

EVALUATION REPORT OF THE UNIT

Ibens - Institut de biologie de l'école Normale Supérieure

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

- École normale supérieure – université Paris Sciences & Lettres - ENS-PSL
- Centre National de la Recherche Scientifique – CNRS
- Institut National de la Santé et de la Recherche Médicale – Inserm

EVALUATION CAMPAIGN 2023-2024
GROUP D

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In the name of the expert committee:

Lucas Jacques Waltzer, Chairman of the committee

Annie Andrieux, Vice-chairwoman of the committee

For the Hcéres:

Stéphane Le Bouler, acting president

Pursuant to Articles R. 114-15 and R. 114-10 of the Research Code, the evaluation reports drawn up by the expert committees are signed by the chairmen of these committees and countersigned by the President of Hcéres.

To make the document easier to read, the names used in this report to designate functions, professions or responsibilities (expert, researcher, teacher-researcher, professor, lecturer, engineer, technician, director, doctoral student, etc.) are used in a generic sense and have a neutral value.

This report is the result of the unit's evaluation by the expert committee, the composition of which is specified below. The appreciations it contains are the expression of the independent and collegial deliberation of this committee. The numbers in this report are the certified accurate data extracted from the deposited files by the supervising body on behalf of the unit.

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:

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Mr Philippe Chavrier, CNRS, Paris (representative of the CoNRS)

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Mrs Stéphanie Miserey, CNRS

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Mrs Anne Christophe, ENS-PSL

Mr Arnaud Tourin, PSL University

CHARACTERISATION OF THE UNIT

- Name: Institut de biologie de l'école normale supérieure
- Acronym: Ibens
- Label and number: UMR 8197, Inserm U1024
- Number of teams: 30
- Composition of the executive team: Mr Pierre Paoletti, director, Mrs. Valérie Hernu, General Secretary

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

Secondary panels: SVE5 & SVE1

THEMES OF THE UNIT

Researchers at the Institut de Biologie de l'Ecole Normale Supérieure (Ibens) conduct fundamental research aimed at deciphering the mechanisms and principles that govern living systems organisation and functioning, at multiple scales of analyses (from single molecules to organisms and ecosystems). To do so, they use various biological models (bacteria, cultured cells, animal models and plants), high-end technologies in genomics, bioinformatics, imaging, optogenetics or electrophysiology, as well as theoretical modelling and multidisciplinary approaches. The main thematic areas of the unit relate to genome expression, organisation and evolution, central and peripheral nervous system development, synapse regulations and neuronal functions, evolutionary processes, biodiversity and ecosystem functioning.

For the evaluation period, the unit was composed of 30 independent teams, plus one 'associated team' from the ENS physics department (not assessed here), organised in four interconnected sections: Functional Genomics (8 + 1 teams), Developmental Biology (five teams), Neurosciences (nine teams), Ecology & Evolutionary Biology (height teams).

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The unit was created in 2010 with the different CNRS and Inserm units at the Ecole Normale Supérieure (ENS) and renewed twice, with Dr Antoine Triller as director until 2019. Dr Pierre Paoletti was appointed director of the Ibens in September 2019 for a first mandate of five years. The unit is affiliated to the CNRS, Inserm and ENS-Université Paris Sciences & Lettres (PSL). All the teams of the unit are located 46 rue d'Ulm, on the ENS Campus, in the heart of Paris Quartier Latin.

RESEARCH ENVIRONMENT OF THE UNIT

The Ibens is located on the campus of the ENS, a prestigious multidisciplinary academic institution in France, with which it has strong links. Notably over twenty members contribute to teaching at the ENS Department of Biology (headed by Dr Paoletti) and the Institute regularly hosts and trains ENS students. The unit also has strong connections with other ENS departments (notably Physics, Chemistry, Mathematics, Geosciences or Cognitive Studies) and hosts a team from the Physics Department.

Ibens is affiliated with Paris University PSL, one of the leading universities in France, which benefits from an Initiative d'Excellence (Idex) program. PSL gathers a number of high-profile research institutes, including neighboring labs from Collège de France (Cirb), Institut Curie, or ESPCI and Mines-Paris engineer schools, with which Ibens teams have collaborations. As part of PSL, Ibens is implicated in and benefits from the 'Institut de convergence' Q-Life for cross-disciplinary projects and Paris Santé Campus Q-Bio for quantitative research in life and health sciences.

All the Ibens teams are associated with the Labex MemoLife, together with twenty other teams in neighbouring institutes (Cirb, ESCPI Paris, Neurobiology unit), which has been running since 2010 and was renewed for five years in 2019. The recently selected 'Programmes et Equipements Prioritaires de Recherche' (Pepr) Atlasea is coordinated by Dr Roest-Crollius, and Dr Garel is associated with the Pepr ProPsy.

Some of the technological platforms are integrated within national networks (e.g. France Biolmaging, France Genomics, Institut Français de Bioinformatique). The Genomics and Imaging platforms obtained an Ibisa label. Ibens scientists also have access to the Ecotron facility, a CNRS 'très grande infrastructure de recherche' (TGIR) located outside of Paris, to perform field ecological experiments.

UNIT WORKFORCE: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	9
Maîtres de conférences et assimilés	15
Directeurs de recherche et assimilés	27
Chargés de recherche et assimilés	36
Personnels d'appui à la recherche	52
Sous-total personnels permanents en activité	139
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	66
Post-doctorants	44
Doctorants	79
Sous-total personnels non permanents en activité	190
Total personnels	329

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons at 31/12/2022. Non-tutorship employers are grouped under the heading 'others'.

Nom de l'employeur	EC	C	PAR
CNRS	0	36	25
ENS-PSL	18	0	13
Inserm	0	26	14
SORBONNE UNIVERSITÉ	1	0	0
UVSQ	2	0	0
UNIVERSITÉ PARIS-CITÉ	2	0	0
Inrae	0	1	0
UPEC	1	0	0
Total personnels	24	63	52

GLOBAL ASSESSMENT

Profile, resources, and organisation

The Ibens is a flagship of fundamental research in various fields of biology, spanning from molecular & cellular biology to neurobiology, development, systems biology, ecology, evolution and bioinformatics. Using high-standard experimental, theoretical and multidisciplinary approaches, it aims at unravelling biological systems functioning and complexity at various scales. These very ambitious objectives are timely and highly relevant. To conduct top-class research, the institute can rely on exceptional financial and human resources as well as on its outstanding local academic environment. The internal organisation of the unit and its management are effective, with new initiatives to increase internal cohesion. A large part of the recurrent funding (significantly topped up with ANR overheads, funding from the Labex MemoLife and small levies on teams' grants) is dedicated to the unit scientific policy and common services, which provide excellent support to most teams. Some platforms (e.g. Imaging, Genomics or Bioinformatics) are at the forefront of their domain. While efforts have been made to modernise the premises, the building still needs major refurbishment to bring it up to the expected level. The unit globally complies with its institutional requirements and actively tries to improve its environmental practices. Despite a reduction in the number of permanent support staff, the general

atmosphere among the permanent staff is very positive. Although some well-appreciated actions have been launched by the direction recently, the integration of foreign students and postdocs should be improved and more efficient procedures are urgently needed to deal with cases of harassment. The gender balance at the PI level is slowly progressing, but further measures will be necessary to improve gender equality and female inclusion.

Attractiveness

The attractiveness of the institute is clearly outstanding as demonstrated by the exceptional capacity of individual researchers to obtain major international (e.g. 7 running ERC-funded projects) or national grants (e.g. 83 ANR-funded projects), or by the recognition of several scientists (e.g. 7 EMBO members, many national prizes and awards – CNRS medals, awards of Science Academies – , invitations to prestigious conferences...). The unit recruited four talented new group leaders and attracted another 22 researchers/professors during this period. It is very attractive to visiting scientists, PhDs and postdoctoral fellows, with a high proportion of foreigners. Ibens' association with the ENS is a major asset to mix multidisciplinary research and training. The unit is involved in several PIA programs, notably the Labex MemoLife and PSL idex (to which the MemoLife is affiliated), with its various initiatives (e.g. Q-Life). Several teams are coordinators or members of international consortia (e.g. Horizon 2020, HFSP, TaraOceans...). The unit has a remarkable capacity to embrace new fields of research and to develop cutting edge approaches (e.g. mathematical modelling, live imaging). Many members of the unit take part in national and international review bodies, institutional steering committees or scientific societies, thereby playing an important role in the science organisation.

Scientific production

The institute's scientific output is exceptional in terms of both number of publications and quality. The Ibens as a whole has made major contributions to scientific discoveries in the fields of genetics, genomics, ecology, evolution, cell biology, development and neuroscience. An impressive number of excellent publications have been produced over the last 5 years in journals such as Cell, Science, Nature Comm., eLife, Neuron, PNAS... More specifically, despite the disruption caused by Covid19, Ibens' work has led to the publication of 842 peer-reviewed articles (with an average of ~23 citations per publication and at least 26 publications with >100 citations since 2017) for ~150 researchers and professors/assistant-professors, 30% of which were in top-level journals. In addition, more than 30 review articles covering Ibens' main fields of study have been published in prestigious journals, with Ibens researchers as principal authors.

Contribution of research activities to society

The unit's interactions with society are excellent. Ibens' main activities are basic research, teaching and training. In keeping with its status as a research centre in the basic sciences, the unit's main contribution to society essentially lies in its teaching activity (25 professors/assistant professors from ENS-PSL, as well as a strong implication of researchers in training at ENS or through international courses). Notably, the unit launched a new MD-PHD program and organises advanced courses and workshops in quantitative biology (Q-Life & Q-Lab initiatives). Also, during the period, 101 PHD thesis and 10 HDR were defended.

Moreover, Ibens offers an exceptional intellectual, collaborative, multidisciplinary and scientific framework which is conducive to economic transfers well exploited by a few teams. This is evidenced by filing of patents (13) and licenses (4), the creation of start-ups (5) and the development of various industrial partnerships (contracts, Cifre PHD fellowships, consulting...). Some members of the Ibens are also involved in external bodies such as the Haut Conseil de la Santé Publique, Santé Publique France, Tara Oceans Foundation... Last but not least, several of the teams make important contributions to public outreach activities (Brain Week, Fête de la science, etc.), as well as a number of specific initiatives toward high-school students.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous report repeated preceding calls for an ambitious refurbishment plan of the lab whose estate was deemed incompatible for scientists and trainees to reach their full potential.

Some actions have been undertaken to improve the situation. Notably, one lab and the administration space have been refurbished and the renovation of two more labs and a cell culture room are programmed for 2023–2024. Most importantly, a 13 M€ worth Contract Plan Etat Région (CPER) has been finally approved in 2022, which should allow a complete renovation of the building (technical installations & energy performance) at the horizon 2027. However, this CPER does not include the modernisation of the research labs, which remains an absolute necessity.

B – EVALUATION AREAS

EVALUATION AREA 1: PROFILE, RESOURCES AND ORGANISATION OF THE UNIT

Assessment on the scientific objectives of the unit

The Ibens is a flagship of fundamental research in biology in France. It develops a variety of research lines to unravel biological systems functioning and complexity at various scales using experimental, theoretical and multidisciplinary approaches. The objectives are of very high standards and particularly ambitious. They are fully relevant to outstanding scientific and societal questions. Ibens research is very well integrated within its environment and perfectly aligns with the multidisciplinary policy of the ENS.

Assessment on the unit's resources

The Ibens has exceptional financial and human resources. Overall the teams are very well funded as they have been extremely successful in obtaining external contracts, part of which is used to implement the unit scientific policy. The staff is highly qualified and evolves in a thriving environment, but the increase in researchers and professors was not sufficiently backed up by the recruitment and replacement of permanent support staff. The Ibens made important efforts to maintain or upgrade its technological platforms, which are a major asset for the unit, but – given the wide scope of research thematics – it has proved difficult to support all the teams and models. The premises of the unit remain a matter of concern and the long-awaited renovation plan may strongly affect the activity of the teams.

Assessment on the functioning of the unit

The unit is very well structured, with a strong leadership from its director. The management team is deeply involved in further improving the functioning of the unit. The unit complies with its institutional requirements in terms of health and safety, scientific procedures or data protection. It took some excellent initiatives to enhance its environmental practices. The researchers and support staff are generally satisfied with the functioning of the unit. Notwithstanding the recent actions taken by the direction, the committee was alerted by the undesirable situation of several PHDs and postdocs, who expressed a very high level of collective dissatisfaction, and by issues affecting female position at Ibens. In light of this, gender issues and RPS require to be considered more effectively.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The Ibens is a leading research institute in the field of Life Science, with a strong commitment toward basic curiosity-driven multidisciplinary research. Its scientific objectives are particularly ambitious and broad as they cover topics from genetics to developmental biology and neuroscience up to ecology and evolution. They tackle timely fundamental questions concerning biological systems organisation, function and evolution, which are highly relevant for general knowledge and could have a profound impact on human health promotion, biodiversity preservation or environmental changes understanding. The Ibens is a rare example of a research institute carrying a holistic vision of life. Their effort to integrate different levels of complexity could bring a unique level of understanding. This strategy is well articulated with the ENS, CNRS and Inserm missions.

The scientific strategy of the unit is defined by the director in coordination with the team leaders and several committees involving various staff members contribute to more specific agendas (eg. platforms committee, ITA committee...). The overarching strategy of the unit is generally well shared. The unit also benefits from inputs of a scientific advisory board composed of internationally renowned scientists who visited the Ibens in 2023 and provided valuable pieces advice concerning the unit organisation and future directions.

One defining feature of the institute is to conduct and integrate research at very different scales, ranging from single molecules and cells to whole organisms and ecosystems. Maintaining a continuum of research along those different scales in the unit is a challenge, but it offers unique opportunities for collaborations and cross-fertilisation between scientific communities. The organisation of the unit into four sections with stronger thematic coherence increases the Ibens visibility. Besides, there are tight connections (collaborations, shared methodologies, converging scientific goals) between teams of different sections, notably between the Development and Neuroscience sections or between the Functional Genomics and Ecology & Evolutionary Biology sections, as revealed by seventeen existing collaborations in 2022 (notably between the 4 new teams and historic groups). To improve the unit structuration and cohesion, collaborative interdisciplinary/cross-thematic projects can be funded now by the Labex MemoLife and a first series of transversal thematic axes have very recently been identified (RNA Biology, Disease Models & Mechanisms, Imaging & Engineering Life; Machine Learning & Big Data for Life Sciences, Impact of Climate change on living systems), which could serve as a basis to foster further cross-section interactions.

Importantly, several Ibens teams stand at the forefront of research in their specific domain and the overall scientific dynamics of the unit is remarkable. For instance, four teams have been recruited in response to international calls (Strick 2017, Charrier 2019, Lambert 2020, Salecker 2021; 1 in each section) in the last 5 years. The core research projects are aimed at increasing scientific knowledge into four interconnected areas of biology. The unit also plays an important role in terms of student training or knowledge transmission, notably within the ENS, whose biology department is headed by the director of Ibens. Along that line, 101 PHD thesis and ten HDR were defended during this contract. Moreover, the unit launched a new MD-PHD program, leads graduate programs at PSL in Earth and Biodiversity as well as in Life Sciences, and organises advanced courses and workshops in quantitative biology (Q-Life & Q-Lab initiatives). Finally, the unit significantly contributes to research valorisation through the registration of patents (13) and licenses (4 licenses), the creation of start-ups (5) and the development of industrial partnerships (10 teams).

Weaknesses and risks linked to the context

Besides laudable efforts to increase unit cohesion and promote interactions between teams, and notwithstanding the impressive quality of the Ibens research teams, the diversity of questions and approaches remains important and not fully integrated. There is a risk of divergent interests between sections and/or teams when it comes to strategic decisions such as new team selection or infrastructure investments. This diversification puts some strains on the platforms and common services, some of which are used by relatively few teams. In addition, some teams may appear or become marginalised and can suffer from a lower level of support (eg. technical staff, benefit from common services...).

While the unit recruited talented teams in each of the four sections, it is unclear whether this recruitment fitted with a specific strategy beyond the maintenance of an equilibrium between the 4 sections.

2/ The unit has resources adapted to its activity profile and research environment, and makes use of them.

Strengths and possibilities linked to the context

The Ibens is a rather large biological institute in France: it hosts around 330 persons, including ~135 civil servants (researchers, professors and support staff) and 120 to 140 PHD or postdoctoral fellows. It presents an outstanding

gathering of scientific talents coming from 36 countries and the number of researchers/professor significantly increased over the last period (+8).

There was a concomitant increase in the recurrent budget of the unit from 1.293k€ in 2017 to 1.471k€ in 2022. In addition, the Ibens has an outstanding capacity to obtain external contracts (~9.800k€/year), part of which (including ~35% of the recurrent budget, ANR overheads and a 2.5% levy on most contracts) is re-allocated to the common budget and is used to maintain or upgrade its platforms and to conduct its scientific policy (hiring of support staff, acquisition of common equipment, seminar series invitations, installation package for new teams, internal calls for transverse projects, help to teams in difficulty...).

Research at the Ibens relies on an exceptional mixture of approaches including genomics, epigenomics, bioinformatics, imaging, optogenetic and opto-chemical manipulations, electrophysiology and mathematical modelling. Moreover, the teams use various biological systems, ranging from bacteria and algae to plants and animal models. Thankfully, some of these activities benefit from the support of strong platforms with dedicated staff (around 20 permanents) which provide expertise, hands-on training or services in genomics (sequencing), bioinformatics (analyses), imaging (confocal and electron microscopy), animal and plant breeding (rodents, zebrafish, *Astyanax*, *A. thaliana*, tomatoes, algae & diatoms). The lab has also set up a Fablab, which produces essential customary scientific instrumentation. Major efforts have been made to improve the Ibens platforms by refurbishing some rooms and investing in new equipment (e.g. FACS, mouse racks, spinning disk confocal, upgrade for AOD two-photon microscope, Promethion, NextSeq 2000) or increasing data storage and computing capacity (~17 Tb GB RAM), as well as by relocating the administration staff (10 permanents) in a centralised and renovated space. Some members of the staff (4 to 5) on the support services are paid on the Ibens common budget.

Another asset of the unit is its excellent integration in its environment, which clearly enhances its operational capacities. Researchers at the Ibens fully take advantage of a rich intellectual environment and are very well inserted into local (Labex MemoLife, DIM-C Brain) national (Pepr Atlasea, Pepr ProPsy; GDR NeuralNet) and international networks (Tara Oceans, EMBL-Ibens-Collège de France partnership; CNRS international research unit iglobes with the University of Arizona, EU H2020 networks) to conduct their projects. The Genomics, Bioinformatics and Imaging platforms are also associated with national infrastructure consortia, which not only foster technological exchanges and promote training but also significantly contributed to local investments (1.8M€ received over 10 years).

Important efforts have been made to renovate some of the outdated spaces (e.g. several teams' lab spaces, L2, Fablab, admin offices, entrance, seminar room...) and to improve the infrastructure of the lab (extension of the bioinformatics facility and animal house capacity, refurbishment of the aquatic facility...).

Weaknesses and risks linked to the context

There was a lot of staff movements (9 departures, 8 arrivals) in the administration service since 2017, putting at risk the organisation of the service. Along the same lines, the total number of permanent support staff decreased during this period (-3). The foreseeable departure of other support staff members will further increase the strain on the common services if their position is not renewed by the governing bodies. The functioning of the Imaging platform, which is used by twenty teams out of 29, might also be impacted by its future restructuration (departure of two staff members).

The wide range of subjects developed at the Ibens limits its capacity to provide basic support to all the teams (e.g. *drosophila* and *C. elegans* media preparation) and to develop common platforms whose activity benefits to most teams.

The size of the different teams is rather heterogenous (ranging from 1 to 7 permanent staffs), with five teams currently hosting a single researcher or professor, and a lot of teams do not have technical support staff.

The Ibens is located in a 60-year-old building, which is globally in poor condition despite some recent investments. Many team leaders rightfully complained about the state of the premise, which is not to up to modern standards. The CPER is a unique opportunity to bring the Ibens building to modern environmental and organisational standards, but the planning of the renovation is not yet very clear. How this will be managed and how this will affect the activity of the teams and services is a major concern. In addition, this renovation will not resolve the status of the research premises.

3/ The unit's practices comply with the rules and directives laid down by its supervisory bodies in terms of human resources management, safety, the environment, ethical protocols and the protection of data and scientific heritage.

Strengths and possibilities linked to the context

The direction and management structure of the unit is very well organised. The Director works in close collaboration with the secretary general and the heads of the four sections. Several committees (team leaders council, unit council, ITA committee, Platforms committee, users' committee, PHD/Post-doc association) and actions (general assembly, platform presentations...) have been set up to ensure that the different categories of personnel are taken into consideration and encouraged to participate in the life of the institute.

The career of the staff is well cared for, with effective actions from the direction and the ITA committee to help them progress in their careers. For instance, during this period, twenty ITA out of 50 had a promotion (against 13 in the last contract) and ten researchers obtained their HDR. The members of the unit are also informed about possible training courses and encouraged acquiring new skills.

The unit gender balance is very good (48% of women) and reflected in the composition of most Ibens committees. Importantly, since 2013, the Ibens recruited five women and five men as group leaders, although it was not sufficient to compensate for the historical imbalance in this category (still 73% of men). A 'gender balance committee' was constituted to raise awareness on this issue, but needs to be reactivated. The Ibens also recently put in place preventive measures against sexual harassment and psychosocial risks (e.g. a listening cell for PHD/postdocs). Several persons are strongly involved in working risk prevention. Newcomers are informed and trained appropriately, with more actions to come in the future, in particular for foreign students/postdocs (electronic information/welcome booklet).

Several events such as the Ibens scientific retreats have been curtailed due to the Covid-19 pandemic but will be reinstated. The institutional life is well organised, with a direct implication of the students and post-doc (SPIbens association) and close interactions with the neighbouring Curie Institute.

Access to the building and research premises are well controlled and adequate security measures for the crucial IT tools have been implemented, notably with a systematic encryption of the hard disks, large back-up storage capacities (CEPH server, RAID5/6 storage arrays, plus LTO tapes in a different building) and secured cloud computing solutions. In parallel, the usage of electronic lab book (eLabFTW) is progressively implemented.

Intellectual property or animal experimentation issues are addressed appropriately.

The unit implication on environmental matters is commendable. In coordination with the ENS, the unit is strongly committed to reduce its carbon footprint and move toward more sustainable practices (establishment of a Sustainable Travel Chart, creation of the Ibens Green Committee to raise awareness and initiate change, reduction of unused computing calculation power...).

Weaknesses and risks linked to the context

Several matters were raised by the different categories of staff concerning the functioning of the unit. The dissemination of information is not fully effective and some researchers expressed critiques about the top down mode of governance. Besides, the Assistant of Preventions coordinator has not been replaced and the location of the occupational health and safety register is not well known. Also, the unit 'règlement intérieur' is not yet approved by the governing bodies.

As noticed in the DAE, women are underrepresented as group leader, but also as directors of research or professors (8/39). Although several women found Ibens a very supportive and inclusive environment for the development of their career, several others complained from sexist remarks and behaviour in their working environment, a feeling of isolation, and unequal treatment when facing difficulties or sharing information. Several felt that their concerns and requests were not considered with the same attention as those of their male colleagues. This experience and concern were not general, but it was voiced by sufficiently diverse voices to deserve special attention from the Ibens direction.

Even though the direction set up a 'listening cell' to help PHD and postdocs and already took some measures to tackle situation of harassment, the committee faced a very high level of discontentment among PHD and postdoctoral fellows on this sensitive subject. Along that line, the committee regrets that posters concerning psychosocial risks, harassment or sexist and sexual violence are not clearly displayed in the institute's premise.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the unit is outstanding as demonstrated by the recruitment of four new teams, the arrival of 26 new researchers or professors (15 new recruits) as well as 122 PHD or postdoctoral fellows from various nationalities. The Ibens obtained eight ERC grants and Ibens teams have been remarkably successful in competitive calls. Several PI are very well recognised internationally and hold prominent positions in academia. The network of international collaboration is impressive. Despite its premises, the unit offers an outstanding research environment thanks to its technological platforms, a broad range of expertise, and local concentration of talents.

1/ The unit has an attractive scientific reputation and is part of the European research area.

2/ The unit is attractive because for the quality of its staff support policy.

3/ The unit is attractive through its success in competitive calls for projects.

4/ The unit is attractive for the quality of its major equipment and technical skills.

Strengths and possibilities linked to the context for the four references above

The outstanding reputation of the institute is firmly established as demonstrated by numerous participation as an organiser, chair or invited speaker in reputed conferences (e.g. chairs in 3 Gordon Research Conference and 3 EMBO Workshops, 1 CSH course) and as editorial board members in scientific journals (Science, eLife, PLoS Biology, PLoS Comp Biol, Development, Current Opinion in Pharmacology, Genetics, Glia, NAR Genomics & Bioinformatics, Evolution...). Several Ibens scientists hold positions in renowned learned societies (7 EMBO members, 2 Academia Europaea, 3 French academy of Sciences, 2 Professors at Collège de France, 2 junior Institut Universitaire de France...), serve as evaluator in international/national committees (2 ERC panels, 5 ANR, 7 CoNRS, 2 CSS Inserm...), stand in scientific advisor boards of various organizations (EU Elixir, French parliament OPECST, Santé Publique France...), or head research consortia (Tara Oceans, Pepr Atlasea, Labex Memolife, GdR NeuralNet). They have also received various national prizes or awards (5 «grand prix de l'Académie des Sciences», 1 Grand Prix Inserm, 1 Silver + 3 Bronze + 1 Crystal CNRS medals, 2 FRM prizes...).

During this period, the unit has been extremely attractive. For instance, it recruited four new PIs, thanks in particular to the opening of two positions of professor at the ENS and the constitution, since 2019, of a 200 k€ starting package on the Ibens/MemoLife/ENS budget. Of note, one of the PI originated from a top-level foreign research institute (Crick Institute) and another one obtained an ERC Starting grant. The Ibens welcomed another 22 scientists (10 within 'mobilities', 12 fresh recruitments), while eighteen left (4 due to retirement).

The unit effectively promotes the career development of its staff scientists: (young) researchers are encouraged to apply for their own funding (8 obtained an ANR and 4 an ERC) and six of them moved in other institutes to start their independent group.

The unit is also very attractive to younger fellows: it currently hosts a high number of PHD students (78 for 62 scientists with HDR) as well as 44 postdocs. PHD and postdocs are encouraged to present their work at internal section seminars and external conferences, and they can enroll in the SPIbens association (or the larger Young Researcher in Life Science Parisian network), which organises social events and scientific seminar series with Ibens funding (5k€/year). Some PHDs and postdocs can also benefit from a fellowship extension to finish their project thanks to the Labex Memolife.

The unit has recently set up an annual welcome day to facilitate the integration of newcomers and normally organises a scientific retreat once every two to three years. It holds an active scientific animation, with more than 150 invited seminars and it fully took advantage of ENS/PSL policy to invite and host eighteen distinguished scientists (mostly from North America). Moreover, Ibens scientists participate as an organiser or speakers in advanced courses, in particular winter schools in quantitative biology, funded by PSL Q-life Institut de Convergence.

Overall, Ibens scientists have been remarkably successful in competitive calls for projects, raising between 7.1 and 12.8M€ each year, with one third of the budget from international grants. For instance, since 2017, they obtained eight ERC (2 Advanced, 1 Consolidator, 4 Starting, 1 Synergy), seventeen Horizon Europe-funded projects, one HSFP, 83 ANR (60 as PI, including 6 ANR 'Young Researchers' and 2 ANR 'ERC Trampoline'). They also obtained substantial funding through R&D contracts (~3.5M€), territorial collectivities (~1M€) and from French charities (~8.1M€; e.g. 7 FRM and 1 LNCC labels, grants from Fondations ARC, Cotrel, Fyssen, NRJ, Rotary...). Ibens is a founding member of PSL index, which includes the program 'Paris Santé Campus' or the Institute de Convergence Q-Life, and Ibens scientists lead the Labex Memolife, the Pepr program Atlasea and are involved in the Pepr PropSY. 80 PHD students obtained a fellowship from the doctoral schools and six Cifre contracts, whereas 16 postdoctoral fellows obtained their own grants (5 EMBO, 11 MSCA).

The unit has established seven technological platforms (Genomics, Imaging, Protein engineering, L2/Transgenesis, Bioinformatics, Scientific Instrumentations), each with one or two dedicated support staff members and a referent scientist, which allow access to various facilities and services at reduced costs. For example, the Imaging platform is at the forefront of research for live imaging, with impressive developments in two-photon imaging for neuronal activity recording. Electron microscopy is now also integrated in this platform. The Genomics platform provides cutting edge computational platforms (Eoulsan) and state-of-the-art long read (Nanopore) and single cell sequencing technologies.

The Bioinformatics, Genomics and Imaging platforms are integrated within national networks and the latter two are Ibisa-labelled. Platforms development was supported by the Ibens and by substantial PIA funds (Memolife, France Génomique, France Biolmaging, Institut Français de Bioinformatique). In addition to annual internal calls for shared equipment (50–80 k€) and a recurrent budget (5–15 k€), the platforms also directly apply to competitive calls from governing bodies and funding agencies (Ibisa, Plan Cancer, Neurodon...), raising ~1.3 M€ over this period for the acquisition of new equipment. Moreover, the platforms obtained ~1.5M€ through internal & external billing to cover their costs.

Weaknesses and risks linked to the context for the four references above

While several teams have an outstanding international reputation, the visibility of some others and their participation in European consortia could be improved.

With twenty departures against seventeen arrivals, the net flux of permanent ITA is negative and it seems difficult to keep qualified support staff in Paris. 38% (33/86) of the ITA are on short-term contract, some of which paid directly on the Ibens recurrent budget, notably in the common services and technology platforms. The loss of staff in the animal house and on the imaging platform is perceived as a threat.

It seems that 'by tradition', the ENS does not, or only very exceptionally, promote assistant professors to the level of full ENS professors. This does not seem well justified and probably does not favour gender equity.

The integration of the foreign PHDs and postdocs is not yet fully satisfactory. More generally, the current distrust expressed by the PHDs and postdoctoral students could deteriorate the unit's attractiveness.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of Ibens is outstanding both in terms of number of publications but also in terms of quality; i.e. the 29 teams have produced major contributions to scientific discoveries (in fields of Genetics, Genomics, Ecology, Evolution, Cell and Developmental Biology and Neuroscience) as illustrated by an impressive number of excellent publications. During this period, Ibens work led to the publication of 842 peer-reviewed articles (30% of which in high-profile journals) with an average of ~23 citations/article. In addition, more than 30 high impact review articles with Ibens researchers as lead authors were published.

1/ The scientific production of the unit meets quality criteria.

2/ The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.

3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.

Strengths and possibilities linked to the context for the three references above

Despite the recent pandemic, the scientific production of the 29 teams has remained impressive, with an average of 140 publications/year, 30% of which in high-profile journals. The original publications cover the fields of Genetics, Genomics, Ecology, Evolution, Cell and Developmental Biology and Neuroscience. From January 2017 to September 2022, 842 peer-reviewed articles have been published. They obtained an average of ~23 citations and at least 26 of them obtained more than 100 citations since 2017. In addition, Ibens researchers published more than 30 review articles in prestigious journals (Annual Review of Genetics, Nature Reviews Neurosciences/Microbiology, Current Opinion in Neurobiology, Trends in. Ecol & Evol, Trends in Biochemical Sciences...). Also, Ibens scientists filed thirteen international patents, obtained four licenses, and created 5 start-up companies, directly stemming from ideas, methodologies and technologies developed at the Institute. Overall, the Ibens scientific production represents a convincing contribution to scientific discoveries both in terms of number and in quality.

The Ibens scientific production is well balanced among the four sections of the Institute. We can note the presence in the list of authors of PHD students' names, in accordance with the requirements of the doctoral schools. PHD students published more than 150 papers as first or co-first author, and postdoc 108 as lead authors during this period. We can also find co-corresponding authorship for junior researchers even though it seems variable among teams. Generally, research support staff also appear to be well included in lists of authors, although the practices are variable among teams.

The Ibens complies with the ethical, security and broader mandatory rules (animal experimentation, GMO etc..) , in accordance with its governing bodies and the European regulations. FAIR principles are well publicised with the help of the Institut Français de Bioinformatique and put into practice. Regarding integrity, Ibens promotes scientific good practices to prevent fraud, plagiarism and confidential scientific information leaks. One can note the promotion of the use of electronic laboratory notebooks within the institute. From an ethical point of view, Ibens try to promote a fair consideration of contributions with a special attention to fostering junior researchers' careers. Ibens encourages researchers to avoid predatory publishers and strongly recommends that research articles are published in open public archives (e.g. biorxiv, HAL). The annual number of publications in open access (deposited on BioRxiv or HAL) steadily increased between 2017 and 2022. An effort is also made for the deposit of data, source codes, algorithms in international repositories and dedicated website. This is in part supported by the Ibens Bioinformatics platform, which hosts web servers and tools, freely accessible to the community (Elixir's labelled Rsat and Genomicus tools).

Weaknesses and risks linked to the context for the three references above

Whereas the overall production of the unit is outstanding, a few teams appear less impactful. Although some important efforts are in progress to promote internal collaborations, the number of publications associating different teams from the unit remains limited and mostly originate from a few teams. The Ibens does not seem to have established and publicised some guidelines concerning authorship for support staff.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The unit's interactions with society are excellent. Ibens activities are focused on basic research and its main contribution to society lies in high-level training and education. Ibens also offers an exceptional research framework which is conducive to economic transfers and very well exploited by some teams, as evidenced by the filing of patents (13) and licenses (4), the creation of and participation to start-ups (4) or the development of industrial partnerships (contracts, Cifre fellowships...). Several teams have made important contributions to outreach activities toward the general public, in particular with high school students.

1/ The unit stands out for the quality and the amount of its interactions with the non-academic world.

2/ The unit develops products for the cultural, economic and social world.

3/ The unit shares its knowledge with the general public and takes part in debates in society.

Strengths and possibilities linked to the context for the three references above

Education and training are at the core of the unit. During the period, 101 students obtained their PHD. The unit also host ~60 postdocs and ten scientists obtained their HDR. Ibens scientists are extensively involved in providing students training, mentoring, giving lectures and organising courses. Notably, the Ibens director is the head of the ENS Biology Department and seven Ibens group leaders are professors or adjunct professors at this prestigious institution. The teaching topics are broad, taking into account the need for multidisciplinary and interdisciplinary knowledge to apprehend modern biology. Training is provided by full faculty members, with contributions from Ibens scientists and external staff. In recent years the ENS training program has been integrated into the larger community of the PSL University (undergraduate and graduate levels). It is associated with two new graduate programs at PSL, with the ambition of combining master's and doctoral degrees through scholarships. Very interesting is the 'Médecine-Sciences' program (equivalent of an MD-PHD track), which provides an early introduction to research for medical students. It is hosted at Ibens and performed together with PSL, Curie and Pasteur Institutes. Every year ten M/S students are enrolled and funded. Such a program, which bridges the gap between medical and biological knowledge, is an exceptional achievement.

At the administrative level, Ibens set up a Teaching Committee 'CodEns' (department's directors, Full Professors, heads of the Biology Studies, elected Associate Professors) which meets every other month and discusses all aspects connected to the educational and organisational teaching and training strategy in the Department.

Various collaborative biomedical projects between Ibens teams and pharmaceutical or start-up companies are underway, and at least 6 Cifre PHD grants have been obtained. Ibens' technology platforms also organise high-level training courses open to both the public and private sectors, actions which deserve to be highlighted. Ibens teams valorised their technological innovations towards the economical world, through the registration of thirteen patents and four licenses, as well as through the creation of five spin-offs/start-ups, directly stemming from ideas, methodologies and technologies developed at the Institute. It encompasses various application fields including :-Experimental devices for in vivo and behavioural studies on vigil animals – New microscopy systems to monitor neuronal activity in 3D – Innovative therapeutic strategies based on plant/microalgae immunity and small RNA technology – Algorithmic methods for EEG signal processing.

The unit makes valuable efforts to communicate toward the general public. Ibens has a website and a Twitter account that report on the scientific activities and major discoveries of the Ibens teams. In addition, several Ibens researchers are actively involved in public awareness initiatives aimed at 'showing off' the science carried out in the laboratories. These include participation in the Fête de la Science, Visites insolites (CNRS), Apprentis Chercheurs and Déclics programs (for secondary school students), Nuit des Sciences et Lettres, Semaine du Cerveau, etc.

Several researchers conduct expertise for various public institutions and organisations, concerned with Health or Biodiversity Conservation, as exemplified by contributions to the Haut Conseil de la Santé Publique at the national level and consulting for the Biodiversity Beyond National Juridictions treaty for the United Nations at the international level. Several teams (in particular with modelling expertise) also actively engaged in developing new research questions during the Covid19 pandemics to guide political decisions and inform the general public.

Weaknesses and risks linked to the context for the three references above

The translational potential of the excellent research performed at the Ibens is not fully exploited, notably in the biomedical and environmental/ecological fields.

Similarly, actions towards the general public or patient associations are not very strong.

ANALYSIS OF THE UNIT'S TRAJECTORY

The unit has a very dynamic trajectory and a clear vision of its future thanks to the collective reflection of the Ibens team leaders and advices from its SAB. Since 2017, four teams were closed, mostly due to the retirement of their PI, and four new team leaders were recruited, maintaining the equilibrium between the different sections but also bringing in new blood and sub-thematics, which open new perspectives of internal collaborations and fit well in the Ibens environment. The dynamic renewal of the staff is also sustained by the arrival or fresh recruitment of many scientists and the departure of researchers to create independent groups or to join other teams in different institutes, with a positive flux for the Ibens (+ eight). One team was recently closed down, three others will not be presented for the next contract as they will stop their activity in 2024, and two more will probably close during the next period with the retirement of their PI. Besides, the unit will have the opportunity to recruit a new group leader in 2023/2024 thanks to the opening of a 'junior professor chair' (CPJ) at PSL and its attachment at the ENS-PSL on the topic 'health and global change'. In addition, the unit will pursue its recruitment policy through international open-calls to attract new talents that will consolidate recently identified transversal axes. A first round of calls for one team in computational biology and one or two in Plant Sciences/Environmental Biology will be opened shortly, but the unit also wishes to open calls to strengthen the Neuroscience (neurophysiology of brain circuits) and Development (organoids) sections by 2025. Whether the recruitment of four to seven new teams can be effectively supported in the next few years remains uncertain. It will be important to select the best fitting candidates to avoid over-stretching the Ibens thematics and technical support. The restarting of the ENS foundation as well as other upcoming opportunities (e.g. PSL Grands Programmes de Recherche) may provide extra means to increase the start-up package (currently 200k€) and improve Ibens attractiveness/competitiveness. Local mentoring and strong institutional support will be needed to guarantee the success of these operations on the long term.

Still, it is crucial, not only for recruiting new teams but also to ensure the security, efficiency and well-being of the current staff, that the much-needed renovation of the Ibens premises proceeds in a timely and ordered fashion, with minimal impact on ongoing projects.

The unit wishes to maintain its thematic diversity and to develop along two main fronts: 'digital biology' and 'biology in context'. These developments are fully consistent with the strengths of the unit in computational biology as well as its expertise in animal/plant models and environmental studies. The broad scope of the unit is well in line with the multidisciplinary philosophy of the ENS-PSL and it has already prompted internal collaborations or discussions between researchers of different fields. The proposed cross-section animations and project funding are welcomed as they should enhance these valuable interactions and help consolidate the cohesion of the unit. This diversity remains a challenge in terms of external visibility and internal policy as it considerably extends the technological needs of the unit and may impair the definition of strategic lines of development, the maintenance of less used facilities or the level of resources sharing.

The unit director, the executive board and the SAB have defined several interesting actions to improve the scientific life of the institute and its general management, which are worth implementing (increase inter-axes exchanges and actions, maintain a strong level of resource sharing, nominate of a deputy director, improve internal communication and social life...). The expertise and support offered by the platforms constitute an important asset of the Ibens. Continuous investment in computing and imaging facilities are necessary and setting up a centralised service for ES/IPS and Organoids would be timely, but it may come with a cost in the much needed basic support to some teams.

The Ibens is also a major player in various national and international initiatives that should help maintain a high level of international exchanges. The implication of its staff in training is remarkable. Although it is essentially oriented toward fundamental research and knowledge advance, it could probably strengthen its societal impact both in terms of communication toward the public and in terms of transfer toward the health and environmental sectors. The ambitious holistic vision of life carried by the Ibens is particularly well suited to have a broad impact on society.

RECOMMENDATIONS TO THE UNIT

Recommendations regarding the Evaluation Area 1: Profile, Resources and Organisation of the Unit

The committee acknowledges the commitment of the direction and welcomes the different initiatives that were launched to increase the scientific coherence of the unit, its resources management and its organisation. Yet, besides these laudable efforts, the committee encourages the direction to take further measures to improve the organisation and life of the unit.

The unit should continue and strengthen its efforts to promote greater integration and synergy in research at Ibens, both from a logistic and intellectual point of view, in particular when recruiting new teams and supporting extant ones, with special attention to the maintenance of strong plant biology expertise and the reinforcement of ecology/evolution to reach a critical mass and improve the relative isolation of some teams. The good fit between the unit platforms and the need of the research teams within the unit should also be a priority. The unit is encouraged to actively promote transversal scientific animation and strengthen the role of commonly identified transversal axes in the research strategy and projects of the teams.

More effective measures to disseminate information toward all the target audiences within the lab are needed.

The committee strongly encourages the entire unit to embrace the issue of parity and discrimination. The direction could for example follow the ALBA network recommendations, which could help avoid possible sexism and discrimination against women within the institute. An organized mentoring within Ibens will ensure that all staff have access to this help.

The nomination of a female PI as deputy director should be very actively considered.

With regard to psychosocial risks and harassment, Ibens management is very strongly encouraged to take full advantage of the various supervisory bodies in order to adopt all the measures that are available (referent for quality of working life, psychosocial risk coordinator, social assistance, sexism and harassment referent, professional equality referent, active listening group, etc.). The procedures for reporting to the supervisory bodies any problem related to psychosocial risks or instances of various forms of harassment in the workplace must be made known and widely disseminated to all Ibens staff. We encourage the posting of such information in strategic areas of the institute to facilitate a direct contact between potential victims and their supervision body. Training to raise awareness of gender-based violence and harassment has recently been made compulsory for ENS employees. This measure should be extended to all employees without exception.

Recommendations regarding the Evaluation Area 2: Attractiveness

The committee recommends that the Ibens continues its efforts to improve the integration of foreign postdocs and students. A mentoring program for postdocs and young PIs could be set up.

For the recruitment of new teams, beyond the excellence of the candidates, the Ibens should take into account accurately how their activity will fit in the unit and which technical platforms will be needed for their success. Lack of technical support in basic tasks, like animal feeding, animal maintenance, media preparation and waste disposal will make teams unattractive for PHD students and for international postdocs. A part-time reallocation of one of the three technicians from the fish facility to these tasks could be beneficial. More generally, increasing or maintaining a critical mass of researchers working on a specific model (plants, fly, worm, fish...) would be beneficial for more effective work and synergies.

Recommendations regarding Evaluation Area 3: Scientific Production

The committee encourages the unit to maintain its outstanding level of scientific production.

Recommendations regarding Evaluation Area 4: Contribution of Research Activities to Society

The Ibens is encouraged to set up more actions toward the general public, disseminating the results of fundamental research, and to support investment of its members, at all stages of their career, in outreach activities. It could also increase its implication in expertise towards diverse agencies, policy-making bodies and non-profit organisations.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Neuronal algorithms
 Name of the supervisor: Mr Boris Barbour

THEMES OF THE TEAM

The research aim of the team is to understand neuronal mechanisms of brain function with a central focus on the cerebellum. The team has interdisciplinary expertise in patch clamp electrophysiology in brain slices alongside computational methods and biophysics. Recently the team has established in vivo electrophysiology and behaviour with an aim to test a central theory of cerebellar function in motor learning.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No major recommendations from the previous evaluation.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

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

EVALUATION

Overall assessment of the team

The team has an outstanding conceptual focus and has made an ambitious and exciting shift from *in vitro* to *in vivo* work to test a novel theory for cerebellar synaptic plasticity. The team has an excellent publication record in the reporting period and an outstanding interaction with society, being deeply involved in public engagement of science. While the group is fairly small, new funding has been obtained and tenured members are planned to arrive soon. Overall, this very strong team continues to make novel discoveries using interdisciplinary approaches.

Strengths and possibilities linked to the context

The PI is senior author on a high-profile study that combined in vitro work with modelling to identify new rules for cerebellar synaptic plasticity. This study has raised central questions about cerebellar plasticity that the group will test in vivo and likely to lead to a highly influential study. Another senior researcher in the team has been particularly productive, with a number of senior and first authorship articles. The lab is highly collaborative with a number of collaborative papers, alongside a methods paper that will likely be broadly useful for many labs performing sorting of extracellular spikes in different brain regions. There is an outstanding level of interaction with the general public, in particular the team leader's organisation of 'PubPeer'. An ANR grant has been obtained recently and new members with funding are expected to arrive soon. The outstanding scientific reputation of the lab has led to the team leader being invited for international conferences. The team is heavily involved in teaching and training with the team leader teaching master's students and is the codirector of an MD-PHD program and the organiser of established doctoral training courses. Two PHDs have graduated from his lab within the reporting period. The novel interdisciplinary approach of the lab allows the lab to address central questions from different angles.

Weaknesses and risks linked to the context

A possible weakness is the small group size, however new tenured scientists are planned to join the group soon and an ANR grant was recently obtained.

Analysis of the team's trajectory

The lab's plan for further in vivo work is outstanding and ambitious. The datasets described in the report show fundamental and unexpected findings that will challenge current theories of cerebellar funding. Equally as exciting is a planned collaborative project to combine 3D super-resolution microscope on recorded pairs of neurons to examine silent synaptic connections. Further funding will very likely follow to support this fundamental work.

RECOMMENDATIONS TO THE TEAM

None

Team 2: Cortical dynamics and coding mechanisms
 Name of the supervisor: Mr Laurent Bourdieu

THEMES OF THE TEAM

The team combines a focus on the coding of sensory information in the cortex with the development of two-photon microscopy for in vivo work. Together, this allows the lab to tackle questions of cortical function with imaging of neuronal activity with unprecedented temporal and spatial resolution. This interdisciplinary team is a focal point for collaborations in Ibens and the broader community.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has addressed the recommendations of the previous assessment. In detail, the team has obtained significant third party funding; the team has worked together with Ibens based Kathala System company that produces cutting edge two-photon AOD scanning microscopes; scientific projects are integrated with the optical development; the team has been invited and attended multiple national and international conferences to enhance their profile. The new scientific focus on predictive sensory coding is an exciting avenue and something recommended in the previous review.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	4
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	3
Doctorants	3
Sous-total personnels non permanents en activité	6
Total personnels	10

EVALUATION

Overall assessment of the team

The team has been outstandingly productive in progress in two-photon microscopy development. The interdisciplinary nature of the lab combining optical development, data analysis and modelling has allowed sophisticated studies in sensory cortical coding. The team has an outstanding track record in obtaining funding. There is a clear emphasis on collaboration and the use of novel technology to address fundamental question in neuroscience. The team has outstanding visibility and presented work at national and international conferences. There are outstanding links to industry.

Strengths and possibilities linked to the context

The development of new optical technology is an outstanding strength of the team. They are fundamental and ground breaking for the field. Specifically, the development of a 3D-CASH is currently the only technique for 3D imaging of neuronal activity at kHz sampling rates. There have also been important publications on the deconvolution of calcium traces, fast confocal imaging in behaving mice and acoustic optic holography. With further important studies on preprint servers, the next publications continue to make fundamental strides. The team has been outstandingly successful in obtaining third party funding has been obtained with 23 grants that together ~four million euro. Links to industry are outstanding with the team securing a patent, creating a new start-up company as well as central involvement in the successful Ibens company Karthala System. There has been excellent interaction with the general public and debates in society with articles and public science events alongside interactions with industry. The team has played a major role in scientific committee work with 28 thesis juries and membership of ten local and national scientific committees. Science communication has been a central aspect of the lab with 22 invited conference seminars and the team is enhancing the visibility of the team. The team has made outstanding contributions to teaching throughout the reporting period both locally and in international school and training courses.

Weaknesses and risks linked to the context

The cost of optical development is high and it is a major challenge to find enough funding. However the group has been outstandingly successful in obtaining grants.

Analysis of the team's trajectory

The projects described that will address the role of attention and anticipation on sensory coding are exciting and should lead to fundamental insights into cortical mechanisms of sensory processing and perception. The technique developments planned for the next years are world class and continue to be at the cutting edge of optical development. In particular photoactivation with cellular resolution in freely moving animals would be a first. The combination of 3D-CASH with the expectation whisker task is a particularly exciting future project.

RECOMMENDATIONS TO THE TEAM

Continue to combine technical developments with the scientific questions both within the group and in collaboration

Team 3: Plant and Algal Genomics

Name of the supervisor: Mr Chris Bowler

THEMES OF THE TEAM

The team led by Chris Bowler is deeply interested in the adaptability of photosynthetic organisms in varying environments and focuses on how the environment can impact genome structure and dynamics. They are focusing on different organisms: *Arabidopsis thaliana* (a higher plant) as well as *Phaeodactylum*, and *Fragilariopsis* (as model marine phytoplankton). In *Arabidopsis*, the team examines how light affects chromatin-level regulation. Concurrently, functional genomics methods are employed in *Phaeodactylum*, along with analysis of Tara Oceans data, to understand the evolutionary and ecological success of diatoms and related phytoplankton groups in today's oceans.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was encouraged to promote career development of women and to develop additional collaboration with ecologists. Both recommendations were taken into consideration. Notably, two researchers (one female and one male) will set up an independent group together in a neighbouring institute and the team had a very fruitful collaboration with Morlon's team at Ibens.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	5
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	10
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	8
Post-doctorants	0
Doctorants	8
Sous-total personnels non permanents en activité	16
Total personnels	26

EVALUATION

Overall assessment of the team

During the last evaluation period, the quality of the scientific production, achievements and international visibility of the team was outstanding. The team published a large number of high-quality publications, acquired prestigious funding (e.g., ERC Advanced and Starting grants), and established local, national and international collaborations. Several permanent researchers of the group (1 DR CNRS and 2 CR CNRS) are about to establish their own research team, showing the quality of the research performed over the five last years.

Strengths and possibilities linked to the context

The Plant and Algal Genomics team has an impressive output in terms of publications (124 articles, including very high quality articles), as well as the number and quality of funding acquired (27 active grants over the period), with two ERC Advanced grants following one another during the evaluation period. The team hosted many PhDs (7) and postdocs (13), several of them coming from abroad. The team is also involved in a large number of international, national and location collaborations. Among other things, it is very involved and actively participates in the large-scale Tara Oceans project. In terms of interactions with the public and society, the PI has appeared on numerous television and radio programs around the world (BBC, France Radio, etc.) and has held the annual 'Biodiversity and Ecosystems' Chair at the Collège de France (2020–2021). Finally, it should be noted that three of the permanent members of the team will establish their own research team and one of whom has just obtained ERC Starting funding. This very clearly shows the exceptional dynamics and scientific quality of the research carried out during the period evaluated.

Weaknesses and risks linked to the context

During the evaluation period (2017–2022), there are no real weaknesses to raise. As mentioned above, all the indicators (production, visibility/attractiveness, inclusion in society) are at an exceptional level. However, for the coming period, the principal investigator will be confronted with the departure of many permanent members of the team. This will require a transition phase and probably the recruitment of new permanent staff.

Analysis of the team's trajectory

With the departure of a certain number of permanent staff, future activities will all be based on further exploration of diatom ecology and evolution. These explorations will be divided into four axes: (i) the exploration of the diatom contributions to carbon fixation in the oceans, (ii) the exploration of gene origins in diatoms, (iii) the dissection of diatom-specific innovations, and finally (iv) the study of adaptation of diatoms in polar regions. All of these axes represent a logical extension with respect to previous studies but also represent important challenges. It is also important to note that funding for these activities has already been secured from different grants (e.g., ERC Advanced award (Diatomic), EU Horizon grant (BlueRemediomics and Marco-Bolo). And finally, these activities will also benefit from already established collaborations, including for example that in relation to the Tara Oceans project.

RECOMMENDATIONS TO THE TEAM

The committee advises the team to keep ambitious goals for publication in highly reputed journals and successful applications to prestigious funding programs. With this in mind, it will be crucial to be able to recruit new permanent members to the team. This concern appears to have already been addressed as a new CR researcher is about to join the team.

Team 4: Development and Evolution of neural circuits
 Name of the supervisor: Mr Jean-François Brunet

THEMES OF THE TEAM

The team's theme centres on studying the developmental, evolutionary, and physiological aspects of visceral nervous system's sensorimotor reflex circuits that regulate vital functions like breathing, digestion, and blood circulation, with the overarching goal of integrating the realms of development, evolution, and physiology.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous evaluation of the research group was notably positive regarding their accomplishments. However, the report did highlight a discrepancy between the team leader's outstanding scientific contributions and their international visibility, particularly in terms of invitations to conferences and seminars. To address this, the committee suggested that the team leader engage more actively in participating in or organising international conferences. Despite having received eight invitations from 2017 to 2019, this recommendation's implementation was hindered by the Covid pandemic. Looking ahead to the upcoming contract period, it is anticipated that this recommendation could be effectively implemented.

Additionally, the committee emphasised the importance of the team leader expanding their team size to further amplify their impressive output. Notably, in 2017, the team leader recruited an assistant professor, a technician, followed by another addition of a DR1 in 2019. The team's continued appeal to postdoctoral researchers and PHD students reflects their steadfast adherence to the right course of action.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

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

EVALUATION

Overall assessment of the team

Despite being a relatively small team, the scientific output is outstanding with an excellent level of publication. The team has published seven research papers all of them of very high quality, six with team members as corresponding authors, and one review. The groups' appeal is evident through the successful acquisition of approximately 1M€ in grants.

Strengths and possibilities linked to the context

Their ground-breaking discovery that genetically classifies the sacral autonomic outflow as sympathetic initiated substantial debates and rebuttals. To strengthen acceptance, they are engaged in a follow-up project to validate their findings. Another key contribution focused on revealing the origin of parasympathetic ganglia from migrating Schwann Cell Precursors, influencing the understanding of the enteric nervous system, but the proposition to redefine the 'vagal crest' concept has yet to gain wide adoption. Their discovery is not acknowledged at its rightful worth, yet they are determined to ensure their breakthrough is finally recognised. The team leader's recognition includes eight international speaking invitations, contributed to two scientific advisory boards and the 'Brixham Foundation' award from FRM in 2018. The other research director also delivered presentations on the international and national stages. The research inquiries are all current, captivating, and engaging. The recruitment and training of human resources have been of high standards, with four PHD students and three postdocs. The groups' appeal is also demonstrated through the successful acquisition of three ANR and one FRM grants as well as one FRM scientific award.

Weaknesses and risks linked to the context

The forthcoming retirement of the team leader is the main weakness of the team. The grant obtained by the team will conclude in 2024. The team leader has expressed concerns regarding the current state of research funding. The team's research quality is exceptional, particularly in the realm of developmental biology, which has the potential to garner substantial funding. The integration of physiological aspects in their study of the nervous system is expected to enhance the team's ability to secure high-quality grants.

Analysis of the team's trajectory

The research team's trajectory has been marked by profound inquiries and innovative explorations within the realms of developmental, evolutionary, and physiological aspects of the nervous system. Their project endeavours are multidimensional and have yielded substantial insights. The team's investigation into the sacral autonomic outflow has not merely unveiled genetic reassignment but has ignited robust discussions and controversy. Their rigorous use of single-cell transcriptomics on the pelvic ganglion provides novel perspectives. This ambitious work addresses the misclassification of the pelvic ganglion as mixed (sympathetic and parasympathetic). This paradigm shift underscores the alignment between ontogeny and physiology in neural circuits, questioning established concepts. The team's focus on Phox2b interneurons within the reticular formation has led to demonstrate an overarching theme of Phox2b's pervasive influence in feeding circuits. The team's plan to uncover evolutionary connections between vertebrate and amphioxus motoneurons. By delving into respiratory rhythm generation, the team seeks to comprehend the robust yet adaptable central pattern generator underlying breathing. Their innovative use of two-photon recordings and holographic excitation aims to visualise burstlet ensembles and establish their significance in rhythm generation. These investigations hold the potential to transform our understanding of the fundamental mechanisms of breathing. In summary, the research group's trajectory has been characterised by groundbreaking studies that challenge established paradigms across various aspects of the nervous system. Their continuous dedication to unravelling complex neural processes and their commitment to bridging ontogeny and physiology demonstrate their profound contributions to the field.

RECOMMENDATIONS TO THE TEAM

Given that the team leader will retire during the next few years, the future of the current staff should be discussed well in advance.

Team 5: Development and Plasticity of Synapses
 Name of the supervisor: Mrs. Cécile Charrier

THEMES OF THE TEAM

The research carried out by the team focuses on human-specific genes expressed in the nervous system, to investigate their role in synapse development and plasticity, human brain evolution and the impact of these genes in brain disease/disorders. Their past achievements include discovering various human-specific genes that together regulate the timing and density of synapse maturation and the balance of excitatory vs. inhibitory synapse development. These gene functions enabled the emergence of characteristics of human synapses, and mutations are linked to autism, schizophrenia and mood disorders.

The current research themes are:

- (1) Using mice to investigate mechanisms and regulation of synaptic development, by partners of SRGAP2 genes, such as FRMPD2B, which enables human neurons to send and receive more information.
- (2) Function of SRGAP2 and their partner GluD1 in synaptic function, plasticity and critical periods.
- (3) Use of human hPSC to generate tagged and shRNA neurons to transplant into the mouse, and then promote their maturation and connectivity.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was officially established as an independent lab in January 2020, following its selection in an international Ibens call for new team leaders and the award of an ERC starting grant in 2019 to the PI. Prior to that, the PI had established her own group of one postdoc and two PHD students, funded by an ANR grant, within another group at Ibens. Thus, she was not evaluated in the previous report.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres 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 d'appui non permanents	1
Post-doctorants	2
Doctorants	2
Sous-total personnels non permanents en activité	5
Total personnels	7

EVALUATION

Overall assessment of the team

This is an outstanding team. The PI has established her team recently and has already had an impressive trajectory, recognised by outstanding funding (incl. ERC Starting grant), multiple awards and prizes (e.g. EMBO Young Investigator Award), and invitations to conferences and seminar. The productivity of the team has been particularly outstanding, publishing in high-profile journals, including PLOS Biology, eLife and Neuron. The team also contributed to teaching at ENS (including on education in ethics in research) and to scientific diffusion toward the general public (e.g. production of various YouTube videos).

Strengths and possibilities linked to the context

The PI is an outstanding scientist. She has received outstanding funding (e.g. a 1.5 million Euro ERC starting grant) and multiple awards and prizes (including EMBO Young Investigator Award, Prix Janine Courier, Prix Coup d'Elan, Prix Irene Joliot-Curie). Furthermore, in the last six years, the PI has been invited to speak at international conferences or give seminars at other institutions in eighteen occasions.

The Charrier team is obviously attractive, as demonstrated by their ability to recruit and maintain new members. The team currently consists of seven team members, including the PI and another Senior Assistant Professor, as well as two postdocs, two PHD students and one IE, CDD.

Their productivity has so far been impressive, with together publishing in high-profile journals, including PLOS Biology, eLife and Neuron. Two further articles are currently in biorxiv.

The past research achievements by the team include:

- (1) Discovering the specific human gene SRGAP2C, a truncated inhibitor of the paralogous SRGAP2A, which slows down the assembly of synaptic scaffold. Furthermore, these proteins influence the balance of inhibitory and excitatory synapse maturation.
- (2) Discovery of a partner of SRGAP2C, the atypical glutamate receptor GluD1, which is involved in trans-synaptic interactions for the formation of inhibitory cortical circuits.
- (3) Discovery of another partner of SRGAP2 in the mouse, called CTNND2, which delays synaptic maturation, and has a protecting role in ageing.
- (4) Technological development and the enabled discovery of novel dendritic spines that receive both excitatory and inhibitory innervation.

Altogether, these gene functions enabled the emergence of characteristics of human synapses, and mutations in these genes are linked to autism, schizophrenia and mood disorders.

The team's involvement in engagement with society includes production of videos and talks within ENS on ethics in science.

Weaknesses and risks linked to the context

The team would benefit from more technical and administrative support by permanent staff. The lack of a permanent technician or lab manager position compromises the research effectiveness of the team, which could be improved with such help.

The unique selling point of the Team's research is the analysis of human neurons. However, most of their research has been and is carried out in the mouse. It is important that they move away from the mouse and focus their research on human cells, human organoids and tissues, in order to validate their findings and sustain the uniqueness of their line of research.

The team commits to greater participation in society activities into the future.

The activities were heavily impacted by the Covid-19 pandemic.

Analysis of the team's trajectory

The trajectory projects of the team focus on the investigation of further partners of SRGAP2, including:

- (1) Mechanisms of synaptic development. Using transgenic mice to manipulate human genes in the mouse, they are investigating SRGAP2 partners such as GluDs and FRMPD2B, which enables human neurons to receive

and send more information. They aim to investigate whether human-specific innovations increased vulnerability of the human brain to neurodevelopmental and neurodegenerative disorders.

(2) Molecular determinants of synaptic plasticity regulations. Here they will test the hypothesis that some human-specific genes differentially regulated in humans regulate synaptic plasticity and shape our adaptive abilities. They will investigate using electrophysiology how the role of SRGAP2 in slowing down the duration of synaptic maturation affects synaptic plasticity and the critical periods. They will also investigate GluD1 and GluD2 in synaptic plasticity and the development of cortical circuits and they affect information processing in the neocortex. And they will investigate the relationship between immediate early genes and human-specific genes and how they influence how human neurons perceive and respond to changes in activity,

(3) New models to directly interrogate the specialisation of human synapses in human neurons. They will differentiate human neurons from human pluripotent cells, which can be genetically manipulated, and these will then be transplanted into the mouse. They will use nanobodies to SRGAP2C to identify further interacting partners using mass spectrometry.

The trajectory project is ambitious but somehow repetitive and vague in places. It would benefit from clearer directions.

RECOMMENDATIONS TO THE TEAM

The PI leads a very ambitious, outstanding and successful team and they should continue working effectively and productively in innovative projects.

The team is attractive and has been able to recruit suitable postdocs and PHD students. It currently comprises seven people, which is a good size to remain productive.

The team's unique selling point is the study of the unique properties of human neurons. However, most of the research is being done in the mouse. It will be important for the team to make the jump to move with human contexts (cells in culture, organoids and tissues).

The ERC starting grant terminates in May 2024. The PI is planning to apply an ERC Consolidator Grant in the next few months. In this context, it will be important for the team to remain productive and get the papers currently in biorxiv published in good journals.

The team would benefit from more technical and administrative support as the lack of a technician or lab manager position compromises the research effectiveness of the team, which could be improved even further with such help.

Team 6: Genome Dynamics and Epigenetic Variations

Name of the supervisor: Mr Vincent Colot

THEMES OF THE TEAM

The research of the 'Genome, Dynamics and Epigenetic Variation' team focused on studying epigenetic processes, specifically DNA methylation, and their impact on heritable differences in traits. They primarily use the plant model *Arabidopsis thaliana* for their experiments. Their research involves various molecular, genetic, epigenomic, and bioinformatics techniques to understand the molecular mechanisms behind the movement of transposable elements (TE) and the transgenerational epigenetic changes associated with TE sequences. Additionally, their studies often consider populations or species to relate their findings to ecological and evolutionary contexts.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous committee did not make specific recommendations for this team.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
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 d'appui non permanents	3
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	4
Total personnels	8

EVALUATION

Overall assessment of the team

The quality of the scientific production and achievements of the team was excellent during the last evaluation period. The international visibility is outstanding. The team published a large number of high-quality articles and made very significant discoveries in the field of epigenetics in plants and beyond. The team also acquired excellent funding (mostly ANR grants). Some permanent researchers of the group established their own research team, showing the excellent dynamics and scientific quality of the research carried out by the 'Genome, Dynamics and Epigenetic Variation' team.

Strengths and possibilities linked to the context

The 'Genome, Dynamics and Epigenetic Variation' team is an excellent team, which is a world leader in the field of transgenerational epigenetic inheritance and TE mobilisation. During the evaluated period, the team

had an excellent output in terms of publications (19 articles, including 5 in Nature Communication, two in Genome Biology and one in EMBO Journal as corresponding author). In addition, the national and international excellence is also evidenced by the large number (15 for the PI) of invitations at international conferences over the last five years. During this period, the team benefited from substantial financial support at the national level, including four ANR grants (2 as coordinator, 2 as partner). The team also hosted three PhDs, four postdocs, and most of the permanent researchers had a very good implication in teaching at different universities in Paris and at the ENS. The PI was also involved in outreach activities and diffusion of scientific knowledge toward the general public. Finally, it should be noted that two postdocs obtained a CNRS position in the team and one also obtained an ERC Starting grant and established his own research team, showing the scientific quality of the research of the team.

Weaknesses and risks linked to the context

While the scientific production and achievements were excellent over the last five years, the team has not had the opportunity to publish his work in very high-profile journals and it did not obtain prestigious grants, such as ERC awards, even though they were well ranked in the case of the ERC Synergy call.

Analysis of the team's trajectory

As the team will close by early 2025 because the PI will retire in August 2025, there is no project and future scientific directions in the document except that the future of the team members is well taken into account.

RECOMMENDATIONS TO THE TEAM

The committee will not make recommendations as this team will close early 2025. However, we would like to acknowledge the work performed by the team over the years as well as the outstanding contribution of the PI to the fields of trans-generational epigenetic inheritance and transposable elements mobilisation.

Team 7: Inhibitory Transmission and Neuronal Computation
 Name of the supervisor: Mr Stéphane Dieudonne

THEMES OF THE TEAM

The group is interested in the understanding of the role of inhibition in the brain. One subgroup works on molecular aspects of inhibitory neurons and another aims to identify the synaptic connectivity and function of inhibitory neurons in the cerebellum. A new approach has been in vivo imaging in behaving animals. The group has further developed a novel and unique multiphoton microscopy for rapid in vitro and in vivo neuronal functional imaging.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was recommended to apply for technology grants and has been extremely successful in grant application with eight grants including one for 1.1 M€ from the NIH Brain Initiative. A second recommendation was to attend more international conferences and the team leader has been invited to a number of high-profile talks at international conferences. The request for further collaborations with 'outstanding external labs' has been achieved and evident from the publication record.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	6
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	3
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	6
Total personnels	12

EVALUATION

Overall assessment of the team

The team has a central interest in synaptic inhibition and the development of new optical techniques. The team has been outstanding in terms of productivity and has outstanding visibility. The development of novel techniques for two photon voltage imaging places them at the cutting edge of neuroscience research. The lab has a number of productive collaborations. The inclusion in society is outstanding partly due the successful optics company Karthala. The team will not be renewed, plans are being made for continuation of team members and integration into other groups.

Strengths and possibilities linked to the context

The research output has been outstanding with the team leader a senior author on multiple high-profile papers that describe the development of cutting edge imaging techniques as well as the development of in vivo imaging of voltage indicators. This is world-leading research. Moreover, the team has contributed to ground breaking international collaborative projects. The subgroup has also been highly productive with corresponding authorship on two papers and collaborative studies on further two more celebrated studies. The development of the RAMP microscopy is ground breaking. The company is growing and their AOD based multiphoton microscope one of the only systems in the world to perform such rapid and stable imaging. The team leader has been involved in teaching on four international courses and teaching throughout the reporting period. Likewise, other staff scientist has been involved in coordination of neuroscience master courses and examinations. During the reporting period, three PHD students defend their thesis. The team leader has been present and multiple high-profile talks and international schools. Notably, one staff was awarded the bronze medal of the CNRS. Outstanding levels of funding have been obtained by the team with eight grants awarded. The further establishment of the company Karthala is a major strength for the team and Ibens at large.

Weaknesses and risks linked to the context

The group will end in 2024, plans are being made to continue the projects and integrate into other teams following the closure of the group in 2024.

Analysis of the team's trajectory

The group will close in 2024. Some team members will move to Bourdieu's team which makes sense with the focus on cortical processing and two-photon microscopy and close ties to the group. This will allow the further development of the RAMP microscopy as well as the continuation of the scientific projects. The first project will test the hypothesis that the cerebellar cortex is arranged into nanozones with are activated by proprioceptive feedback from specific muscles or groups of muscles with activity monitoring and cutting-edge anatomy. A second project is to examine the role of Golgi cell mediated inhibition in cerebellum pattern separation, this is generating ground breaking data with the first voltage imaging in vivo during behaviour.

RECOMMENDATIONS TO THE TEAM

The team will close.

The relocation of all staff members is a priority, in particular all assistant professors.

It is important for the institute to find a new head of the optics platform.

Team 8: Evolution of *Caenorhabditis*

Name of the supervisor: Mrs. Marie-Anne Felix

THEMES OF THE TEAM

The team is studying natural variation in *C. elegans* and other nematodes, mainly *Oscheius tipulae*. They are focused on gaining an increased understanding of the variational properties of developmental cell fates, using nematode vulva development as a model system. Other work includes focusing on the interactions with naturally associated microbes and natural variation in epigenetic memory duration.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

While one of the main recommendations from the previous report, involving increasing the size of the group, does not appear to have been addressed, the recommendation regarding the team developing new research direction has been addressed adequately.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

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

EVALUATION

Overall assessment of the team

The scientific quality of the work is overall excellent and is of an international standard in this field of research. The team production is excellent; it has made significant advances in an increased understanding of the cellular and molecular signalling network in nematode vulva development. The team has an outstanding international visibility. It continues to play a leadership role in the *C. elegans* community and it is very attractive to PHD and post-doc. The team also developed strong interactions with the non-academic worlds. However, the small size of the group could be an issue for the future sustainability of the group.

Strengths and possibilities linked to the context

The team's visibility is outstanding and is very well established scientifically. This is reflected in the number of conferences (international 12; national 5) and invited seminars (international 18, national 6) that team members,

predominantly the team leader, have attended, together with their organisation of major conferences. The PI has a leading role in the *Caenorhabditis* community. The team is also involved in important international collaborative linkages with the Sanger Institute, Imperial College London, the University of Glasgow in the UK; with Northwestern University, San Diego State University, Washington University in the US and with the Indian Institute of Science and the University of Toronto. The team leader is a member of EMBO and in 2019, received the Légion d'Honneur for their work in this scientific area.

The team was very well supported by competitive grants (3 ANR, 1 FRM, 1 Cefipra, 1HFSP...) and several postdoctoral fellows joined the team with their own fellowships (EU Marie Curie, EMBO, FRM).

The overall scientific productivity is excellent. The team combines evolutionary, ecological and quantitative biological approaches to study the nematode worm *C. elegans*. They are striving to gain an increased understanding of the variational properties of developmental cell fates, using nematode vulva development as a model system. They are also undertaking pioneering work on the isolation of natural populations of the worm and the study of their ecology and evolution in the wild. In addition they are studying the evolutionary variability in the phenotypes of these wild isolates, together with their interactions with bacteria, viruses and Microsporidia as well as other life history characteristics, with many significant discoveries on their natural history and genetics. The total number of publications is 29 which is quite impressive, given the modest size of the team. The impact of the work is reflected in a 2017 paper on 'The natural biotic environment of *C. elegans*' which has to date been cited 198 times.

The non-academic activities within the team are mostly centred around their work on antiparasitic agents and with their involvement in an advisory Committee for the Office for Science and Technology of the French Parliament.

Weaknesses and risks linked to the context

The team has highlighted problems with their laboratory infrastructure, particularly with respect to media pouring facility and a cold room. In addition the team lacks infrastructural support in particular for the maintenance of their populations and experiments. These issues could negatively impact on the future trajectory of this team of rather modest size.

The integration of the team leader in the institute is a matter of concern.

Analysis of the team's trajectory

The team plans to continue their work on Wnt signalling pathway sensitivity in both *C. elegans* and in *Oscheius tipulae* and in its quantitative evolution within and between these two genera.

In addition, they aim to characterise the evolutionary variation associated with different *C. elegans* phenotypes that they have observed relating to exposure to high temperature and RNAi together with characterising the effect of associated microorganisms. They hope to identify metabolite(s) that may be involved in suppressing multigenerational phenotypes and this may offer the team an opportunity to collaborate with groups involved in metabolomic analysis. They also plan to continue their work on natural variation in response to horizontally transmitted RNA viruses. Appropriate and relevant collaborative linkages with other research groups have been described, which will facilitate the implementation of this proposed work.

RECOMMENDATIONS TO THE TEAM

The modest size of the team remains a concern, particularly given the breath of new topics being studied by the group and the major dependency of the team on the leader. Efforts should be made to develop the future career development opportunities of the two postdoctoral researchers who are currently in the group, so as to ensure the future sustainability of the group.

The team should build on their virus and bacterial work, particularly with respect to bacterial interactions in *Caenorhabditis* and the attachment of bacteria and viruses to the intestinal epithelium of the worm. This could open up a new research line for the group.

Team 9: Eco-Evo-Math
 Name of the supervisor: Mr Régis Ferrière

THEMES OF THE TEAM

The team studies eco-evolutionary feedback affecting the dynamics of populations, communities and ecosystems, with a strong involvement in the development of mathematical models. The team has focused on the study of microbial systems, combining theoretical, statistical and experimental approaches, with 3 main questions: 1) cooperation and its consequences on emergence on collective behaviour and major life transitions (multicellularity, symbiosis, sociality), 2) feedback between the evolution of microbial communities and their environment affecting macroecological structures, ecosystem functioning and large-scale biogeochemical cycles, 3) development of statistical methods to infer processes shaping non-stationary population dynamics, with a strong focus on epidemiology.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report made very few recommendations to the team but to improve their interactions with non-academic world (e.g. on the topic of climate warming). The tragic demise of a team member in 2018, who was particularly interested in interactions between environment and society, has slowed down the developments on subjects such agroecology and adaptation to climate change. The involvement of the team with the non-academic world has, however, been strengthened in the period by the strong contribution on expertise on various Public Health issues through role as a member of Haut Conseil de la Santé Publique and of the Scientific Advisory Board of Santé Publique France, two national agencies with a major role in National Health policies, strategies and surveillance, as well as through research on the epidemiology of COVID-19 during the pandemics. An interesting interdisciplinary program was also led by the team during the period on cognition and cooperation with regards to climate change, with however little detail yet on the results of this ongoing project.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	4
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	9
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	2
Total personnels	11

EVALUATION

Overall assessment of the team

The quality of the scientific production of the team is excellent to outstanding, with the development of an innovative research program, strong integration between theory and experiments and several breakthrough in the analysis and inferences from transient dynamics in epidemiology. The visibility of the strong and pointed expertise of the team in mathematical biology is outstanding, with in particular a very strong level of international recognition exemplified by the dual appointment of several team members in other institutions. The investment in other missions is also excellent to outstanding, with strong investment and responsibilities in teaching (e.g. director of a Graduate program) and important roles of expert for Health national agencies.

Strengths and possibilities linked to the context

The team holds extremely strong, pointed and well-established expertise in mathematical ecology and evolutionary biology. This high recognition is, furthermore, shared by several members of the team (e.g. external faculty at the Plön Max Planck Institute for Evolutionary Biology, external faculty at the Institut des Hautes Etudes Scientifiques, deputy director of France-Arizona Institute for Global Grand Challenges, member of the Haut Conseil de la Santé Publique), which makes it a particular fertile environment to train a new generation of talented theoretical ecologists. The team is very well connected to the international community, hosting in the period nine well-established visitors from the USA for stays of variable length (e.g. Chaire Blaise Pascal to Weitz), organising four international workshops and symposia, with four keynote invitations for the team in the period, and directing an International Research Laboratory at the University of Arizona. The network of collaborators is diversified and very solid both at the national and international level.

Twelve PHD students and four postdocs have been or are being trained by the team during the period (which contains 4 members with HDR, indicating a commensurate, high quality investment in training), with several very impactful innovative publications co-authored or led by young researchers on the topics of speciation for instance (a study in 2018 has been cited 12 times more than an average publication in the same year and same field), astrobiology (a study in 2020 cited 10 times more than an average publication) and epidemiology (22 times more than an average publication, with up to 7 publications co-authored by a former PHD student in the period). The team is strongly involved in various training and teaching activities of high reputation, exemplified by the responsibility of director of Graduate Program in Earth and Biodiversity Sciences Paris Sciences et Lettres University, teaching various courses at ENS at graduate and undergrad levels or the organisation of an International Winter School on Viral Dynamics.

The research led by the team is highly original and interdisciplinary, involving mathematics, biology, physics, biogeochemistry, planetary sciences, mixing theoretical developments, sophisticated data analysis and experiments. The scientific environment at the ENS is a strong asset in this regard because of the proximity of both colleagues with different expertise in other departments (as well as in the different Paris universities) and students with excellent, diverse, quantitative training. The focus on microbial systems and the interest for eco-evolutionary feedback at various scales of organisation allow a nice conceptual integration of the different projects led by the team. The team also collaborates regularly with other ecology teams at Ibens. Among the remarkable achievements of the evaluated period, one can note: (i) an increased understanding of the emergence of collective behaviour through an original integration of general theory (e.g. on the evolution of heritability through the selection of developmental programs) and mechanistic details of cell interactions, (ii) the successful launching of a thought-provoking interdisciplinary research program on the impact of microbial evolutionary processes on planets geochemical cycles and habitability, (iii) the continued efforts development of sophisticated statistical inference methods from ecological dynamics applied to numerous epidemiological data sets and to the Covid19 pandemics in particular with important conclusions for human health. This work has been published in visible journals with a wide readership, both generalist and more specialised for the technical developments and is well cited. Success in obtaining funding from various sources (ANR, labex, university PSL, Region) is excellent and allows supporting the mostly theoretical research projects developed by the team.

Weaknesses and risks linked to the context

Beyond collaborations with some specific ecology/evolution groups at Ibens, the team has little interactions with other Ibens groups in particular in other sections, and suffers from a weak representation of ecology in the Ibens research landscape. With the retirement of an engineer, there is a lack of technical support for the development

and dissemination of computational methods and packages, a need shared by other teams strongly involved in the development of quantitative methods at Ibens. The dual appointment of several members of the group showcases the recognition of their expertise and sustains a strong international integration of the team, but the team must ensure that the presence of researchers at Ibens is sufficient to contribute to a lively scientific environment for trainees and staff. Despite strong conceptual integration, there are very few co-publications between PIs in the team in the period. Given the exciting subjects tackled by the team (cooperation, epidemiology, habitability, astrobiology), there is underexploited opportunity for team members to engage more in communicating their findings to the general public via various outreach media. There are projects that would strengthen the team outreach activities, but still in maturation.

Analysis of the team's trajectory

The team projects for the next five years are in strong continuity with their current questions and approaches and correctly identify promising areas of development along three axes:

1) evolution of collective behaviour in microbial communities, combining sophisticated theory inspired by physics and evolutionary biology with experiments in microcosms, integrating multilevel selection and mechanisms of cell interactions; the future projects will tackle this question along a gradient of community relatedness, from communities of highly related cells to multispecies communities, which is very relevant. Collaborations are in place and these projects are funded by ongoing ANR and labex grants led by the team, 2) eco-evolutionary feedback responses to environmental change; the team correctly identifies the need to empirically demonstrate the role of eco-evolutionary feedback involving microbial community both at the local and global scale, now that their potential role has been suggested by theory developed in the team; to reach these goals, they are associated to large collaborative projects funded by NSF (which investigate how genetic adaptation, acclimation and assemblage processes affect ecosystem function) and by Nasa (linking microbial ecology and evolution to astrobiology to inform the study of exoplanets and the inferences from spatial expeditions). In each of these projects, the team will be in charge of model and theory development, but more details could have been given on how data acquisition will be used to confirm or infirm this theory (a difficult task);

3) the last axis concerns the development of statistical methods of inference from epidemiological data, addressing the technically difficult but highly relevant questions (as was illustrated by the case of the covid19 pandemics) of inferences at an early stage of the epidemics where issues of non-observability and identifiability of parameters are a strong concern, and of optimal control when the optimisation criterion is not the total number of cases throughout the epidemics but the height of the peak (because of hospital capacity). Applications of these methods concern the links between climate change and emerging zoonoses in a One Health perspective. These limits of current methods of analyses are very well identified, the team has the analytical capacity to make significant progress on these fronts. Seed funding from the CNRS MITI program has been obtained and grant requests submitted to ANR through a collaborative project.

RECOMMENDATIONS TO THE TEAM

The team is encouraged to maintain the excellence and originality of its research, its strong international network, high level of expertise and strategic role in training students to work at the frontier between ecology and mathematics. It should maintain its links with the national ecology community both within and outside Ibens where they have an important role to play. By its ability to study and model complex feedback at various scales, the team has the potential to contribute to a stronger integration of research conducted at Ibens and should therefore keep an eye on promising collaborations with teams from different sections if opportunity presents itself. A greater investment in transfer of research findings towards various stakeholders in health, climate change adaptation and biodiversity conservation and more generally public outreach is also encouraged.

Team 10: Brain Development and Plasticity

Name of the supervisor: Mrs. Sonia Garel

THEMES OF THE TEAM

The team investigates the wiring of forebrain circuits during development and how this is affected by exogenous factors, such as the microbiota and inflammation. They have found that microglia can have distinct functions in different states, and they aim to disentangle these functions. Current projects aim to understand:

1. the function of early neuronal activity in brain formation.
2. the function of microglia in connectivity, tissue integrity.
3. the function of microglia in myelination.
4. impact of prenatal inflammation in microglia and the development of neural circuits.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report on the team was a glowing report. No weaknesses were found and the committee encouraged her to continue to work in the same way, creatively and productively and maintain her ambition. This has clearly been achieved as the team is still producing outstanding and original work.

The committee recommended maintaining sufficient workforce to enable her to reach the research objectives. Following this recommendation, the PI has created a second lab, whilst maintaining a long-term collaboration with her ex-post-doctoral fellow, who now has moved out of Ibens and formed their own group at College de France. The PI now co-leads a second research team at the College de France.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	6
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	9
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	3
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	6
Total personnels	15

EVALUATION

Overall assessment of the team

The team's work is highly original and has implications on neural health. Its production is outstanding, with publications in high-profile journals with the PI as corresponding author. The team international reputation is outstanding. The PI has been recognised by multiple prestigious prizes (e.g. EMBO member, French Academy of Sciences) and 28 invitations to speak at high-profile international conferences. The team was extremely attractive, acquiring major grants (ERC Consolidator, FESR, ANR...), and fostering the development of a second team at College de France with a former postdoc.

Strengths and possibilities linked to the context

The PI is an outstanding scientist, with international reputation, recognised by multiple prizes awarded since the last report, and including: FSER, Brixham, NRJ Prize for Neuroscience, Cajal Club Award, Elected to French Academy of Sciences and EMBO membership. She has been invited to speak at high-profile international conferences (e.g. Gordon Research Conference, Cold Spring Harbour, Fens, EuroGlia, Keystone) including to give three plenary talks.

Her previous postdoc and now co-PI has also been extremely successful, receiving multiple prizes as well (e.g. Prix Delheim for young PIs and French Science Academy). Together, they have been very productive and sustaining regular publications either as first or last authors in high-profile journals in this evaluation cycle (e.g. Cell Reports 2019, Nature Communications 2018 and Cell 2018). They have also published review articles in high-profile journals (e.g. Nature Reviews Neuroscience 2022, Science 2018, Nature Neuroscience 2018).

The lab was funded by a prestigious 2 M€ ERC Consolidator grant that ended in 2021.

Their work focuses on early brain development and most particularly on the roles of microglia. Their past achievements include:

- (1) Neuronal activity during neural circuit formation in development influences neuronal migration and survival. This is independent of sensory experience and instead relies on a prenatal, developmentally controlled, burst of serotonin. This has implications for understanding the consequence to brain formation of preterm birth.
- (2) The genetic depletion of microglia leads to the discovery that microglia have multiple functions that take place at different time points and depend on distinct microglial states. These include enabling connectivity and protecting tissue integrity.
- (3) Environmental signals, such as microbiota, can influence microglia in a sexually dimorphic manner, influencing the brain. Although the mechanism is unknown, this could explain why pathologies associated with microglial dysfunction such as autism, schizophrenia and autoimmune diseases are sexually dimorphic.

Their research relies on the use of multiple technical approaches, and to achieve this they have established collaborations with multiple teams, including at Ibens, France and internationally.

Both PI are also involved in teaching at College de France.

One ex-post-doctoral fellow has now created her own team at College de France, co-directed by the team PI. They appear to work well together, with joint group meetings, joint projects and some independent projects.

Weaknesses and risks linked to the context

The success of the team relies heavily on technical support within the team and in facilities. However, both are lacking permanent positions. Lack of technical support could jeopardise the productivity of this team.

In the previous evaluation cycle, the team benefited from an ERC Consolidator grant, which terminated in 2021. Since then, funding has been considerably reduced and all funding is due to end by December 2024. The PI has applied for other grant(s) and is planning a submission to an ERC Advanced grant as soon as they publish the paper currently in preparation. It will be important that the team obtains sufficient funding to sustain their ambitious research plans.

Analysis of the team's trajectory

This is an outstanding team and leader, that promise to continue to deliver ground-breaking science.

The team plan to investigate: (1) The function of early neuronal activity in the emergence of brain circuits, and the impact for understanding neurodevelopmental disorders such as autism. (2) Microglial states and their different functions in regulating neuronal connectivity, tissue integrity and myelination. (3) The impact of prenatal inflammation in circuit development. They use a wide variety of technological approaches, including mouse lines deficient in microglia, and to facilitate this they have engaged with a broad group of collaborators.

The proposed project is well thought and very ambitious, for which the group will need to have enough funds that may only be provided by EU grants or similar, something is not easy to achieve despite the outstanding production of the team. The team is currently well funded through two ANR grants, FRC and FRM. It will be critical that the PI ensures sufficient funding, to attract researchers to deliver on their ambitious aims.

RECOMMENDATIONS TO THE TEAM

As before, to continue working with ambition and creativity to sustain the outstanding productivity.

To aim for an ERC grant to sustain the research ambitions and deliver on objectives. Funding – to the lab or institutional – would also enable the provision of technical support.

Team 11: Computational Bioimaging & Bioinformatics
 Name of the supervisor: Mr Auguste Genovesio

THEMES OF THE TEAM

The team aims to decipher the morphology and the dynamics of the cell, the basic unit of life, through quantitative exploitation of data, whatever they are images of cells obtained by microscopy or genomic data. This is a transversal theme that grounds a tight network of collaborations with experimental specialists. The theme of the team largely evolves from unveiling mechano-transduction mechanism in the transcriptional dynamics to the complete reconstruction of the development process. This research activity engages to develop advanced deep learning modelling to uncover spatiotemporal and functional relationships in cell-based imaging experiments.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous committee acknowledged the outstanding science performed within the team, and the innovative ambition to close the gap between genomics and microscopic imaging. The committee also supported the excellent training provided to the next generation of biologists. Nevertheless, they recommended to focus more on their experimental lines of research to avoid dispersion. Since that evaluation, the team shifted resolutely more towards computational development and mathematical modelling than towards experimental autonomy, regarding the biological data. This is totally assumed with important development of deep learning algorithms to scale up to dataset size and accurate analysis of images. This strategy was very successful, as demonstrated by numerous high-quality publications since 2017.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
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	1
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	4
Doctorants	4
Sous-total personnels non permanents en activité	10
Total personnels	11

EVALUATION

Overall assessment of the team

The team's performance remains excellent with respect to publication record quality and originality. The team is outstandingly attractive, mentoring many young scientists (6 postdocs, 10 PhDs, 9 engineers, 11 masters) and obtaining high levels of funding. It is strongly involved in teaching and in interactions with biotech companies. Of note, the collaborative network is impressive and the team is a sustainable angle stone of transversal collaborations within Ibens, positioning it as an essential asset in the unit's strategy.

Strengths and possibilities linked to the context

The team has an impressive output with respect to publications (26 papers including 12 as corresponding or last authors, 14 as co-authors), and high-quality collaborations mainly within Ibens or in Paris. The production includes computational and modelling developments for image and NGS data analyses as well as collaborative works on various biological questions involving bioinformatics analyses. The team benefited from substantial financial support at the national level, including three ANR (2 as coordinator, 1 as partner), one Plan Cancer and one ITMO grants. Also, the team had collaborations with three private companies Ksilink, Synsight and Minos bioscience, associated with industrial contracts and a Cifre PHD fellowship. Of note for the attractiveness valence, the PI is the head of the functional genomic section. In addition, the team hosted many PHD (10) and postdocs (6), several of them coming from abroad. The research line to develop AI to understand cell morphology at large scale is especially remarkable considering the human resources (1 DR Inserm, 2 engineers as permanent positions). The main strength is to have readily adapted to set their expertise in linking artificial intelligence and biology. They are one of the international experts in this competitive field.

Weaknesses and risks linked to the context

There are some considerations that concern not only this team but the ones in computational science at large. It is about hardship to keep an even gender balance, as artificial intelligence could be 'repulsive' to women. Nevertheless 7/16 female postdocs are counted during this period. It is also about the frustration to recruit good researchers and engineers, due to the fact that industry offers much nicer salaries but also due to the fact that interdisciplinarity is here really challenging. One can regret the frustration for researcher trained as a biologist to become an expert in deep learning, and reversely for researchers trained in deep learning to fully grasp the difficulties of biological sciences.

The team is composed of a single permanent researcher.

Even though the team was very well funded, one puzzling point is the absence of contract after 2021 despite the blooming of calls asking for AI.

The participation of the team to international conferences or consortium seems limited.

Analysis of the team's trajectory

Based on the strong expertise acquired from decades in computational and mathematical modelling of large-scale biological datasets, the team is ready to step up into modelling and training any biological system into a deep neural network model. This should provide more than a description of the biological systems but more interestingly an interpretation and a prediction of the complex relationships between molecular and morphological data. This knowledge is seriously secured by outstanding collaborations with biological experts in their fields, at Ibens for ependymal cells in in vivo models, or at ESPCI for energy metabolism of memory in *Drosophila*, to name just two. The renaming proposed as 'Deep learning biological processes' should adequately fit with that ambition.

RECOMMENDATIONS TO THE TEAM

We advise the team to continue its excellent work in embracing the opportunities given by AI to interpret and predict the complex relationships between molecular and morphological data. Also, we acknowledge that the team is the angle stone transversal collaborations with numerous teams of the institute. We recommend sticking to biological questions. A recruiting strategy taking care of the gender balance should be set up more actively, while further funding could be secured, including at the international level. Last, more connexions with the society could be leveraged as the public is eager to discover and understand innovative applications using AI.

Team 12: Data modelling, Predictive Modelling & Computational Biology
 Name of the supervisor: Mr David Holcman

THEMES OF THE TEAM

The team is interested in understanding brain function at the molecular, cellular and network scales and they develop mathematical models, algorithms and machine learning-based methods for predicting and understanding domain organisation at these different scales. Their interests are broad including fundamental questions related to domain organisation of the endoplasmic reticulum in dendritic spines in relation with synaptic connections and plasticity, analysis and modelling of single receptor trajectories in several cellular compartments including ER, several plasma membrane subdomains such as glial protrusions or dendritic spines and nuclear organisation. They are also interested in developing adaptive algorithms to analyse transient features existing in EEG signals for anaesthesia monitoring.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report recommended to reinforce the team and continue the focussing effort. Both recommendations still hold true.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	6
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	7
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	6
Total personnels	13

EVALUATION

Overall assessment of the team

The achievements, track record and visibility of the team are outstanding. It published a high number of quality papers in computational sciences and mathematical modelling. The team is very attractive for young researchers and obtained remarkable levels of competitive fundings. The team leader is regularly invited in international conferences and seminars. The team ability to engage in very successful collaborations at the national and international levels are also noticeable. Their interactions with society are outstanding, with strong socio-economic valorisation and important interactions with the general public.

Strengths and possibilities linked to the context

The team published 54 papers covering various aspects of the group's interests mostly in highly visible journals in computational science and mathematical modelling (PloS Computational biology, J Comput Phys, ...), Physics (Phys Lett, Physical Rev...), neurobiology (Neuron) and general biology (Nat Cell Biol, PNAS, Nat Commun, Sci Adv, Adv Sci, Sci Rep, Cell Rep...). During this period, the team also published 25 review articles in journals with high coverage. Based on the small hole model developed earlier on by the group, they developed original methods to analyse single particle trajectories and asymptotic methods and Brownian simulations adapted to the understanding of chemical reactions in microdomains and voltage computation in nanodomains. The team also developed breakthrough methods for analysis and prediction of brain state based on EEG signal processing using artificial intelligence for improved monitoring, dose control and coma prediction during anaesthesia. This work received high public outreach with several articles in well-established newspapers and online media coverage. This work generated two patents and led to the creation of a start-up by the PI and a former neurobiology PHD student aiming at developing and improving algorithms for brain state prediction during anaesthesia.

The team attracted several young researchers with high potential at postdoctoral and PHD levels. The team leader is highly creative and visible. He has been invited to present his work in several highly visible international conferences and seminars and was highly successful in attracting competitive funding (~5M€) including an ERC Advanced grant in 2020. The work of the group during this period is outstanding.

Weaknesses and risks linked to the context

The team had difficulties to recruit very good engineers, who are more interested in applying for industry, and to respect the gender balance (computational science is less populated than biology).

Analysis of the team's trajectory

The proposed project on the development of analytical methods to understand the regulation of motion and particle trajectories at the population level based on molecular diffusion and electrodiffusion model is very original and should be a breakthrough. Collaborative projects addressing neural network interactions at multi-scale level and the modelling of phototransduction and sensory transduction networks in olfaction have high potential and should be pursued.

RECOMMENDATIONS TO THE TEAM

The team should pursue its different directions of research, while maintaining focus on the biological questions and keeping the high level of research excellence, success and attractiveness.

Team 13: Eukaryotic Chromosome Replication

Name of the supervisor: Mr Olivier Hyrien

THEMES OF THE TEAM

The team is focused on DNA replication with specific interests in quantitative descriptions of replication origin firing and replication fork progression in eukaryotic genomes (yeast and human cell lines). Their strategy is based on developing novel replication mapping techniques at both the cell population and the single molecule level. They also contribute mathematical models of genome replication.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report was generally very positive with the team seen as excellent on most accounts. Recommendations on scientific production and activities were mainly on recruitment and teaching, and a more international profile. In the ensuing period, the team has indeed expanded. Moreover, international collaborations have resulted in publications in renowned scientific journals indicating successful actions towards the internationalisation.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

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

EVALUATION

Overall assessment of the team

This is a well-established and competitive team with personnel, technologies, funding, collaborations in place, thus, the team has excellent visibility and attractiveness. There are coherent and ambitious goals, which together with dedicated and quality-oriented execution makes this a very strong team with excellent to outstanding scientific productivity.

Strengths and possibilities linked to the context

The team is mid-size with good funding. The personnel composition is mainly of experienced researchers (permanent and postdocs), though PHD students have also been trained in the lab. This indicates competitive attractiveness of the team. The achievements are scientifically considerable in the basic science field of Eukaryotic DNA replication. The team has contributed markedly to the field by describing features of replication, importantly, they have continued to develop methods that allow precise mapping and detailed analysis of replication initiation and termination events. These developments led to important findings and publications as well as to two US patents.

The team has excellent visibility with multiple oral presentations (also invited) at major international scientific meetings. There are contributions to committees as well as engagement in reviewing tasks. The team has engaged in national but also international collaborations, a notable example resulted in a publication in *Cell* (O.H. second-last author). Additional publications from the team (last authored) were published in well-respected, peer-reviewed journals such as *Nucleic Acids Research*, *Genome Biology*, and *Nature Communications*.

Weaknesses and risks linked to the context

The upcoming retirement of the team leader (due to the approaching age limit) appears as a risk for the team and projects. Multiple projects are listed, and the relative order of priority is not clear in light of the available period of research. Otherwise, the team has excellent ideas, capacities, personnel, collaborations, and funding to execute the exciting research.

Analysis of the team's trajectory

The team has outlined an impressive future research plan with multiple original and important research lines that should further our basic understanding of genomic replication, a prerequisite for life. The movement into more modified systems (such as the genomic editing based project) is particularly exciting. Funding, personnel and possibilities for collaboration are in place for the execution of the programme. Notably, the team leader extension appears as a prime point of interest to allow this to unfold.

RECOMMENDATIONS TO THE TEAM

The team should continue its current scientific directions, though this should be with appropriate consideration of the limited time available for the team due to PI retirement.

Team 14: Stochastic Models for the Inference of Life Evolution

Name of the supervisor: Mr Amaury Lambert

THEMES OF THE TEAM

The team Smile is active in the research fields of Evolution, Ecology and Quantitative Biology. Their main contributions centre around developing algorithms, models and methods in phylogeny, applying them for a better and quantitative understanding of biodiversity – and the loss thereof; for analysing macroevolution, focusing on gene trees and their relationship to our understanding of speciation events; to study population genetics, trait acquisitions and correlated evolution; and to investigate the evolution of microbes, focusing mostly on human pathogens. They have developed and applied a wide range of models and methods to address these evolutionary questions, and in doing so have broadened the concepts and toolsets available for evolutionary analyses.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

This new team was not evaluated in the previous report.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

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

EVALUATION

Overall assessment of the team

The productions, achievements, the national and international visibility, as well as attractiveness of the Smile team is outstanding. Though highly involved in teaching, they have managed to be highly productive in terms of publications, collaborations, funding, education and outreach activities. Of note is their excellent record in citations for some of their publications, as well as their success in contributing to national, as well as international research consortia, which is reflected in co-authored publications in very high quality scientific journals and in organising a large number of scientific meetings. Moreover, their involvement and contribution to the society and public are outstanding.

Strengths and possibilities linked to the context

The Smile team has produced a large number of publications in various research areas. Their strength in combining experts in mathematics and biology is reflected in their portfolio and makes them a strong team in evolutionary biology. Their most notable and best-cited work centres around the quantification of biodiversity loss. The tools ABGD and ASAP are designed to quantify species from samples, which will, in the longer term, allow them to quickly establish the amount of extinction risk and population decline of species. In this, they are also leading the international Redcode consortium for assessing the risk of species extinction quantitatively. It should, however, be noted that they are also highly successful in the other three research axes they follow with respect to both output and visibility.

The Smile team have also acquired an impressive amount of funding over the last period, as both, coordinator, as well as partners. Amongst these was an ERC starting grant, as well as several fellowships for PHDs or postdocs. The international collaborations, as well as the conference organisations and attendance of the Smile team highlight their national, as well as an international reputation and visibility. As such, the team is highly attractive for junior researchers. This is reflected in the fact that the group has trained thirteen PHD students and nine postdoctoral research scientists during this period, resulting in a high level of human capital development.

As the Smile team works on at least two subjects that are highly relevant for today's society (biodiversity and human pathogens), members of the team were very active in interacting with society, in the form of interviews, newspaper coverage, as well as public speeches.

With two full professors in the team, the Smile team has significantly contributed to teaching and thus, attracting young students to their team, as well as to this field of research.

Weaknesses and risks linked to the context

If any, there are three potential weaknesses in the team:

1) the lack of staff, who could help in code dissemination and maintenance (which is an important asset for a team working in software development).

2) while the success of two of the permanent researchers highlights the quality of the team, the loss of these two members could also impact the work output of the team, especially since all 4 research axes seem to be also proposed for the next period. This seems, however, already considered as the team leader proposes to invest in efforts to hire new permanent researchers/teachers.

3) it seems that the team is highly attractive for students/postdocs from top institutions in France; however, it seems that not many international fellows have been recruited to the team in the last period.

Analysis of the team's trajectory

The proposed research follows logically to the already well-established research axes followed by the Smile team, taking the projects to the next level. Particularly interesting will be their contribution to Conservation Genomics, further developing their approaches to quantitatively assess biodiversity and include new data/types (Axis 1). Likewise, the idea of phylogenetic inference of co-evolutionary scenarios is innovative and should reveal interesting novel hypotheses (Axis 2). In the third research axis, the team wants to analyse the interplay between somatic evolution and the genetic program, looking specifically at the development of cancer. This should bring forth potential novel important germline mutations (or features) that could lead to tumour formation in life. Finally, in research axis 4, the team will further investigate the evolution of human pathogens, including the SARS-CoV-2 origin, as well as antibiotic resistance of human pathogenic bacteria.

RECOMMENDATIONS TO THE TEAM

The team should continue its excellent work in the different research axes. In addition, there are several recommendations that could be considered by the team leader.

Firstly, due to the loss of two permanent researchers, the Smile team has lost part of its senior level. The team should make a concerted effort to attract researchers to apply for permanent positions or teaching positions. This is already highlighted in their top priorities. Secondly, the lack of a CDD in a large and productive team as the Smile team is harmful to the long-term success of the team, as a permanent CDD is able to not only maintain publicly available software the Smile team distributes, but also keep the knowledge in the team as the PHD students and postdocs migrate through the team and leave. Thirdly, due to the thinner layer of permanent researchers, the team could think about lowering the number of PHD students and postdocs being supervised, especially as the team's heads are also highly involved in teaching. Alternatively, a good structuring of the personnel with more senior postdocs involved in supervision of the PHD students could be a viable alternative, for the time being.

Team 15: Bacterial Infection & RNA Destiny

Name of the supervisor: Mr Alice Lebreton

THEMES OF THE TEAM

The team is investigating molecular crosstalk during infection of human epithelial cells by the intracellular bacterium *Listeria monocytogenes* (Lm). They are focused on time and space aspects of Lm infection. Their findings may later be extended to other bacterial infections. They investigate the dynamics of the host gene expression in response to infection which includes a variety of regulatory aspects. Moreover, they investigate subcellular niches of host cells that appear key for new *Listeria* lifestyles.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was started during the past report period (i.e. 2015), hence, the previous report recommendations were quite few and focused on production of primary publications from the team. It is noted that the team has published primary publications in this new evaluation period.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

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

EVALUATION

Overall assessment of the team

The team has started to publish primary research in this first full review period. The scientific quality of the work is very good particularly given the modest size of the group. The attractiveness of the team is very good as assessed by the collaborations, the recruitment of staff and obtaining regular funding. The overall assessment of the team is very good.

Strengths and possibilities linked to the context

The team's visibility is very good and it is very well established scientifically. This is reflected in a) active involvement in teaching activities bioinformatics and molecular cell biology and infection, b) in thesis committees and juries, c) The team leader is invited speaker at research conferences both nationally and internationally, including as key note speaker, d) Numbers of PhDs and postdoctoral research scientists trained

is commensurate with the size of the group, e) Good level of research funding obtained to undertake their research with 1 active grant running from ANR, f) the complementary expertise of the group members and their multidisciplinary collaborations are a strength.

The scientific production is very good and it has centred around the two main areas, namely host responses to infection and the heterogeneity of *Listeria intracellular* lifestyles, together with the collaborations that have been initiated, will ensure the future productivity of the group. Altogether seven primary publications, two signed by the team, with PLOS Pathogen as the major paper.

The non-academic activities within the team are excellent and there is clear evidence of the team being involved in activities with the general public including radio programmes, documentaries and with high school students. This is to be welcomed.

Weaknesses and risks linked to the context

The team is heavily involved in teaching, and it is still undertaking the supervision of quite a large number of BSc/MSc students. Care must be taken that these activities do not negatively impact on the overall scientific productivity of the team.

The lack of technical support for the group continues to be an issue, particularly with respect to knowledge retention and lab management. This concern was also mentioned in the previous evaluation report.

From the seven papers highlighted, four were signed as senior authorship by members of the team. It is important that the team develops a line of publications that originate within the lab and are signed by the team. The main model, Lm, is not a major clinical challenge, hence, the sole focus on this bacteria can be a weakness for long-term societal impact and the ability to attract funding.

The need for improvements in microscope possibilities within the Imaging Platform is also noted.

Analysis of the team's trajectory

The team has an exciting line of projects that connect well with earlier research within the group, as they follow the two tracks of a) host responses to Lm infection with focus on transcription-translation aspects, and b) the intracellular niche for Lm. The second line of research (Lm niche) appears as the most promising line at the moment in terms of conceptual novelty and potential for scientific impact. This may be extended to other clinically important bacterial infections.

The group appears ready to harvest the fruits of their methodological developments and findings, including exploiting the fluorogenic probe FAST and characterising eSLAP. Multiple (mainly French) collaborations are set up that allow the relatively small team to conduct a rather wide range of activities. It should be a priority that the PI leads collaborations; at this stage in her career, it makes sense to have a dedicated focus on projects that originate within the team.

RECOMMENDATIONS TO THE TEAM

The team is conducting high-quality research that has some translational potential. Extending the research focus to include additional clinically important pathogens (beyond Lm) could strengthen the team impact and visibility. Publishing primary research papers in renowned journals should still be a major focus for the team, it is important that researchers focus on their own lines of research (i.e. maintain corresponding authorship). The group composition is good in terms of additive areas of expertise, though additional permanent staff recruitment would be a great advantage. If possible, the reduction of teaching load would free the PI to focus on research and grant writing.

Team 16: Expression of eukaryotic mRNAs

Name of the supervisor: Mr Hervé Le Hir

THEMES OF THE TEAM

The team investigates the exon junction complex (EJC), which is deposited onto nuclear mRNAs by the splicing machinery and as such EJC marks processed mRNA which it accompanies to the cytoplasm. The EJC communicates with cellular machinery involved in transport, translation, and quality control of mRNAs. This group combines biochemistry, biophysics, molecular and cellular biology as well as transcriptomic approaches to study EJC assembly and functions. They also use a variety of Eukaryotic model systems, including yeast.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was evaluated with very positive remarks, and there were no major recommendations beyond recruiting more postdocs and continuing the good work.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	5
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	3
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	5
Total personnels	10

EVALUATION

Overall assessment of the team

The team is internationally recognised for the EJC research, and several original research projects have been conducted indicating excellent to outstanding scientific production. Projects are running with very productive national and international collaborations. The group is small to mid-size, but the attractiveness of the team is very good to excellent as assessed by the funding level, collaborations, and the recruitment of permanent staff.

The overall assessment of the team is excellent to outstanding.

Strengths and possibilities linked to the context

The team research is carried out by several staff categories, including permanent researchers, engineers/technicians and PHD students. There is limited engagement of postdocs, as only one has been connected with the team (2018-22). Thus, attractiveness is very good to excellent.

The team has an excellent capacity to obtain grants from national agencies including ANR and INCA. The PI is also coordinator on several of these grant. There are several invitations to scientific meetings, including prestigious conferences (EMBO, FASEB). There was an organisation of one international scientific meeting.

The team has an excellent scientific production with a dedicated focus on the EJC. The team research has been very successful in elucidating aspects of EJC function, which includes EJC assembly and mapping such as the important role of CWC27 as a partner of CWC22 and eIF4A3 that mediates EJC complex recruitment. Another successful line of research involved a collaboration with another team at Ibens. Their results indicate an EJC-dependent mRNA trafficking towards the centrosome that might have a role in neuronal contexts. Altogether, this has resulted in eighteen publications (of which 2 are reviews), often published in well-established relatively broad-scope journals (several corresponding author papers in Nature Communications and NAR). The production is of very high quality.

Weaknesses and risks linked to the context

The team is experiencing difficulties to attract highly motivated postdocs, the recruitment of PHD students may also be challenging. Moreover, there are issues in securing the employment of engineers, which creates challenges for teams with quite broad research approaches as the Le Hir team.

Analysis of the team's trajectory

The research questions, ideas, capacities, and collaborations are at a very high level. Five exciting projects are outlined, which may be to the high side for a group of this size. It is noted that the group has a dedicated focus, hence, conducting multiple projects may be feasible. With the molecular biology focus, the team has major collaborators outside Ibens.

RECOMMENDATIONS TO THE TEAM

The team should consider the means to address the recruitment issues for PHDs and postdocs. Connecting early and actively with prospective candidates at meetings, courses or similar appears as a possible approach going forward.

The trajectories point to several (5) project lines, which may be challenging in light of the recruitment issues, perhaps the team should prioritise the scientifically most rewarding projects.

Team 17: Programmed Genome Rearrangements in Ciliates

Name of the supervisor: Mr Eric Meyer

THEMES OF THE TEAM

The project of the team focuses on the genome-wide DNA rearrangements that occur during the development of the polyploid somatic macronucleus in *Paramecium* species. The main objectives are to characterise the mechanisms of recombination events and their epigenetic regulation that target the excision of numerous transposable element insertions to reconstitute functional genes. Different lines of research are conducted: the recognition of SCNRNA-independent IESs, the evolutionary history of IESs in the *Paramecium aurelia* complex, the identification of new factors involved in IES excision, and finally the analysis of the co-optation of the Internal Eliminated Sequences (IESs) excision machinery and SCNRNA pathway for the heritable inactivation of cellular genes.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

It was recommended to train earlier stage researchers. No significant improvement was achieved along that line during this period (3 PHD students trained) and the team complained about difficulties to attract students on their thematic of research.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

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

EVALUATION

Overall assessment of the team

The research performed by the group is excellent with important contributions in different lines of research. The team is internationally recognised for its work on genome rearrangements in *Paramecium* species and several original research projects are running that, in several instances, involve well renowned national and international experts in the field. Considering its small size, the attractiveness of the team is excellent as assessed by the long-standing collaborations, the recruitment of non-permanent staff and obtaining regular fundings. The overall assessment of the team is excellent.

Strengths and possibilities linked to the context

This is a relatively small team composed of three permanent members, three PHD students, two postdocs and one engineer during the period. The team is working on different aspects of programmed genome rearrangement in ciliates. The results obtained contributed to the characterisation of mechanisms used for the specific recognition and elimination of TEs during development of the polyploid somatic macronucleus (MAC), of the innovations required for continuous recognition and precise excision of such a diverse set of sequences, and of the co-optation of these mechanisms for the regulation of cellular genes. More recently, the team has contributed to the progress towards the complete assembly of the germinal MIC genome and characterised a new class of transposable element called helitrons among 61 identified germline transposable elements. They also revealed an enzymatic activity responsible for rolling circle replication in the developing MAC nucleus. Furthermore, they characterised the expression of six paralogs of the nucleoporin Nup98, some of them specific for the MIC or the MAC nucleus, opening the way to develop affinity purification schemes to isolate the different types of nuclei. In the last three years, the team has also been engaged with physicists to study and model an entire sensorimotor system responsible for the control of spatial navigation by *Paramecium*.

The team has produced as leader three original articles since 2017 in very good journals such as *Genome Biology* (2017), *Nucleic Acids Research* (2018), *Genome Biology and Evolution* (2020), and one review in *Annual Review of Microbiology* (2017). They also contributed through collaborative works four papers including one in *PLoS Biology* and one in *Nucleic Acids Research*. Importantly, most of the work characterised in recent years has yet to be published, in 2024 as the team will not be renewed.

The team has an excellent visibility because of their seminal studies with original approaches to characterise programmed genome rearrangements in *Paramecium*. The team is well integrated in national and international networks of geneticists and biologists interested in genomic rearrangements in ciliates, collaborations that favour funding and publications with other teams.

The work has been funded by national agencies as principal investigator (1 ANR, 1 FRM) or as partner (1 ANR).

Weaknesses and risks linked to the context

Since the team will not be renewed, it is important to publish before the end of 2024 the original results obtained.

Analysis of the team's trajectory

The team will not be renewed.

RECOMMENDATIONS TO THE TEAM

The committee will not make recommendations as this team will close early 2025. However, we would like to acknowledge the work performed by the PI and his collaborators for the seminal studies performed on ciliate biology over the years.

The team has yet to publish the results obtained in recent years.

Team 18: Cell Division and Neurogenesis

Name of the supervisor: Mr Xavier Morin

THEMES OF THE TEAM

The Morin group is interested in understanding how the choice between asymmetric and symmetric cell division is controlled in the neural cord during development to understand how cell proliferation and differentiation affect the development of the central nervous system. They use the chick embryo as a model where they can observe *in vivo* the stages when cells chose between the two different modes of division. Using single cell transcriptomic approaches, they are searching transcripts that are differentially expressed, to isolate new genes defining which division mode is taken by a given cell. One of their main interests is to find cellular mechanisms affecting the cell polarity, which they analyse at the cellular level focusing on the behaviour of either the centrioles or the mitochondria.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report was very positive about the team's performance. The evaluators suggested the team introduces work on Human ES cells. This has not yet been done by the team, probably because the difficulty that including such new research model in the laboratory implies.

The report also suggested increasing the group's visibility through attendance to international conferences and the writing of reviews. At least one review in *Current Opinion in Neurobiology* was published in 2021 by the team, and the group was invited to present their work in several international conferences and workshops almost every year.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

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

EVALUATION

Overall assessment of the team

The team develops original and sound lines of research to analyse, *in vivo*, how symmetric and asymmetric cell divisions result in neuron amplification versus specification. The team has published excellent work during the evaluated period. Its visibility is excellent too as attested by successful collaborations, invitation to international conferences and acquisition of competitive grants.

Strengths and possibilities linked to the context

One of the group's main strengths is the study of neurogenesis in chick, which allows direct *in vivo* analysis. The capacity to perform somatic genetic manipulation *ex vivo*, as suggested by the team, could be particularly important, making the chick a system to understand the function of genes controlling neurogenesis at stages when this cannot be easily analysed in other vertebrates.

The team has published excellent work in the evaluated period, especially in 2017–2018 (Neuron, Current Biology, PLoS Biology, EMBO reports). In 2019–2022, most of the team's publications appeared as collaborations in highly respected journals (One in Angew Chem Int, and two publications in Nature Communications). The effect of the Covid-19 crises and the reorientation of the group's work towards a new focus (symmetric vs. asymmetric neural progenitor divisions) are likely to be responsible for the decrease in the group's output.

The team have introduced single cell transcriptomic analyses in chick and have compared their data with that of other researchers applying this technique in mice with the aim to identify factors that may be influencing the cell's decision to perform a symmetric vs. an asymmetric division. A new avenue of research looking at how the mitochondria may affect cell polarity and neural specification is also being explored, although this is at a preliminary stage. The team has been well funded with more than 1.3 M€ through several national grants including ANR, FRM, Labex and foundation Simone et Cino del Luca. The work of the group in this period is excellent.

Weaknesses and risks linked to the context

Given the small size of the community studying neurogenesis in the chick, there is a risk that the team's work is not as well known as that of teams working on other mammalian models where knockouts can be performed.

Analysis of the team's trajectory

The team has published excellent work in the 2017–2022 period, especially in the first two years (2017–2018, with publications in Neuron, Current Biology, PLoS Biology and EMBO reports). In the last years, most of the team's work appeared in highly respected journals (Angew Chem Int. and two publications in Nature Communications) as a collaboration with other laboratories where the team did not lead the work. The effect of the Covid-19 crises and the reorientation of the group's work towards a new focus (symmetric vs. asymmetric neural progenitor divisions) is likely to be the cause for the small decrease in the group's output. The team has been very well funded during this period through several national grants including ANR, FRM, Labex and The Foundation Simone et Cino del Luca with more than 1.3 M€. The work of the group in this period is excellent. The team is reorienting its work towards a new focus – the control of symmetric vs. asymmetric neural progenitor divisions – using a molecular and cellular approach. Especially innovative is their analysis on how mitochondria may affect this process.

RECOMMENDATIONS TO THE TEAM

It may be advantageous to consider setting in the laboratory human organoid models that could reinforce or confirm observations made in the chick model. Alternatively, the team could explore possible collaborations with other Ibens teams working in *in vivo* models.

Team 19: Modelling Biodiversity

Name of the supervisor: Mrs. H  l  ne Morlon

THEMES OF THE TEAM

The team develops and maintains widely used statistical inference tools, based on mathematical models, which, combined with large data sets, allow answering questions about processes shaping genetic, phenotypic and species diversity at a global scale, with applications to the macroecology and macroevolution of multiple marine and terrestrial groups, from microbes to vertebrates. The team studies the process of diversification with models considering the variation in evolutionary rates across time, groups and environments, the role of interspecific interactions, or highly multidimensional phenotypes. They have recently applied their models to study the evolution and ecology of microbial communities in the oceans and in gut microbiomes, developing inference methods from metabarcoding.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No recommendation was made in the previous report about the team research and investment in other missions, which were judged outstanding, but the need for permanent support in maintaining the developed tools and packages, as well as the data sets used by the team, was noted. The same need is expressed by the team 5 years later (as well as several other teams at Ibens).

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Cat��gories de personnel	Effectifs
Professeurs et assimil��s	0
Ma��tres de conf��rences et assimil��s	0
Directeurs de recherche et assimil��s	1
Charg��s de recherche et assimil��s	4
Personnels d'appui �� la recherche	0
Sous-total personnels permanents en activit��	5
Enseignants-chercheurs et chercheurs non permanents et assimil��s	1
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activit��	5
Total personnels	10

EVALUATION

Overall assessment of the team

The quality of scientific production by the team is outstanding, with a large impact on a wide community of users of innovative methods to analyse and model macroevolution and diversification processes (e.g. the software RPANDA or a study on the effect of temperature on diversification belong to the 1% most cited papers in the field of Ecology of the year), the visibility and attractiveness of the team is outstanding as well as exemplified by the training of numerous young researchers with a successful career, prestigious prizes such as the CNRS Silver Medal and an expertise sought for by many scientific institutions (including the CoNRS with strong commitment for the scientific community during the evaluated period). The level of investment of the team in teaching and very active outreach is also excellent to outstanding.

Strengths and possibilities linked to the context

The team leader has outstanding and very well-established expertise in mathematics and bioinformatics methods applied to macroevolution and macroecology. The tools developed, maintained and improved by the team members such as RPANDA, or BEAST are used by a very wide community of researchers using phylogenetics and comparative methods and the team's research has allowed several breakthroughs in the period about the kinds of analyses and questions that can be addressed with these tools (such as modelling heterogeneous evolutionary rates, combining fossils and genetic data, integrating interspecific interactions and better modelling uncertainties affecting inferences). The application of these methods to different data sets within the team has also allowed major discoveries about the evolution and spatial structure of biodiversity on the planet, among which one can cite showing how temperature in the distant past has affected diversification processes or revealing different modes of transmission of gut microbiota across different groups. Both these aspects explain why the research conducted by the team has been extremely impactful, their work highly visible and well cited. The quality of research has been recognised by numerous prizes to the team leader in the evaluated period (CNRS Médaille d'Argent, Prix Irene Joliot-Curie, KU Leuven Chair, nominated « Chevalier de l'Ordre National du Mérite), 56 invited conferences, and her expertise sought by many various national and international institutions (CoCNRS section 29, Cesab scientific council, Tara Oceans Consortium Board, evaluation of projects for NSF, ANR, ERC, etc., but also roles of associate editors for reputed journals such as Ecology Letters or PLoS Biology).

Success in obtaining funding in the past period and global attractiveness of the team has been outstanding as well (with in particular the coordination of an ERC grant and a large ANR project, 3 Marie Curie Fellowships and a Mogpa grant hosted in the team), which has allowed the training of six PHD students and thirteen postdocs in that period. Young researchers in the team have been extremely productive (8 of them have more than 4 publications in the period, up to 10), publishing their work in journals of high reputation with a high impact in terms of citations (e.g. the publication of RPANDA is cited 35 times more than an average publication in the same field in the same year, the publication of ClaDS in 2019 is cited 20 times more, or the work on the influence of temperature on diversification 23 times more). Many postdocs publish both with the team leader and their own independent work, and several of them have since obtained a highly competitive position at CNRS as permanent researchers.

The team is involved in many national and international collaborations on various topics and model systems and the expertise sought by a very extended network of collaborators, both theoreticians and empiricists (as illustrated by the integration in a recent large European project). Within Ibens the team is very involved in fruitful collaborations on the analysis of data from the TARA Oceans expeditions, where the breakthrough in terms of methods of analysis of metabarcoding data has allowed impactful publications on the biogeography and evolution of yet relatively unknown compartments of marine biodiversity and ecosystems. The team also regularly collaborates and co-supervise students with two other teams on model development. This puts the team leader in a good position to coordinate the animation of the ecology & evolution section at Ibens.

The team is also very involved in teaching with one member currently with an ATER position at ENS (192 hours per year at various levels), the team leader teaching short courses in a great diversity of universities (Paris, Lyon, Grenoble, Sweden, etc.) and the whole team being involved in the organisation and lecturing of an online course from the program 'Transmitting science' on the RPANDA tool that they develop. The team leader is also very active in various outreach activities, including prestigious wide-audience conferences (e.g. Collège de France, Théâtre des variétés) and many interviews in various media (radio, press).

Weaknesses and risks linked to the context

While being globally very attractive and led by a very successful woman researcher, the gender composition of the team is very unbalanced, suggesting difficulties in recruiting female students and postdocs on these topics. The recent recruitment of a young female researcher in the team may help change this situation. The recruitment of two CNRS researchers in the team will also strengthen the team where the leader was the only permanent researcher until this year. The maintenance in the long-term and diffusion of tools and packages to a wide audience is a key activity of the team, a very time-consuming, and also a scientific challenge overall for this field of research, for which there is no dedicated permanent technical support.

Analysis of the team's trajectory

The team projects are follow-ups of their current questions, which are very diverse, original and with very large potential impact. In particular, the team will continue to explore the internal and external factors driving diversification by integrating many of their recent methodological advances in the same analytical framework, which will allow integrating molecular and fossil data, jointly reconstructing phylogeny, diversification processes and phenotype evolution for highly dimensional 3D morphological data. This part of the project is funded by an

ANR grant. Such integration will represent a very significant advance in our ability to test more and more sophisticated scenarios of trait evolution. From a methodological perspective, the team will also continue to explore novel computational possibilities allowed by the use of machine learning. Research on ocean planktonic ecology and evolution initiated during the last contract remains a key goal of the team, where the combination of rich fossil data, past climate models and long-read metabarcoding has indeed high potential for the application of the team new models to significantly increase our understanding. This work is funded by a European project and an advanced ERC project will be resubmitted. Finally, an original project linking macro and microevolution has just been launched, supported by a PHD scholarship. All these projects are very innovative, promising relevant and in the reach of the team given their expertise and secured funding.

RECOMMENDATIONS TO THE TEAM

The science and the trajectory are outstanding and the investment in different missions (outreach, teaching, collective responsibilities) excellent, so we have no recommendation in this regard. With respect to the two points of concern expressed by the team, the lack of attractiveness for female students could be acted upon by further increasing activities such as teaching or outreach where role models play an important part, but the bias starts early in education so this is a far-reach long-term endeavour. Given that the lack of support for software development is expressed by several teams and modelling a clear strength of Ibens, one could discuss the recruitment of staff that would work with different concerned teams at Ibens, even though the specificity of the models and softwares is a challenge in this regard.

Team 20: Small RNA-directed reprogramming of gene expression in host-bacteria interactions

Name of the supervisor: Mr Lionel Navarro

THEMES OF THE TEAM

The team's current research interests are focused on the genetic and epigenetic based mechanisms controlling the reprogramming of gene expression during antibacterial defence and how this is relevant in disease resistance. In particular they are focusing on the involvement of DNA demethylation and small RNAs in these processes. To achieve this, they are employing *Arabidopsis* and *Chlorella* together with human epithelial cells as model systems.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous recommendation regarding extending the group's plant work to include crop species has been followed, and approaches of the team in extending their work into the *Chlorella* and *Shigella* areas is to be welcomed.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres 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 d'appui non permanents	1
Post-doctorants	1
Doctorants	5
Sous-total personnels non permanents en activité	7
Total personnels	9

EVALUATION

Overall assessment of the team

The scientific quality of the work is very good and is of an international standard in the field of research. However, this quality is not fully reflected in the scientific production of the group in terms of published outputs. The group has outstanding interactions with industry and with start-up companies in particular, and this particular focus may have resulted in this reduced scientific production. Notwithstanding this, the visibility of the group is excellent and they are also very active in outreach activities involving relevant stakeholders.

Strengths and possibilities linked to the context

The team visibility is excellent and it is very well established scientifically. This is reflected in the number of national and international conferences (36) and invited seminars that team members have attended and at which they have presented their work.

Visibility is also attested by the involvement of staff in teaching programmes at ENS-PSL and at the University of Versailles, at Pasteur and at the Saclay summer school amongst other activities in this sphere. The team is involved in collaborative linkages nationally with University Grenoble Alpes, IBPC (Paris), IRD, Institut Pasteur, Université de Perpignan and the University of Toulouse and internationally with the University of Cambridge, University of Bielefeld and Indiana University, Bloomington.

The overall scientific productivity is very good. The team are employing state-of-the-art approaches to study the transcriptional control of defence genes by DNA methylation and demethylation in *Arabidopsis*. They are also studying the clinical pathogen *Shigella flexneri* in the context of the role of small RNAs in the vacuolar rupture process involved in infection. The total number of publications is however modest, particularly given the number of permanent members in the team. However some of the work is making an important contribution to the field as reflected in the 2021 paper which describes the erasing of DNA methylation at promoter-regulatory regions, which has already been cited 37 times. In addition, the number of PhDs and Masters supervisions, together with postdoctoral researchers that have been trained is commensurate with the size of the team.

The non-academic activities within the team are outstanding particularly with respect to interactions and partnerships with start-ups and with industry. These are based on four patents that the team have with *Chlorella*- and RNA-based therapeutic and biocontrol applications. In particular during the reporting period they have been involved with ENGreen and with AGS Therapeutics and AGS manufacturing. There is also clear evidence of the team's involvement in appropriate outreach activities with relevant stakeholders such as schools, and with the general public.

Weaknesses and risks linked to the context

While the overall scientific production is very good, the number of publications is quite modest, particularly given the number of permanent members in the team. In addition to the profile of some of the journals in which the scientific outputs have been published, does not appear to match the quality and significance of the work. A number of papers are, however, in preparation and will be submitted for publication soon.

While the team have successfully undertaken work in the area of technology transfer involving start-up companies using the experimental systems that they have developed, this may have had the effect of reducing the overall scientific productivity of the group.

Analysis of the team's trajectory

The team plan to continue to build on their expertise on *Arabidopsis*, *Chlorella* and human cells to evaluate and compare gene regulatory mechanisms within these different systems. They also plan to study epigenetics and RNAi in the context of host-bacteria interactions. Finally, they plan to leverage their technology transfer knowledge in the field of anti-infectives. The trajectory project involving gaining a better understanding of the nature and causes of epigenetic variations in *Arabidopsis* will build upon the group's expertise in this area. The potential role of endogenous plant sRNAs in modulating the bacterial expression of pathogenic and/or symbiotic, which builds on work being undertaken on *Sinorhizobium meliloti*, will form the basis of an ERC Advanced grant is also relevant to the team's research interests and has the potential to result in exciting advances in the *Arabidopsis* field. The proposed work in the area of bacterial-mediated suppression of RNAi and of host counter-attack involving *Arabidopsis* mutants that inhibit RNAi suppression triggered by the archetypical bacterial GW-effector HopT1 will also open an interesting avenue of future research; particularly if insights can be generated that are relevant to *Legionella pneumophila*. Appropriate collaborative linkages are in place to implement this work. Finally, the approaches aimed at discovering novel anti-infectives by focusing of antimicrobial peptides, AGO4 which is involved in siRNA mediated gene silencing, LegK1 which is involved in modulating macrophage defence or inflammatory responses in *L. pneumophila* together with the proposed work on host susceptibility factors are all exciting and valid approaches, with appropriate collaborative linkages and industrial collaborators.

However, while these proposed exciting projects represent an opportunity to generate high quality scientific results in the future contract, care must be taken in two respects. Firstly, given the size of the group it is important that they do not dilute their scientific efforts in too many different directions. Secondly, given the involvement of industrial partners in their work – which may generate IP issues – care must be taken that this does not endanger the group's ability to publish the scientific outputs from their work.

RECOMMENDATIONS TO THE TEAM

The team publishing strategy should be improved. They should strive to publish their research outputs in scientific journals that have a broader audience reach.

As previously highlighted, care should be taken that the group do not dilute their scientific efforts by working in too many different directions. Also care must be taken to ensure that in projects involving industrial partners/start-ups that IP issues do not preclude the group's ability to publish the key scientific outputs from these projects.

Team 21: Glutamate Receptors and Excitatory Synapses

Name of the supervisor: Mr Pierre Paoletti

THEMES OF THE TEAM

The team is interested in understanding the principles of glutamatergic synapse and NMDA receptor (NMDARs) functions in neurotransmission and excitatory synapse function. Their approaches are multi-scale and pluridisciplinary and focus on the molecular characterisation of NMDAR structure and allosteric switch control and the design of specific drugs to target different receptor subtypes, the understanding of the consequences of receptor composition and signalling diversity on brain function and the impact of the synaptic microenvironment including the role of zinc in neurotransmission modulation.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report was extremely positive and made no major recommendation.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	3
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	7
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	4
Doctorants	3
Sous-total personnels non permanents en activité	7
Total personnels	14

EVALUATION

Overall assessment of the team

The track record and visibility of the team are outstanding. The group established strong collaborations at the national and international levels and contributed to important research articles and reviews. The team leader has been invited to present his work in several highly visible international conferences. He is clearly recognised at the international level and holds important scientific responsibilities. The PI and senior scientists of the team were also very successful attracting competitive funding (~4M€), including an ERC Advanced grant in 2017. The team was very attractive to international PhDs and postdocs. Its expertise resulted in strong links with industrial actors.

Strengths and possibilities linked to the context

The track record of publication and recognition of the team are outstanding. They published 16 original papers in highly visible journals in neurobiology and pharmacobiology (Neuron, J Physiol, ChemPhotoChem) and

general biology fields (eLife, Nat Commun, EMBO J, Science, PLoS Biology, Cell Rep, iScience...). The team also published eight review articles/comments in high impact journals (Trends Biochem Sci, Curr Opin Physiol, Nat Rev Neuro, Neuron,).

Using a combination of experimental and modelling approaches, the team made significant progress in the understanding of the fine regulation NMDARs at the ultrastructural level and found different allosteric mechanisms for GluN2A and GluN2B receptors (EMBOJ 2019, Nat Comm 2021, Neuron 2021). Based on previous work from the team that used protein engineering to design photo-controllable NMDARs, the team validated the incorporation of photo-convertible unnatural amino acids as a suitable strategy to control receptor activation and they succeeded in developing photosensitive ligands that should be very valuable to manipulate NMDAR function in vivo (eLife 2017, ChemPhotoChem 2021). They extended their understanding of the role of vesicular zinc as a component of the synaptic microenvironment and found that zinc also acts positively on neurotransmission in the neocortex (eLife 2017, Nat Comm 2018, Neurobiol Dis 2020, Cell Reports 2022). Finally, the team provided novel evidence for the association of GluN1 and GluN3 subunits to form atypical NMDARs, which are sensitive to extracellular glycine (and hence called excitatory glycine receptors, eGlyRs) and regulate emotional behaviour (Nat Comm 2018, Science 2019, Neuron 2022).

The team leader has been invited to present his work in several highly visible international conferences and seminars. He was awarded the Grand Prix Lamonic de Neurologie of the French Science Academy (2017) and he was elected as a member of Academia Europaea (2019). The PI and senior scientists of the team were also very successful in attracting competitive funding (~4M€) at national and international levels including an ERC Advanced grant in 2017.

The team's composition is an excellent balance of experienced senior scientists/associate professors and younger researchers at postdoctoral and PHD levels. The group established very successful collaborations with established teams, which provide valuable knowledge and knowhow and complement the team's main expertise.

The team contribution to society is also remarkable, with collaborative contracts and scientific consultancies for major pharmaceutical companies (Genentech, Pfizer, Boehringer Ingelheim...).

Weaknesses and risks linked to the context

The team leader is aggregating the directions of Ibens, ENS Biology Department and laboratory of excellence (labex) MemoLife. He is the proposed director of the two structures for the next five-year period. Despite a high load of administrative duties, the PI together with his collaborators, maintained a high level of achievement and visibility. However, the present conjunctural struggle in hiring young scientists at predoc/postdoc level may represent a risk for the group for maintaining its productivity and realising its aims.

Analysis of the team's trajectory

The team capitalises on recent progress and findings and will pursue the work on eGlyRs by elucidating the molecular organisation of the GluN1/GluN3 receptors using cryoEm and engineering small ligands and nanobodies for a functional characterisation. This work will be extended to poorly understood Delta receptors (GluD1 & GluD2). They will develop new tools to decipher the role of components of the synaptic microenvironment in vivo and intend to analyse the specific contribution of different receptor subtypes using subtype-specific optopharmacology tools. They also propose to use Evo-devo approaches based on non-vertebrate marine species to better characterise the function of non-glutamatergic ionotropic glutamate receptor (iGluR). This research program has high potential and should be pursued.

RECOMMENDATIONS TO THE TEAM

The team should pursue the different directions of research and maintain a high level of research excellence, and attractiveness. The team should maintain and reinforce existing collaborations with several national and international established teams to complement the team's expertise and manpower.

Team 22: Neurophysiology of Brain Circuits
 Name of the supervisor: Mrs Daniela Popa and Mr Clément Lena

THEMES OF THE TEAM

The team investigates how computations by the cerebellum shape actions and representations in the forebrain and how dysfunction in this circuit leads to pathologies. This is centred on the hypothesis that executive brain function requires the functions of the cortex, basal ganglia and cerebellum and that pathological states can result from the failure to compensate for the dysfunction of one structure by the others. The team uses the mouse as a model organism in their research.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was established in 2016. The previous report praised the excellent publication record of the team, the healthy size of the team and their effective organisation and delivery.

They also praised their excellent internal collaborations, but saw as a weakness the lack of international collaborations. The committee recommended international collaborations should be established. In the current report, there is mention to the participation to two European Marie-Curie ITN (Inavigate, CEN).

The committee recommended that particular attention was paid to promote the career progression of Dr Popa. The current report explicitly demonstrates the individual reputation of each of the PIs, and their invitations to speak at conferences, involvement in committees, and independent funding. This indicates that this point is being taken care of.

The committee saw that the potential for translational and clinical research could strengthen the success of the team. The current and trajectory project does investigate on pathological conditions, but it does not explicitly mention how findings will be translated into clinical outcomes. For example, there is no mention of possible collaborations with industry or hospitals/medics.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	3
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	1
Doctorants	8
Sous-total personnels non permanents en activité	10
Total personnels	13

EVALUATION

Overall assessment of the team

This is an outstanding, effective team, that carries out innovative, high risk, high-gain research, leads by two PIs. They have sustained an outstanding publication record as senior authors in high-profile journals, including eLife 2017, 2022, Nature Communications 2020, 2023 and review in Neuron 2021. The team secured very high level of national and european fundings and was very attractive to PHD and post-doc. Both PI have strong international reputation, as demonstrated by invitations at many reputable conferences.

Strengths and possibilities linked to the context

This is an outstanding team, carrying out innovative, high risk, high-gain research and internationally recognised as pioneers in the field of cerebello-cerebral coupling.

They work as an effective, well-organised two-PI team, supervising ten researchers (1 CR, 1 postdoc, 8 PHD). They have been very productive in this evaluation cycle and have an outstanding publication record in high-profile journals as senior authors, including multiple articles in eLife (2), Nature Communications (3) and a review in Neuron.

Both PIs have an international reputation demonstrated by their regular invitations to speak at international conferences (including as chair for a GRC), and their involvement in multiple evaluation committees (e.g. HCERES, CoNRS, CSS...).

The team is well funded by ANR (7, incl. 5 as coordinator) and FRM grants and it is involved in 2 MSCA-ITN. It hosted a very high number of PHD students (16) as well as a few postdocs.

The research achievements of the team are based on their conceptual novelty and technical breadth, using a model organism, and include:

(1) The finding of a novel type of connection from the cerebellum provides to the sensory-motor system in the cortex and basal ganglia. They investigate how this regulates skilled locomotion, sensory exploration and emotional conditioning. They demonstrated a role for the cerebellum in the consolidation of skilled learning and the regulation of emotional memory.

(2) The finding that the cerebellum continuously updates the brain internal model of the body in space. This has implications for understanding and recovery from pathological conditions.

(3) Investigating how the cerebello-cerebral circuit is dysregulated in pathological conditions. This is based on the hypothesis that executive function in the brain depends on the integration of cortex, cerebellum and basal ganglia, and that pathology results from failure to compensate the deficits in one of these structures by the other. They have found that diseases that affect locomotion, like Parkinson's disease, can be improved by stimulation of the cerebellum. This reveals functional plasticity in the connections involving cerebellum, cortex, basal ganglia and thalamus, and has tremendous clinical potential and implications.

The two PIs are also involved in teaching at ENS and Université Paris Cité.

Weaknesses and risks linked to the context

The team is well funded by ANR, ITN and FRM for the next couple of years. However, for a two-PI team this size, it would be even better if they could recruit more postdocs. They should apply for ERC grant(s), after they have sent those papers that are currently in preparation.

The lab is distributed across three different floors at IBENs, which is not ideal, but refurbishment work is under way and they hope that in around two years' time the lab arrangement will have improved.

The team is aware of the translational potential of their findings, and they tried to obtain funding to carry this through, but so far, they have been unsuccessful due to the surprising, innovative nature of their findings. They are still planning to keep trying, and they aim to compile some further preliminary data that would make the case more compelling for critical reviewers. Their findings could have a tremendous impact that would benefit their own research and also society as a whole.

Their involvement in activities for society and public engagement are limited.

Analysis of the team's trajectory

The team is pioneer and expert in the cerebellar-cerebral pathways.

Their project aims to identify the forebrain functions under cerebellar control and identify the pathological processes during learning and adaptation. This is done in the mouse, as a model organism, using transgenesis, opto- and chemo-genetics, electrophysiology and behaviour analysis. The objectives are:

(1) to investigate how experimental models of Parkinsons' disease and other dystonias disrupt the cerebellar-cortical circuit and whether cerebellar stimulation can rescue these locomotion deficits.

(2) Investigate the multiple functions of the cerebellar-cerebral circuit, in emotional learning, spatial orientation, motor learning and somato-sensory and motor integration.

RECOMMENDATIONS TO THE TEAM

This is an outstanding team that works effectively, in highly innovative, high risk, high-gain research, sustains an outstanding publication record, in high-profile journals, and is well funded until 2025. Their hypotheses are original and they are well-recognised experts in their field. They should continue to work effectively to continue to deliver in their project aims.

Attracting further funding and postdocs is critical to the sustained success of the team. They should apply for (an) ERC grant(s), and independent postdoctoral fellowships. They could use available social network platforms, conferences, etc. to advertise themselves to attract postdocs who could apply for fellowships.

Their idea to compile more preliminary data to request further funding to further explore translational opportunities will eventually pay off.

Team 23: Genome Organisation and Dynamics

Name of the supervisor: Mr Hugues Roest Crolius

THEMES OF THE TEAM

The main focus is comparative genomics applied to the understanding of genome evolution and function with elucidation of the complex evolutionary histories of regulatory circuits, genes and genomes, especially those involving whole genome duplications.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

An increased publication rate was recommended to reflect the large body of work that was done in the team. This has been fully met by the Dyogen team.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

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

EVALUATION

Overall assessment of the team

The team's performance in the last evaluation period was outstanding, with respect to publication, funding acquisition, as well as national and international collaborations and visibility. Though the team is comparatively small, they published 21 papers, with four more publications accepted since the writing of the report. They are actively involved in building and maintaining the INSB Bioinformatics infrastructure. The team has an outstanding national and international reputation, reflected in the team members collaborative projects and their involvement in international research consortia. The team is also outstanding with respect to society contribution, with their involvement with the ERGA and their coordination of the AtlaSea project.

Strengths and possibilities linked to the context

The Dyogen team has had an impressive research output, with 21 publications as main or co-authors. Their contribution to the field of genome structure evolution especially in fish were and still are undisputed, as is their release of toolkits for studying genome evolution in diverse contexts (Genomicus, Scorpios). The team was also highly successful in acquiring funding, especially with the now newly funded AtlaSea project, whose results will generate valuable resources for the entire research community.

With its international visibility and its international collaborations represents a highly successful and attractive team that should attract junior researchers, and students at all levels. Though the team leader chose to downsize the group in light of heavy administrative loads in the past in writing the Atlasea project. However, the team is projected to grow again with the acquired funding. The team has a very good size, with four permanent staff, three of which are involved in research and thus can help in supervising Postdocs, PHDs and Master students. Of note, the strategy to adjust the human resources to the work load of the PI is clearly explained and can be acknowledged as it defined the quality of mentoring and care towards people in the lab.

The team's members have also been well involved in teaching, and in interacting with society, for instance, as co-organisers of 'Nuit des Sciences et Lettres' or 'Les Origines' and other public events.

Needless to state that the administrative contributions of the team members, and especially the team leader, have helped shape the bioinformatics community at CNRS for the last years.

Weaknesses and risks linked to the context

As the team has currently only one PHD student, the presence of only one HDR does not provide a threat. With hiring more students, it is well appreciated that a second team member aims to defend the HDR this winter.

With the prospect of growing with the newly acquired funds, the limited space allocated to the team could hinder its growth and prosperity.

Analysis of the team's trajectory

The proposed project evolves around the Atlasea program, of which the team leader is one of the coordinators. It aims at cataloguing on a molecular level the breadth of eukaryotic species in the French economic zone and will lead to a greatly valuable resource for the entire research community. The Dyogen group will develop novel algorithms that can deal with the amount of data. Especially phylogenetic analysis is compute-intensive and novel algorithms will be developed to speed up this process. Furthermore, the team will be in charge of providing the wealth of data collected by the collaborating groups to the researchers, making it easily available, visually analysable and mineable. Several other projects are also proposed, centring on the evolution of CNEs, the development of deep learning approaches to comparative genomics, such as the very ambitious aim of being able to predict evolution, or to predict anatomical features based on genomic traits. While some of the projects are very ambitious, all of them will yield valuable and relevant information, as well as make available novel algorithms to the community.

RECOMMENDATIONS TO THE TEAM

We advise the team to continue its outstanding work in all areas and to fully exploit the new opportunities with the Atlasea project. We acknowledge the care taken to the human resources, to adapt the recruitment according to the workload of everyone, and possibly too to the gender balance.

Team 24: Visual Circuit Assembly
 Name of the supervisor: Mrs. Iris Salecker

THEMES OF THE TEAM

The team investigates cellular, genetic and molecular mechanisms of neural circuit assembly, using the development of the *Drosophila* visual system because of the unmatched opportunities it offers for genetic manipulation and visualisation of neurons and glia with single cell resolution. They research how neurons and glia organise giving rise to the highly complex layers and columns of the visual system neuropils, which enable retinotopy. The themes currently investigated are:

1. Layer formation of direction-selective neurons by segregation.
2. Role of neuron-glia interactions in astrocyte branch morphogenesis and circuit function
3. Role of glia in controlling layer refinement by developmental neurite remodelling.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was not considered in the previous evaluation as her group has only recently moved to Ibens. Her scientific career as a principal investigator was carried in the United Kingdom where she worked in London at the NIMR Mill Hill of the Medical Research Council UK and at The Francis Crick Institute.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

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

EVALUATION

Overall assessment of the team

The PI is an outstanding world expert in the development of the *Drosophila* visual system, analysing how genetic and molecular mechanisms drive neuronal target selection and connectivity to enable the retinotopic organisation of the visual system. The team joined Ibens in 2020 and has only had a short time to establish itself. As a result, the team currently includes only one postdoc and one PHD student. Before joining Ibens, the team produced important findings at The Crick Institute, UK.

Strengths and possibilities linked to the context

How neural circuits are organised is one of the remaining complex issues to be solved in biology. Several international initiatives are currently being developed to address this question and this group is amongst those at the forefront.

The team investigates how neural circuits are established during development, using the visual system of the fruit-fly, *Drosophila*, as an in vivo context. This model organism allows sophisticated genetics to manipulate genes, label neurons and glia with single cell resolution and to directly observe the system as it develops, including in real time. The team is well known for their landmark contributions including: establishing the Flybow system for stochastic labelling of single neurons in the *Drosophila* brain in vivo; their discovery of genetic and molecular mechanisms that drive target selection and connectivity, to enable the retinotopic organisation of the visual system; discovery of neuron-glia interactions that are instructive to both neural circuit formation and glial morphogenesis; discovery of a novel mechanism of neurogenesis from neuro-epithelial cells into migratory progenitors. The current projects continue in this trajectory of outstanding science. They are currently unravelling: (1) a novel mechanism of sequential repressive interactions that enables axons to segregate to distinct target layers. (2) The mechanisms controlling astrocyte glia morphogenesis, their involvement in glial-glia and glia-neuronal communication and spatial arrangement in circuits. They have identified the involvement of the LRR transmembrane protein Lapsyn and gap-junction channels (called Innexins in *Drosophila*) in these processes. (3) Mechanisms of neurite remodelling during development and the role of glial cells in this process. For these new projects, the team will be using Ibens cutting-edge technologies, including adaptive lattice sheet microscopy (AO-LLSM), 2-photon calcium imaging, transcriptomics, and label-free mass spectrometry. Furthermore, to these aims, she has established high-profile collaborations, including with Academia Sinica, Taiwan and FU Berlin, Germany. The recent results of the team lay a very strong basis for future publications at Ibens.

Overall, this is excellent to outstanding research led by a scientist of high international reputation. Proof of her international attractiveness are: her regular invitations to speak at international conferences; collaborations with high-profile scientists; her involvement in evaluations (e.g. EMBO Global Investigator Network Committee, ATIP-Avenir interviewing committee, etc.), grant reviews, promotion panels, and editorial board roles. She is the recipient of prestigious awards (e.g. EMBO member) and consistently publishes in high-profile journals (e.g. Nature Communications, Nature Neuroscience, Neuron, etc.).

The PI has substantial commitments to lecturing and teaching administration at the ENS. The team is normally very active in outreach activities, including hosting school children/young people in the lab, collaborating with artists, creating films and delivering lectures for the public.

Weaknesses and risks linked to the context

The group has recently settled in Paris after years working in the United Kingdom. This has caused severe disruption in their research that will take some time to get over, as the PI not only has to set a new laboratory but also has to adapt to the specific ways in which research is financed in a new country.

The group uses *Drosophila*, a model that is not prevalent at Ibens. This implies that very basic tasks, like making fly food has to be done by the team members, as it is not a centralised service in the institute. This will detract time and resources from research.

Analysis of the team's trajectory

This is an outstanding team that addresses relevant questions of fundamental developmental neuroscience. Their discoveries will have an ultimate impact in understanding how the brain is structured and the impact of brain disease in brain function.

In the past, the team has sustained regular productivity in high-profile journals, invitations to speak at conferences and to evaluate the research of other teams internationally. The PI has carried out research in Germany, the United States, United Kingdom and France and is internationally recognised for her outstanding work, demonstrated by prestigious awards. Based on her current research aims, it can be anticipated that the team should maintain this productive, high-profile and internationally recognised trajectory also into the future.

The team has recently moved to Ibens from the Francis Crick Institute (London). The relocation caused disruptions to the momentum of the team, its size decreased and it is now in a regeneration phase. An expansion in the team's workforce and technical support will be critical for the sustained success of this team.

RECOMMENDATIONS TO THE TEAM

The team has recently been reduced in its workforce, as a result of her relocation from UK to France, combined with the global pandemic period. It will be important that she expands her team again, with new PHD students and postdocs, to regain the momentum that will enable them to continue to produce cutting-edge, high-profile research. In this context, a permanent researcher position for her team would be of considerable help.

It would be desirable to increase the *Drosophila* research mass by recruiting senior researchers to the team or to the unit. Furthermore, technical help such as from a permanent technician position in her team will be important in the long-term, e.g. to look after *Drosophila* stocks.

The committee was concerned that Ibens does not have a *Drosophila* facility and has not provided the team with technical support for making and disposing of fly-food. Having her team doing these tasks is very wasteful of talent and skills and detracts the team from doing their research. The institute could provide technical support for *Drosophila* as they do for other animal facilities. This could be in the form of shared animal-facility technical staff, as a few hours per week would suffice for making fly-food and to process fly waste. This could be done by technicians already post, e.g. working in the fish facility.

Team 25: Cilia biology and neurogenesis
 Name of the supervisor: Mrs. Nathalie Spassky

THEMES OF THE TEAM

The 'Cilia Biology and Neurogenesis' team is working on the cilia of multiciliated ependymal cells, whose beating is crucial for the circulation of cerebrospinal fluid in the cerebral ventricles. Defects in the formation or number of motile cilia are often associated with pathologies such as neurodevelopmental disorders. The overall aim of the team is to study cilia development using the mouse brain as a model system. More specifically, the group leader investigates how progenitors are specified in ependymal cells, the mechanisms by which cilia are formed and oriented in these cells and how ependymal cells contribute to ventricular morphogenesis and adult neurogenesis. Other staff scientist explores how these multiciliated cells escape the programme controlling the number of centrioles to amplify these organelles during their differentiation, and the second one is dissecting the cellular mechanisms involved in the differentiation and maintenance of ependymal cells.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations of the previous Hcéres evaluation were as follows

'A – Recommendations on scientific production and activities

Maintaining the remarkable productivity of this relatively large team might require efforts in the design of the research projects (see below).

B – Recommendations on the team's organisation and life

None.

C – Recommendations on scientific strategy and projects

The brief description of the future scientific programme suggests that a significant number of the future projects will use mostly descriptive approaches relying in particular on imaging experiments. Maintaining the productivity of the team and reaching its ambitious goal might require a broader range of experimental approaches than those described in the proposal.'

Clearly, the team has been able to maintain an exceptional scientific level thanks to a clear vision of the field and quality of the questions asked. The emergence of an interdisciplinary project linking nuclear mechanics and cell differentiation has been a response to the concern expressed in the previous report together with the emergence of multidisciplinary approaches in the team.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	6
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	5
Total personnels	11

EVALUATION

Overall assessment of the team

The scientific production of the team is outstanding with articles signed as lead author by the team's PIs in high-profile journals such as *Science* (2017), *Nature Communications* (2018), *Neuron* (2019), *Nature Cell Biology* (2019), *Cell Reports* (2022), *Nature Reviews Molecular & Cellular Biology* (2021). The team has outstanding attractiveness and visibility: it has been successful in grant applications (ERC consolidator grant, five ANR grants, équipe FRM, fellowships from charities and several other grants from local programs); its training activities is above the standard with six PHD students and 4 postdocs; members of the team contribute to several committees (ENS, Inserm, EMBO conferences) and have been invited to more than twenty conferences, including fourteen abroad.

Strengths and possibilities linked to the context

The team's scientific output is exceptional. It should be emphasised that the three senior researchers published work as lead author, reflecting a healthy collegial governance and emulation. Similarly, most past PHD students and postdocs have published their work as first authors. Some of the team's most outstanding findings includes: 1) primary cilia regulate both cortical neurogenesis and ventricle morphogenesis by acting as a brake on the mTORC1 pathway (Foerster et al. 2017, *Development*); 2) adult neural stem cells and multiciliated ependymal cells share a common lineage regulated by the Geminin family members (Ortiz Alvarez et al. 2019, *Neuron*); 3) the p53/p21 pathway for DNA damage response controls the development of multiciliated ependymal cells (Ortiz Alvarez et al. 2022, *Cell Reports*); 4) the mitotic oscillator drives motile ciliogenesis (Al Jord et al., *Science* 2017); 5) massive centriole production occurs in the absence of deuterosomes in multiciliated cells (Mercey et al, 2019, *Nature Cell Biology*); 6) cilia beating in ependymal cells induces the formation of an actin network that protects centrioles against shear stress (Mahuzier et al, 2018, *Nature Communications*).

The team has outstanding attractiveness and visibility. The group leader has been awarded one of the most prestigious international research grants (ERC consolidator grant, 2016–2022). She was awarded the 'Camille WORHINGER' prize of the FRM. In total the team collected five ANR grants (2 as coordinator, 3 as partner), an équipe FRM grant, several PHDs and postdoctoral fellowships from national charities such as La Ligue and ARC, and several grants from local programs such as the Labex IPGG. All the permanent researchers have been successful in grant applications. Training is also outstanding with six PHD students and four postdocs. Members of the team contribute to several committees (ENS executive board, Inserm CSS4, EMBO conferences). The three permanent researchers have been invited to more than twenty conferences, including fourteen abroad. Finally, the team as a strong contribution to teaching since one member is a part-time Professor of Biology at Ecole Polytechnique.

Weaknesses and risks linked to the context

This team has no weaknesses, but the lack of mention of nonacademic interaction and interaction with the public is regrettable.

Analysis of the team's trajectory

The main directions proposed to capitalise on the team's most important discoveries, such as the role of the DNA damage response in physiological development, the mechanisms behind the action of the mitotic oscillator in ependymal cell differentiation, the role of mTOR in the control of ependymal cell development. A collaborative and interdisciplinary axis aimed at understanding the role of mechanical forces applied to the nucleus in ependymal cell differentiation. The trajectory is therefore very promising and there is no doubt that the team will maintain the excellence of its scientific output.

RECOMMENDATIONS TO THE TEAM

The committee encourages this team to maintain the excellence of its research.

Team 26: Molecular Motors and Machines

Name of the supervisor: Mr Terence Strick

THEMES OF THE TEAM

The project of the team focuses on the mechanistic understanding of fundamental processes in DNA metabolism, including DNA transcription, replication and repair. By using different single molecule approaches and by developing new tools and methodologies, they characterise in detail a number of processes and pathways with important fundamental and technological impacts.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report made no particular recommendation.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	6
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	3
Total personnels	9

EVALUATION

Overall assessment of the team

The research performed by the group is excellent to outstanding with important contributions in different lines of research. The team is internationally recognised for its work on molecular motors and machines and several original research projects involve national and international experts. The visibility of the team is outstanding as assessed by the collaborations, publications, recruitment of PHD students and obtaining regular fundings. The outreach activity is excellent to outstanding with an important of the team in teaching and for the development of tools for innovation. The overall assessment of the team is excellent to outstanding.

Strengths and possibilities linked to the context

This is a well-established team composed of five permanent members (2 Professors, 1 CR CNRS and 2 assistant-professors), nine PHD students (5 defended), two postdocs and one engineer during the period.

The team is working on different aspects of DNA metabolism, in particular in processes involved in DNA repair, transcription and replication. By using a variety of single molecules approaches (DNA nanomanipulation and

single molecule fluorescence), by developing a new DNA-based DNA nano-sensor (called DNA forceps), the team is contributing new insights and paradigms into mechanistic processes of DNA metabolism.

The production of the team is excellent to outstanding over the last six years. The team has produced as PI more than ten papers in very good journals such as Nature Nanotechnology (2019), Nature Structural and Molecular Biology (2018), Nature Communications (2019), PNAS (3 papers in 2017, 2020 and 2021) and Nucleic Acids Research (4 papers in 2018, 2019, 2020 and 2021). They also contributed four reviews, two in the Journal of Molecular Biology (2018 and 2019), one in a book (RNA Polymerase as Molecular Motors, 2022) and one in Current Opinion of Chemical Biology (2019).

The team has an outstanding national and international visibility because of their seminal studies with original approaches to characterise various processes of DNA metabolism. The team is involved in fruitful collaborations with high-level partners from all over the world (in France or Bristol, UK, Sweden, Houston, USA, Rotterdam, Netherlands, Pennsylvania State University, USA. The PI has been editor of a special issue of Current Opinion of Chemical Biology and of one book (RNA polymerases as molecular motors). The work has been importantly funded by national and international agencies as principal investigator (1 ANR, 1 Ligue contre le Cancer, 1 Fondation Bettencourt-Schuller, 1 Inserm) or as partner (2 ANR, 1 FRM Alzheimer, 1 NIH, 1 MSCN). The PI received a coup d'élan from the Bettencourt-Schuller foundation. Members of the team participated to 19 international conferences.

The involvement of the team in innovation is excellent to outstanding as it has filled one patent and received two rounds of early-stage start-up funding. The involvement in teaching is remarkable with the PI being responsible for the Graduate program in Life Science of PSL University and giving or organising different courses at different levels for ENS students.

Weaknesses and risks linked to the context

Because of the original expertise of the team in a range of single molecules approaches, a number of collaborations have been established to apply those approaches to different biological questions. In several cases, the ability to carry out these studies depends on the availability of biological systems provided by the collaborating teams. The only project based on the laboratory's own expertise concerns the control of DNA topology in archaea. It might be safe for the laboratory to develop a few biological themes of its own. The establishment of new collaborations within Ibens could enable a detailed characterisation of processes studied within the unit.

Analysis of the team's trajectory

The trajectory of the team has not been very much described. The report of the team lists a number of projects (6) which are in the continuity of the actual studies and rely in most cases on external collaborations.

RECOMMENDATIONS TO THE TEAM

The team was very successful in implementing original methods to characterise various processes in DNA metabolism. In addition to these collaborative studies, the team may wish to invest autonomously, in the medium or long term, in the study of a particular biological process.

Team 27: Neural Circuit Dynamics & Behaviour
 Name of the supervisor: Mr German Sumbre

THEMES OF THE TEAM

The team investigates the dynamics of extensive brain circuits and their interplay with cognitive functions and behaviour. To achieve this, they employ zebrafish and *Astyanax mexicanus* larvae as experimental models and multidisciplinary approach, incorporating cutting-edge techniques, to monitor the dynamic activities of sizable neuronal networks, including the entire brain. Additionally, they utilise mathematical methodologies to analyse intricate, high-dimensional datasets. By merging diverse disciplines and utilising intact, behaving animal models, they gain insights into the foundational mechanisms of sensory perception, the functional significance of inherent brain dynamics, and the evolutionary aspects of sensory processing.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report recommended that focusing on the correlation between network activity and behaviour could enhance collaborations within the Team and Ibens, thus boosting overall productivity. The updated report emphasises central themes: sensory perception mechanisms, intrinsic brain dynamics, and sensory processing evolution. Recent investigations focused on spontaneous brain activity, revealing structured patterns vital for visual detection. Despite successfully establishing the network-activity-behaviour link, collaborative engagement within Ibens remains limited.

The team leader adeptly managed multiple students and projects, a consistent achievement. Hcéres proposed involving Master's students to support project aspects, resulting in the recruitment of an M2 and an L3 student. While the mention was made, its relevance might be limited as the team already comprises a substantial number of PHD students and postdocs.

The main concern was the mismatch between the presentation's impact on the committee and the outstanding data. An approach emphasising questions at the beginning was recommended. Written reports include an opening paragraph outlining lab goals and well-presented project questions. Manuscripts and oral presentation distinctly outline result significance and novelty, incorporating previous committee recommendations.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres 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 d'appui non permanents	3
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	5
Total personnels	11

EVALUATION

Overall assessment of the team

The team's performance, reputation, and appeal have been assessed as outstanding by the panel. Over the past five years, Team 27 displayed remarkable productivity with seven articles and three reviews published in prestigious journals (Neuron, Current Biology, Cell Reports...). Awarded an ERC consolidator grant in 2016 and subsequent HFSP and ANR grants, the team leader's prominence is reflected in numerous national and international meeting invitations. The training through research is exceptional.

Strengths and possibilities linked to the context

The team consistently demonstrates a strong track record in innovating in vivo experimental methodologies for investigating sensorimotor inquiries. Employing state-of-the-art techniques including spim, optogenetics, and big data analysis, the team engages in complex computational investigations within a biological and behavioural framework. Recent studies have uncovered patterned structures in spontaneous brain activity, forming pivotal networks for visual detection. The identification of criticality in whole-brain activity enhances brain function optimisation. The team's competence was further extended by their exploration of brain evolution through the study of *Astyanax* cave fish, revealing adaptations despite vision loss and offering insights into neural circuit evolution. Their adoption of cutting-edge techniques aligns their projects with a high-risk, high-reward profile. The lab's strategy is geared towards publishing fewer articles but with substantial impact, maintaining the tradition of PHD students as first authors.

The attractiveness of the team is exceptional. It hosted six PHD students and three postdocs (including 1 with an MSCA fellowship), most of them coming from abroad. It was awarded an ERC consolidator grant in 2016 and subsequently an HFSP and two ANR grants. The team leader's prominence is reflected in numerous national and international meeting invitations.

The team leader holds significant roles, including membership in the scientific committee of the Raices French-Argentine network since 2022. Furthermore, they are the founder and organiser of the French Neuroethology Club, affiliated with the French Society of Neuroscience and the International Neuroethology Society, signifying their growing involvement within the French scientific community. The team leader is also involved in several outreach activities.

Weaknesses and risks linked to the context

The extent of the team leader's involvement in prominent French committees such as Inserm, CNRS, and ANR has been minimal.

Analysis of the team's trajectory

The research group's trajectory is marked by a series of pioneering studies across three distinct projects. The first project focuses on investigating spontaneous brain activity, specifically studying the functional roles of neuronal assemblies within the optic tectum. In the second project, the team delves into the role of glial cells in brain computation. In their third project, the team collaborates with experts to explore brain evolution using the *Astyanax* cave fish model. The team remains dedicated to unravelling the complexities of brain phenomena across various dimensions. Their commitment to employing advanced methodologies and engaging in collaborative efforts underscores their mission to uncover ground-breaking insights into brain dynamics, glial cell involvement, and the evolutionary changes within neural circuits. In essence, their endeavours challenge traditional notions, fostering a deeper understanding of the intricate workings of the brain.

RECOMMENDATIONS TO THE TEAM

The team should pursue the different directions of research and maintain high level of research excellence,

Team 28: Experimental Evolutionary Genetics

Name of the supervisor: Mr Henrique Teotonio

THEMES OF THE TEAM

The team uses a combination of theoretical models, quantitative genetics and experimental evolution with the nematode *C. elegans* to explore various questions in evolutionary biology of broad interest, such as the evolution of epigenetic effects in variable environments, the evolution of reproductive systems, the evolution of genetic architecture for complex polygenic phenotypes.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

While the quality of the science produced was judged excellent in the previous report, it was recommended to increase the size of the team to have the workforce necessary to achieve its various goals. The absence of a PHD student in the team was also noted as a weakness. During the evaluated period, one of the postdoc in the team has obtained a tenured position at Inserm and as adjunct professor at ENS. There are now two researchers in the team. One visiting professor spent extended time in the team and contributed significantly to theory development in particular. A very good funding level has allowed to hire four postdocs and four engineers and assistant engineers to support the experimental work in the team. One PHD student has joined the team in 2019. The self-evaluation however still underlines the size of the team as being a limiting factor despite growth in the evaluated period.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
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	2
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	2
Total personnels	4

EVALUATION

Overall assessment of the team

The quality of the scientific production of the team is excellent to outstanding, testing theoretical predictions in dire need of experimental confirmation, but also developing impactful new theory on the evolution of epigenetic transmission, which could shed light on many different research programs at Ibens. The visibility of this research is excellent, with a very relevant network of national and international collaborations with key actors in evolutionary genetics, invitations to conferences, and roles of editor for reputed journals in the field. The team involvement in teaching is excellent to outstanding with significant teaching duties and responsibilities, as well as interesting outreach initiatives.

Strengths and possibilities linked to the context

The research developed by the team addresses very interesting questions in evolutionary biology with a strong level of generality. The combination of theoretical predictions and their tests with sophisticated experimental evolution using the fast cycling worm *C. elegans* is particularly powerful and has allowed a number of breakthroughs. The collection of recombinant *C. elegans* inbred lines (which is also used as a resource for other labs) is a strong asset for the quantitative genetics research in the team in particular. The team has contributed to the development of theory on the evolution of maternal and epigenetic effects, a field of research attracting a lot of interest in recent years and having quite flourished since then (their theory paper in 2017 belongs to the 25% most cited papers in evolutionary biology that year). More originally, their clever lab system has allowed them to test their theoretical predictions by letting epigenetic effects evolve in variable environments, which is a significant advance as such evolutionary theory is in need of validation. This new line of research for the team appears as very fruitful. The quantitative genetics/genomics work of the team on the genetic architecture of complex traits and the identification of QTLs for complex life history traits such as matricide has also attracted a lot of attention (two papers in 2021 and 2017 belong to the 15% most cited in the field of genetics of those years). The use of recombination modifiers in *C. elegans* also allows clever tests of theories about the evolution of sex that are in dire need of empirical validation, in collaboration with well-recognised experts in this field of research. Finally, the team has contributed to with their experimental system (but not led) a study testing predictions of the Red Queen Hypothesis about coevolution, which was the subject of much interest (the 2019 publication belongs to the 2% of the

most cited in ecology that year), again because experimental validations of these old theories are rare.

The attractiveness of the team is illustrated by several international and national collaborations with key experts in evolutionary biology and the frequent visit in the team of researchers and students who are trained on its unique experimental system. The team leader has also contributed to visible reviews, which establish *C. elegans* as a biological model for experimental evolution. The expertise of the team leader is sought by several Society journals of a very good reputation with a role of associate editor and guest editor (*Journal of Genetics, Evolution, Genetics*) and by diverse research funding agencies as a reviewer (ERC, ANR, NSF, DFG, etc). Recognition is also illustrated by invitation to two Jacques Monod conferences and to the Kavli Institute for Theoretical Physics.

Both the team leader and a team member are strongly involved in teaching at the ENS, they coordinate and lecture an important volume of courses at ENS and other Paris universities. An international course of high reputation on experimental evolution is jointly organised with the Vienna Graduate School of Population genetics. Four postdocs and one PHD student have been trained in the period. The postdocs have published between two and seven papers during the last years, both with the team leader and on their own projects. All publications are in excellent reputation journals and the team members are strong proponents of ethical publishing and open science (e.g. submitting their work to *PCI Evolutionary Biology*). The research has been very well funded over the past period (with the coordination of three ANR projects and the supervision of a Marie Curie Fellowship).

Weaknesses and risks linked to the context

The capacity of the team to attract PHD students remains lower than expected given the interest of the science conducted in the team, its level of funding, the proximity of ENS students with their own funding and the frequent contact with students through teaching. The team leader suffers from a lack of visibility due to his current position as assistant professor, which is unusual for group leaders at Ibens, and the near impossibility for ENS assistant professors to be promoted as full professors while staying at Ibens by the ENS rules. Both PIs have heavy teaching duties, which makes support to maintain their experimental projects particularly critical. The lack of permanent support staff for their complex experimental system is also a risk if funding becomes less successful and because of the need to train new staff regularly. Collaborations with other teams at Ibens are not well developed despite a lot of potential areas of common interest: e.g. common biological model with complementary approaches, epigenetics, evolution of multivariate phenotype, role of drift and selection in evolution. The sex ratio of the team is also very unbalanced with women only among the technical staff, and none cited among the collaborators.

Analysis of the team's trajectory

The research objectives for the next five years are very exciting follow-ups of the team current findings. In particular, better understanding theoretically the conditions under which epigenetic effects over multiple generations evolve seems really important to interpret the observations made by the team and other groups on various systems about such intriguing carry-overs. Conducting experimental evolution of matricide seems equally promising in shedding light on the ultimate determinant of this intriguing plastic life history trait, informing more generally on parent-offspring conflicts. The project on the evolution of aging in populations where sexual conflicts in hermaphrodites are manipulated also sounds very exciting and novel. The use of recombination modifiers and the analysis of patterns of evolution at the genomic level will also represent a major breakthrough. The experimental work on the evolution of genetic variances and covariances in multivariate phenotypes will

also be very valuable. However, the lack of already secured funding for these projects is worrying and should be a priority in the near future.

RECOMMENDATIONS TO THE TEAM

The team should continue their efforts to train more PHD students and co-supervision of students across teams at Ibens on topics of common interest could be a fruitful experience for everyone, fostering more integration. Efforts to balance the sex ratio in the team should also be pursued. The two worm teams at Ibens could benefit from shared facilities and support staff covering their basic need. The current status of the team leader is an anomaly with respect to his responsibilities, experience and overall scientific achievements, causing a lot of frustration, and a solution needs to be found to fix this situation.

Team 29: Computational Systems Biology

Name of the supervisor: Mr Denis Thieffry

THEMES OF THE TEAM

The team combines *in silico* approaches to model the behaviour of molecular regulatory networks. These bioinformatics approaches are largely based on experimental data exploitation. The first axis is to develop computational tools for the analysis of functional genomic data (ChIP-seq, transcriptome) to delineate cis-regulatory regions and their role in the control of gene expression. The second axis is computational methods for the joint analysis of large-scale functional genomic data (RNA-seq, ChIP-seq, ATAC-seq data) to decipher the molecular mechanisms driving specific biological states. Last, the third axis is to implement algorithms and software tools devoted to the dynamic modelling, the analysis and the simulation of large signalling/regulatory networks. Of note, the main research line is to apply these tools to decipher regulatory networks that control cell specification, differentiation and reprogramming, with a special focus on immune cells.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous committee acknowledged the synergistical partnership between the team leader and the permanent researchers, together with outstanding scientific outputs and an appealing international reputation. It underlined how the team could play a pivotal role in single-cell genomics data analysis and recommended having collaborations at Ibens and coaching/hosting bioinformatic researchers. Accordingly, during this period, the team embraced single cell genomics through collaborations and contributed to analysis of scRNA-seq and ATAC-seq data. They extended the software Eoulsan to robustly process scRNA-seq data, they benchmarked existing tools for the inference of gene networks from single-cell data, evidencing limitations. Appropriately, novel developments were engaged to overcome these limitations. The team has a pivotal place at Ibens, this trait should become even more critical, with the increasing demand for bioinformatics and single-cell genomics. Indeed, they publish PDC authors more than 30 papers in top tier journals. The PI was largely involved in teaching with a full-time professorship at ENS and the charge of a master in Life Science at PSL/ENS. Another scientist was also deeply involved in teaching at ENS and at the head of the sibi – Société Française de Bioinformatique – for two mandates. Last, the funding is impressive.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	5
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	7
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	5
Total personnels	12

EVALUATION

Overall assessment of the team

The team's performance is excellent and shows attractiveness and visibility with respect to publication record, teaching, funding acquisition. Of note, the collaborative network is impressive. Also, the team has been for years a pillar of bioinformatics at Ibens, despite having only few internal collaborations with Ibens biologists.

Strengths and possibilities linked to the context

The strengths of the team still align with the previous assessment that underlined a remarkable work synergy within the team as well as excellent scientific outputs (exemplified by numerous high rank publications), intensive international teaching, and an outstanding international reputation and visibility. Notably, during the evaluation period, they published as PDC authors more than 30 papers in top tier journals. Also, the Pi kept his full-time professorship and coordination of a master in Life Science at PSL/ENS. He co-organized advanced courses in countries such as Singapour, Mexico, Norway, Lebanon. The second staff scientist was also deeply involved in teaching at ENS and at the head of the SFBI – Société Française de BioInformatique – for two mandates. The funding is impressive, with the acquisition of six ANR and five ITMO Cancer grants. The team was very attractive to PHDs (8) and postdocs (5). The international visibility of the team is very strong as demonstrated by the role of D.Thieffry as an editorial board member of reputed journals (PLoS Comp Biol, NAR Genomics & Bioinf, BMC System Biol) or their participation to various international conferences. The team also had a significant activity in valorisation: it developed 3 software suites and obtained one contract with the biopharma Sanofi.

Weaknesses and risks linked to the context

No obvious weakness was apparent from the report. The closure of the team before the end of its term was seemingly due to departure of two female PIs, one, who went to another Ibens team; and one PI who went to Institut Pasteur with an ERC starting grant.

Analysis of the team's trajectory

There is no trajectory since the team was closed at the end of 2022.

RECOMMENDATIONS TO THE TEAM

Not applicable.

Team 30: Cell Biology of the Synapse
Name of the supervisor: Mr Antoine Triller

THEMES OF THE TEAM

The team aim to decipher how microglia, brain-resident immune cells, sense and regulate synaptic activity, especially inhibitory synapses, as crucial indicators of brain states. Their research explores non-neuronal contributions to brain function.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The committee recommended that the team continue their pursuit of ground-breaking research, emphasising the importance of publishing at the highest level. Additionally, they encouraged the team to persist in their unique and unconventional approach to addressing intriguing questions. The team's achievements encompass publishing nine articles in prestigious journals such as EMBOJ and interdisciplinary platforms like the Biophysical journal. Their prominence in the field is evident from the four reviews published in exceptional journals. The committee also proposed that the team leader leverage the newly available time, post directorial responsibilities, to engage more deeply with students and postdocs. The team has overseen the work of four postdocs and one PHD student. All of this information underscores their commitment to following the guidance of the prior committee's suggestions.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

The team has stopped its activity during the evaluation period. So, this item is no longer relevant.

EVALUATION

Overall assessment of the team

The achievements and international visibility of the team was outstanding. The quality of the scientific production was excellent publishing nine articles, one as senior author, and four reviews. The team leader's role as Secrétaire Perpétuel de l'Académie des Sciences since 2021 and involvement in esteemed panels reflected influence. The other research director, an École Normale Supérieure professor, contributed to MD-PHD leadership, ENS entrance exams, and prestigious lectures, highlighting exceptional training standards.

Strengths and possibilities linked to the context

Overall, the team's closure in 2020 did not hinder their impressive productivity and far-reaching contributions to the field. Their research, international collaborations, leadership roles, and commitment to training have left an indelible mark on the scientific community. Their dedication to scientific progress was evident. Recognition exceeded research, with an ERC Synergy grant in 2021 showcasing international collaboration. The team leader's role as Secrétaire Perpétuel de l'Académie des Sciences since 2021 and involvement in esteemed panels reflected influence.

One of the team's notable achievements was the discovery of a novel role of microglial TNF α in regulating cortical inhibitory synapses during sleep. This groundbreaking work highlighted the connection between TNF α production triggered by neuronal activity and synaptic GABAAR enhancement through CamKII phosphorylation. This intricate relationship between microglial plasticity and GABAAR enrichment had significant implications for slow waves and sleep-related memory consolidation. The team's research further elucidated the role of microglial TNF α in controlling inhibitory synaptic plasticity through CamKII phosphorylation, a process crucial for sleep-related kinases (MAPK, MARK), as well as synaptic proteins that play a pivotal role in sleep homeostasis.

Weaknesses and risks linked to the context

None

Analysis of the team's trajectory

In 2020, the team concluded its activities due to the retirement of its leader. Subsequently, all previous members transitioned to another team within the institute. The team leader has now achieved emeritus status, a well-deserved recognition.

RECOMMENDATIONS TO THE TEAM

Not applicable

CONDUCT OF THE INTERVIEWS

Dates

Start: 25 septembre 2023 à 8 h 30

End: 26 septembre 2023 à 17 h

Interview conducted: on-site or online

INTERVIEW SCHEDULE

Hcéres scientific advisor (CS): Ina Attrée, Yacine Graba

DAY 0, Sunday 24 September – arrival - 20:00 Dinner – Committee + Hcéres CS only

DAY 1, Monday 25 September

- 8:30 – 8:45** Preliminary meeting of the expert committee (closed hearing)
- 8:45 - 9:00** Presentation of the HCERES evaluation to the unit (SO)
- 9:00 - 10:00** Presentation of the research unit by the Director (40' +20' questions)
- 10:00-10:35** Platforms (30' +5')
- 10:35-10:45** **Break**
- 10:45-12:30** Parallel team presentations SC1 /SC2 :
 - 10:45-11:20 [Bowler](#) / [Léna-Popa](#)
 - 11:20-11:55 [Colot](#) / [Brunet](#)
 - 11:55-12:30 [Meyer](#) / [Spassky](#)
- 12:30-13:30** **Lunch**
- 13:30-15:50** Parallel team presentations SC1 / SC2:
 - 13:30-14:05 [Félix](#) / [Salecker](#)
 - 14:05-14:40 [Ferriere](#) / [Charrier](#)
 - 14:40-15:15 [Hyrien](#) / [Dieudonné](#)
 - 15:15-15:50 [Lambert](#) / [Garel](#)
- 15:50-16:15** **Break**
- 16:15 - 18:00** Parallel team presentations SC1/SC2: Teams 8-10
 - 16:15-16:50 [Le Hir](#) / [Barbour](#)
 - 16:50-17:25 [Lebreton](#) / [Morin](#)
 - 17:25-18:00 [Thieffry](#)
- 18:00-18:25** **Break**
- 18:25-19:00** closed door meeting for each subcommittee; debrief /day 1
- 19:30** **Dinner (Committee + Hcéres CS)**

DAY 2, Tuesday 26 September

8:30-10:50 Parallel team presentations **SC1 (+LeClainche)/SC2 (+Haberman)**: team 11-14

8:30- 9:05 **Genovesio / Bourdieu** Salle 324 / Salle Favard

9:05-9:40 **Morlon / Holcman** Salle 324 / Salle Favard

9:40-10:15 **Navarro / Sumbre** Salle 324 / Salle Favard

10:15-10:50 **Strick / Paoletti** Salle 324 / Salle Favard

10:50-11:15 Break

11:15-12:25: Team presentations **SC1**; **SC2: visit of the unit if possible**

11:15-11:50 **Roest-Crollius** Salle 324

11:50-12:25 **Teotonio** Salle 324

12:30-13:30 Lunch

13:30– 14:00 Meeting w/supervising bodies Salle 316

14:00-14h45 Meeting w/staff - Parallel meetings (3 subcommittees)

- Meeting with technical and administrative personnel (in French) Salle Favard

- Meeting with thesis students and post-docs Salle 316

- Meeting with researchers and professors Salle 324

14:45-15:15 Meeting with the head of the unit/deputy director Salle 316

15:15-16:00 closed door meeting for each subcommittee; debrief day 2 Salle 316 + salle 324

16:00-17:30 closed door meeting for the whole committee Salle 316

Nota: teams presentations - 15 min presentation + 10 min questions + 5 min with PI only + 5 min debriefing of the committee (35' all inclusive)

GENERAL OBSERVATIONS OF THE SUPERVISORS

Arnaud TOURIN

Vice president for research and outreach

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Director
Research Evaluation Department
HCÉRES

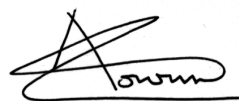
Paris, December 20, 2023

Référence : DER-PUR250024125 - IBENS - Institut de biologie de l'école Normale Supérieure.

Dear Director,

The supervising bodies of the IBENS unit warmly thank all the Committee's experts for their evaluation work. They have no comments to make on their report.

Yours sincerely.



Arnaud Tourin

The Hcéres' evaluation reports are available online:
www.hceres.fr

Evaluation of Universities and Schools
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