-driven molecular nanotechnology and synthetic biology, with rich opportunities in science, technology, and translation.

Context-related weaknesses and risks

This is a newly assembled group with complementary but distinct expertise and cultures. Without deliberate effort toward shared governance, joint supervision, and integrated projects, there is a risk of a "two parallel labs" effect (DNA vs proteins) rather than a fully fused hybrid-design team.

The vision—algorithmically designed hybrid architectures, self-repairing assemblies, de novo protocells—is high-risk/high-gain. Timelines to robust demonstrators can be long, and negative or incremental results may challenge funding continuity and evaluation expectations. Managing milestones and interim outputs will be critical.

Success relies on complex resources (cryo-EM, HPC, custom software) and a small number of highly skilled people. Turnover, overload, or technical downtime could significantly slow progress. Redundancy in skills, robust documentation, and cross-training are not yet clearly secured.

Global competition in *de novo* protein design, DNA origami, and nano-delivery is intense (US, Europe, Asia). Larger consortia may outpace the team if it does not rapidly produce distinctive proof-of-concept systems (e.g. uniquely programmable hybrids, in vivo efficacy). Risk: being perceived as technically strong but overshadowed if flagship applications are delayed.

Transitioning from elegant nanostructures to clinically relevant nanomedicines involves immunogenicity, stability, manufacturing, regulatory challenges. If these aspects are not integrated early through clinical/industrial collaborations, the translational narrative may remain aspirational, weakening long-term impact.

The team's ambitions span algorithm development, AI/ML integration, DNA origami, de novo proteins, hybrid vesicles, cancer targeting, vaccines, protocells and diagnostics. With a still modest core team, there is a tangible risk of overextension, leading to delayed publications and diffuse impact if priorities are not clearly staged.

Overall, these potential weaknesses are manageable but demand explicit structural choices: prioritization, shared leadership, risk management, and early external partnerships.

ANALYSIS OF THE TEAM'S TRAJECTORY

The proposed trajectory is coherent, staged, and upward-looking:

Phase 1 – Foundations in design and assembly. The team consolidates algorithmic DNA origami (ENSnano, curved and isothermal structures) and state-of-the-art de novo protein design using generative AI. In parallel, they establish a feedback loop combining high-throughput screening and structural validation by cryo-EM. This phase anchors technical credibility and differentiates their approach from purely empirical nano-engineering.

Phase 2 – Hybrid DNA–protein nanostructures. The next step is the true signature of the team: integrating proteins as functional modules on DNA-based scaffolds in one-pot, physiological assemblies. This is where the convergence of expertise becomes unique—enabling programmable architectures that can sense, compute, and actuate at the nanoscale.

Phase 3 – Application-driven demonstrators. Flagship applications in targeted oncology (HER2, PDAC) and bioorthogonal protocell-like compartments create concrete testbeds. Success here would validate the platform, attract industrial partners, and provide high-visibility outputs (therapeutic vectors, smart vesicles, advanced biosensors).

Phase 4 – Toward synthetic cellular systems. Longer term, the team envisages modular "operating systems" built from DNA scaffolds and de novo proteins, approaching protocellularity: compartments with controlled

permeability, signaling, and response behaviors. While ambitious, the roadmap from current tools to this vision is logically articulated and technologically plausible given the environment.

This trajectory is tightly aligned with the institute's reinforcement of Synthetic Biology and SynBio ART, National and European priorities in AI, advanced materials, and precision medicine, global trends in programmable therapeutics and data-driven molecular design.

Key to success will be the rapid delivery of one or two compelling hybrid nanostructure case studies; maintaining strong links to structural biology, immunology, and clinical partners; ensuring that algorithmic and AI components remain genuinely integrated, not decorative.

Overall, the trajectory is visionary yet structured, with clear potential to position the team as a leader in programmable molecular technologies.

RECOMMENDATIONS TO THE TEAM

To maximize impact and reduce risk, the team would benefit from defining two to three near-term flagship demonstrators, such as a validated hybrid DNA–protein carrier with specific tumor targeting or a functionally characterized *de novo* peptide vesicle. Delivering such concrete proof-of-concept systems early would help differentiate the team from international competitors and secure high-visibility outcomes. In parallel, the implementation of genuinely shared projects—including co-supervised students and regular joint lab meetings focused on hybrid systems—will be important to prevent siloing between DNA- and protein-centered activities. Strengthening internal resilience will also require systematic cross-training of team members in ENSnano, cryo-EM workflows, and AI pipelines, along with thorough documentation, to reduce reliance on a small number of key experts.
From a translational perspective, it will be essential to formalize early collaborations with clinicians, immunologists, and industrial partners so that issues related to pharmacokinetics, safety, and manufacturability are addressed from the outset, particularly for oncology-oriented applications. Finally, the team is encouraged to actively pursue Horizon Europe, PEPR, and AI-focused funding opportunities, capitalizing on its distinctive combination of AI, nanotechnology, and synthetic biology, while continuing its commitment to open-source tool development in order to establish itself as a reference hub for programmable molecular design.

CONDUCT OF THE INTERVIEWS

DATES

Beginning: 01 décembre 2025 à 08h00

Ending: 02 décembre 2025 à 17h00

Interview conducted: on-site or remotely

PROGRAMME OF THE INTERVIEWS

Interview programme – CBS evaluation visit
Day 1 – 1 December 2025
08:30–08:45 Committee private meeting
08:45–09:00 Committee presentation
09:00–09:50 Unit presentation
Team presentations
09:50–10:20 Team 1 – Delhommel
10:20–10:40 Team 2a – Bernado
10:40–11:00 Private pause / debriefing
11:00–11:25 Team 11/new3 – Robert
11:25–12:00 Team 4 – Labesse / Lionne
12:00–12:25 Team 5 – Lemaire
12:25–13:00 Team 7 – Nollmann
13:00–14:00 Private debriefing + lunch
14:00–14:35 Team 8 – Pedaci / Nord
14:35–15:10 Team 10 – Bonnet
15:10–15:25 Team 11 – Cambray
15:25–15:45 Private pause / debriefing
15:45–16:20 Team 9 – Doucet / Milhiet
16:20–16:40 Team new11 – Bellot / Courbet
16:40–17:05 Team 6 – Barducci
17:05–17:20 Team 2b – Sibille
17:40–18:20 Private interviews

Day 2 – 2 December 2025
08:30–09:30 Doctoral / Postdoctoral interviews
09:30–10:30 ITA interviews
10:30–11:30 EC/C session
11:30–12:30 Platform visit
12:30–14:00 Debriefing + lunch
14:00–14:45 Private meeting of the committee with supervising bodies
14:45–15:45 Private meeting of the committee with the Unit Director
15:45–17:45 Committee report briefing

PARTICULAR POINT TO BE MENTIONED

The head of Team 3 did not submit a contribution to the common evaluation report of the unit, and this team could therefore not be assessed within the present HCERES framework. This situation is linked to an ongoing conflict between the team leader and the unit management. It is established that the team leader will leave the unit, and discussions with the supervisory bodies are currently underway to identify a suitable host laboratory. In addition, a significant conflict emerged between the two co-leaders of Team 2, which resulted in the oral presentation of two distinct scientific projects for this team, although only a single written report was provided in the evaluation file. It is established that one of the two co-leaders will leave the unit, and the supervisory bodies are currently seeking an appropriate and coherent solution for her future positioning.

GENERAL OBSERVATIONS OF THE SUPERVISORS

UNIVERSITÉ DE MONTPELLIER

MONTPELLIER
Le 4 mars 2026

Monsieur Arnaud TOURIN
Directeur du Département d'évaluation de la recherche
HCERES
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OBJET : Rapport d'évaluation - DER-PUR270025786 - CBS - Centre de Biochimie Structurale

Monsieur le Directeur,

Je tiens à remercier le comité de visite HCERES pour la qualité de son rapport d'évaluation concernant l'unité de recherche CBS - Centre de Biochimie Structurale - dirigée par Monsieur Emmanuel MARGEAT.

Le directeur de l'unité et moi-même avons pris connaissance des recommandations formulées par le comité de visite.

Vous trouverez ci-après les observations de portée générale du directeur de l'unité.

Nous vous prions d'agréer, Monsieur le Directeur, nos salutations distinguées.

La Vice-Présidente chargée de la recherche

Agnès MIGNOT

Centre de Biologie Structurale

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Direction de la recherche et des Études Doctorales (DRED)

Université de Montpellier

Montpellier, le 2 mars 2026

Object : observations de portée generale, rapport HCERES

Reference : DER-PUR270025786- CBS - Centre de Biochimie Structurale

We would like to thank the committee for his work and its helpful comments and constructive suggestions. In general, we agree with the points raised by the committee and their recommendations, and there are no points that we feel necessary to comment or argue.

Sincerely.

Emmanuel MARGEAT

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