Institut de biologie systémique et synthétique

Rapport Hcéres

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

Section des Unités de recherché

Evaluation Report

Research unit :

Institut de Biologie Systémique et Synthétique (ISSB)

University Evry Val d'Essonne

April 2009

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Section des Unités de recherche

Evaluation Report

Research unit :

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University Evry Val d'Essonne

Le Président de l'AERES	Section des unités de recherche
	Le Directeur
Jean-François Dhainaut	**Pierre Glorieux**

April 2009

Evaluation Report

The research unit :

Name of the research unit : Institut de Biologie Systémique et Synthétique (iSSB)

Requested label : UMR

N° in case of renewal :

Head of the research unit : Mr Francois KÉPÈS

University or school :

University Evry Val d'Essonne

Other institutions and research organization:

CNRS

GIP Génopole

Date(s) of the visit :

15 April 2009

Members of the visiting committee

Chairman of the commitee :

Mr Vítor MARTINS DOS SANTOS (Helmholtz Center for Infection Research, Germany)

Other committee members :

Mr Stefan WIEMANN (DKFZ, University Heidelberg, Germany)

Mr Sven PANKE (Swiss Federal Institute of Technology Zurich)

Mrs Elisabeth PECOU (University of Nice-Sophia Antipolis)

Mrs Isabelle VERSTRAETE (University of Paris 7)

CNU, CoNRS, CSS INSERM, représentant INRA, INRIA, IRD.....) representatives :

Mr Thierry GRANGE (CoNRS section 22)

Mrs Isabelle VERSTRAETE (CNU Section 65)

Observers

AERES scientific representative:

Mr Jacques BARATTI

University or school representative:

Mrs Jeannine TORTAJADA VP CS (University Evry Val d'Essone)

Research organization representative (s) :

Mr Gilbert DELEAGE (CNRS)

Mrs Françoise RUSSO-MARIE (Génopole)

Evaluation report

1 • Short presentation of the research unit

The unit (except two teams) is located in Evry on the Genopole building and will migrate to the new Biology building in construction. It is made up of four academic teams and one industrial team. The total number of members is 22 with 17 researchers and 5 technicians:

- 4 Université staff: 1 professor and 3 "maîtres de conférences"
- 4 CNRS researchers
- 6 from the US company Sandia
- 3 others: CNRS postdoc, Genopole, Egide
- 5 technicians
- 5 Ph students

Among them 4 HDR and 0 PEDR and 17 are publishing researchers.

2 • Preparation and execution of the visit

All the documentation relevant for the assessment and visit was sent in advance per e-mail to all commission members, who have then read and prepared the assessment visit. The documents sent were reasonably clear and informative on the past activities, achievements and planned research by each individual team, except in the case of team 4 : "Reprogrammation génomique des bactéries par traslittération d'analogues nucléïques", the description of which and of its embedding within the unit was found to be insufficient. The organisation structure, recruitment and dissemination policies, allocation of resources and valorisation strategies were described appropriately.

The visit took place at the headquarters of the Genopole on April 15th according to the schedule provided below. The AERES official thoroughly briefed the committee members on the assessment process, criteria to be applied and the visit itself.

The oral presentation by the director-to-be well described the organisational and research strategies of the unit. However, the long-term vision, scientific goals and anticipated "edge" of such a unit were not made entirely clear.

The presentations by the individual members were generally clear and representative of the running and planned activities. However, the research plan presented by team 4 (by a representative of its group leader) was unclear and not distinguishable from ongoing work at the company. Furthermore, the presentation did not make sufficiently clear the connections and synergies with the remaining projects.

The envisaged synergies and cooperations among the various teams are recognised as potential value, albeit not entirely convincingly depicted in the presentations.

In addition to the presentations by the director-to-be and the individual group leaders, the visiting committee met with representatives of the institutions involved as well as (separately) with the researchers, students and technical staff involved.

Program of the visiting committee

Date of the visit : Wednesday April 15, 2009
Site for the visit : Genopole® Headquarters,
91030 EVRY cedex

7 h 45 : Welcome to the committee

1. Centering of the committee

8 h 00 - 9 h 00: Preliminary meeting of the committee (closed hearing)
Attending: Committee members, AERES scientific delegate

2. Scientific part

9 h 00 – 9 h 05 : Introduction of the committee members (AERES scientific delegate)
9 h 05 – 10 h 00 : (30 min presentation + 25 min discussion with the committee)

Presentation of the unit project by the head of the unit
Attending: Committee members, AERES scientific delegate, representatives of institutions, unit members

10 h 00 – 11 h 00 : (by team: 15 min presentation + 15 min discussion with the committee).
Presentation of the project of team 1-2:
10 h 00 – 10 h 30 : Presentation of the project of team 5 (by the group leader)
10 h 30 – 11 h 00 : Presentation of the project of team 3 (by the group leader)
Attending: Committee members, AERES scientific delegate, representatives of Institutions, unit members

11 h 00 – 11 h 15 : break

11 h 15 – 12 H 45 : (by team: 15 min presentation + 15 min discussion with the committee).
Presentation of the project of teams 2-5:

11 h 15 – 11 h 45 : Presentation of the project of team 2 (by the group leader)
11 h 45 – 12 h 15 : Presentation of the project of team 1 (by the group leader)
12 h 15 – 12 h 15 : Presentation of the project of team 4 (by the group leader)

Attending: Committee members, AERES scientific delegate, representative of institutions, IFR members

12 h 45 - 13 h 45: Lunch

3. Meeting with representatives of Institutions

13 h 45 – 14 h 15 : (30 min discussion with committee members)
Meeting with representatives of the Institutions
Attending : Committee members, AERES scientific delegate, representative of institutions,

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

14 h 15 – 14 h 45: *in parallel the committee splits into three groups.*
Meeting with researchers
Meeting with technicians
Meeting doctoral students and post doctoral fellows
Attending: Committee members, AERES scientific delegate, without the representative of institution, without the direction of the unit and without team leaders

5. Meeting with the unit Director

14 h 45 – 15 h 15: (30 min discussion with the committee)
Attending: Committee members, AERES scientific delegate, Unit Director

15 h 15 – 15 h 30 : Break

6. Debriefing of the committee

15 h 30 - 17 h 00 : (90 min)

Deliberation of the committee (closed hearing)
Attending : Committee members, AERES scientific delegate

17 h 00 : Thanks and leave of the committee

3 • Overall appreciation of the activity of the research unit, of its links with local, national and international partners

Four Academic groups and one industrial "reverse spin-off" group aim to bundle their activities in the fields of Systems and Synthetic Biology and address scientific questions broadly related to a) epigenetics and cellular differentiation; b) evolution and generation of regulatory networks and, c) development and optimisation of bio-inspired algorithms. To this end and to foster synergies, the group presented a plan for creation of a formal Research Unit at the Génopole. Since the unit as such does not exist at the moment, the appreciation on activities, links with local, national and international members will be done for the individual members as per point 4.

In general, however, the members as a whole have been carrying out relevant research activities and made valuable contributions to their fields of activities. The unit-to-be has achieved some notoriety at national and international level in specific areas and is reasonably well connected with local institutions, namely the Génopole and the University Evry Val d'Essonne. The teams are intensively involved in teaching and training for and by research. The relationships with socio-economics partners show a good potential for valorisation of research results. The committee recognises and considerably values the significant scientific, technological and training potential of the unit.

4 • Specific appreciation team by team and/or project by project

Team 1 : Génie métabolique pour la bioproduction

Its team leader has been doing very good work in areas of scientific relevance. He has been productive in both high impact publishing and in acquisition of projects. He has shown originality, independence, some degree of risk taking and eagerness to innovate. The committee recognizes the potential of the team leader to conduct and to also lead research in the proposed areas. Stronger intertwining with experimental lab work would be warranted. The committee also felt that the goals mentioned were somewhat timid.

Nom de l'équipe : Génie métabolique pour la bioproduction

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

Team 2 : Groupe de biologie synthétique

The panel recognises the strong engagement of the team leader in the field of Synthetic Biology and in the development and deployment of computational tools relevant for research in the area. The team leader has been productive and published abundantly in the last few years. The committee appreciates the creativity, energy and originality, as well as the diversity of methods and variety of ideas generated. However, the panel also has concerns with regard to dispersion and, possibly, superficiality (also in the modelling activities) that can derive from this diversity. As this may undermine potential future achievements, the panel would recommend to give more priorities and to focus the research activities around selected poles.

Nom de l'équipe : Groupe de biologie synthétique

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

Team 3 : Modélisation et ingénierie de l'architecture génomique

The committee acknowledges the networking and animation efforts of the project leader in the Systems Biology community, namely on the setting-up and conducting of the Epigenomics project and associated activities, but also the strong involvement in the setting-up of a European MSc program in Synthetic Biology. The panel also recognizes the vision and efforts towards technological implementation and valorisation. The team leader has made relevant contributions to the field and has published a number of good publications in the assessment period. However, the panel finds that the track record is not as strong as desired at this career stage and that there is some degree of stagnation of ideas and concepts. A clear, mid- to long-term vision of cutting-edge research goals for a research in this career stage was not sufficiently evident from the presentations and discussions. Furthermore, the management concepts and implementation are not found to be sufficiently solid. This is reflected as well (but not only) on the failure to secure the strong, specific and integrated commitment from all team members, namely, team 4.

Nom de l'équipe : Modélisation et ingénierie de l'architecture génomique

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

Team 4 : Reprogrammation génomique des bactéries par traslittération d'analogues nucléïques

The panel praised the originality, depth and scientific standing of the project leader-to-be, who has made several significant contributions to the field and has shown remarkable risk-taking and ground-breaking features. The contribution to valorisation as well as obvious strong relationships with socio-economic agents is strongly valued. However, although the panel appreciates the potential of the team to development and consolidation of the unit-to-be, the specific envisaged contributions to the unit and the interactions with the other potential members were starkly unclear from both the documents presented and the oral presentation. This raised serious concerns on the real commitment by the team to the unit and, consequently, of the added-value to it.

Nom de l'équipe : Reprogrammation génomique des bactéries par traslittération d'analogues nucléïques

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

Team 5 : Metamorphosis

The team leader has an outstanding track record, has shown strong leadership and notoriety in his field. The decision to undertake research activities outside his comfort zone (development) reflects risk-taking capabilities. The panel was however concerned, as yet, on how specifically the team would interact with the remaining partners, which could both undermine his own potential (given his step outside his expertise) and that of the unit (precisely due to possible lack of synergies).

Nom de l'équipe : Metamorphosis

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

5 • Appreciation of resources and of the life of the research unit

As the unit is formally not in place and three of the teams are recent creations, an accurate assessment is as yet not possible. However, the analysis of the documents presented and the various discussions held show that the basic management issues are tackled satisfactorily. The staff supports the laboratory strategy and common services are provided. Several staff members, however, have pointed out weaknesses with the Information Infrastucture (IT) and systems infrastructure availability. Both PhD students and postdoctoral researchers expressed satisfaction with the organization and mentoring, several specifically mentioned the value of the existing interdisciplinarity and collaboration possibilities and were generally satisfied with their integration in the different teams and interactions. There are ample training possibilities in place. Researchers (staff PhDs and postdocs) have all praised the Epigenomics activities as an instrument enabling networking and training. Outreach activities include, among others, the publication of books, press articles and in other media.

6 • Recommendations and advice

— Strong points :

The panel clearly sees the potential of the unit-to-be in this emerging and highly interdisciplinary field. The academic teams are motivated and, as 3 of them have been set up recently, there is a good opportunity for a flexible shaping of a common vision and concept. The teams are reasonably well positioned in the field of Systems and Synthetic Biology and have so far produced good science. Several teams are well connected internationally, which should facilitate the seeding and consolidation of the unit. The various related institutions (CNRS, Genopole, university) have shown commitment in terms of mission, resources and even novel recruits (specifically, the University to support and consolidate team 1 : "Génie métabolique pour la bioproduction".

— Weak points :

Major weaknesses are the lack of clear and innovative vision running throughout the unit as well as the lack of a common theme that would enable synergies to focus on and integrate the diverse expertises having been assembled. The proposed director has not shown sufficient leadership and the scientific drive to successfully develop the unit and make it a national or "flagship" in the field with the potential to become an internationally recognized signature activity of French science. There are communication gaps between the teams and collaborations appear thus far a little artificial. The expertise is limited in some areas and there is not yet enough (true) interdisciplinarity. As an example, the vision around the "high-throughput cloning facility" seems to be not adequately developed, even though it seems to play a major role in some of the experimental plans. In addition, given the limited resources that will be imparted to the different research groups and the resulting focus on shared resources, it is not entirely clear how the unit will deal with the presence of various model organisms. Furthermore, there seems to be a very broad conceptual area covered from system-wide data gathering to system synthesis, which might not be quite adequately covered by a nucleus of only 5 teams.

— Recommendations :

More true interdisciplinarity and interaction is warranted, and additional international recruitments are strongly advised both on the computational/mathematical and experimental sides. A common, strong vision is an absolute requirement. Leadership should be improved/strengthened.

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

Université d'Evry-Val-d'Essonne
Cabinet de la Présidence
Affaire suivie par :
Emery Olivier
Téléphone :
01.69.47.80.46

Evry, le 21 juillet 2009

Le Président de l'Université

à

Monsieur Jean-François DHAINAUT
Directeur de l'AERES

Objet : Rapport d'Evaluation du projet « Institut de Biologie Systémique et Synthétique, ISSB » – S2100015511

Monsieur le Directeur,

Le rapport d'évaluation du projet de création d'une unité mixte CNRS-UEVE intitulé « Institut de Biologie Systémique et Synthétique », (ISSB) que vous m'avez transmis, a été adressé à François KEPES porteur de ce projet et directeur pressenti de cette unité. Vous trouverez ci-joint, en réponse à ce rapport ses remarques et commentaires.

Pour ma part, je souhaite m'associer à ses remerciements pour la qualité de cette expertise, qui sur la base d'une analyse détaillée et pertinente des activités de recherche des différentes équipes, souligne pour chacune d'elle, leur potentiel de recherche et leur positionnement au plan national et international dans un domaine en émergence et de surcroît hautement pluridisciplinaire.

Le comité tout en relevant la qualité, l'originalité et la prise de risques des projets de recherche affichés, pointe sur un déficit de synergie entre les différentes équipes. Le regroupement de toutes ces compétences au sein d'une même unité est la solution qui pourrait à terme conduire à l'émergence de projets partagés non seulement au sein de l'unité mais aussi avec les acteurs du campus évryen.

La biologie systémique et synthétique est en effet un thème prioritaire du projet de Recherche/Formation que l'Université d'Evry affiche dans son prochain contrat quadriennal. Ce domaine de recherche structurera à l'orée 2011, au sein du futur « Institut de Biologie », une grande part des activités de recherche des laboratoires du pôle « Génome, post-génome : applications à la santé et à l'environnement », axe central et fédérateur de l'Université (soutenu par les tutelles, CNRS, INSERM, CEA, INRA et le GIP Genopole) qui regroupe des biologistes, des biostatisticiens, des bioinformaticiens, des biochimistes et des biophysiciens.

La reconnaissance d'une unité de recherche dans ce domaine est un acte majeur dans notre politique scientifique. Aussi, je prends note des recommandations émises par le comité d'experts concernant notamment le choix du futur directeur de cette unité. L'Université souhaite vivement avec l'aide et l'appui du CNRS accompagner au mieux la création de cette unité et s'efforcera de trouver la solution la mieux appropriée en ce qui concerne sa direction.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de mes salutations distinguées.

Le Président de l'université
d'Evry-Val-d'Essonne

Richard MESSINA

Research unit: Institut de Biologie Systémique et Synthétique (iSSB)

OBSERVATIONS BY THE PROPOSED DIRECTOR

July 8th, 2009

We wish to thank the AERES Committee for useful comments and recommendations. We note with satisfaction that point « 3 Overall appreciation » is only positive and recognizes the iSSB unit notoriety at international level in specific areas.

However, some criticisms appear in the detailed evaluation. We take good note of them, and we further provide a few observations below.

1- It is noted in the strong points that, « *as 3 academic teams have been set up recently, there is a good opportunity for a flexible shaping of a common vision and concept.* » All the more so, we would like to interject, that the unit is built around recent or emergent scientific domains where flexibility is essential for proper exploration and rapid adaptation. We certainly mean to seize this good opportunity by a) strongly emphasizing the use of traditional instruments of laboratory animation, and in addition one-week think tanks as already experienced at the Epigenomics Project, and b) by systematically favoring transversal cooperation at scientific and methodological levels. Based on past experiences, we trust that common themes will emerge as the unit is created and matures, and the chance of success of this happening is increased by the multidisciplinary nature of the teams.

2- We share with the Committee the vision to develop the unit into *an internationally recognized signature activity of French science.* However, before being developed, it must be created and receive means, and the existing core teams must learn to work together even more closely towards a strong structuration. This is currently our major focus. Besides, a variety of concrete signs, including the rapid convergence of the first three academic teams from abroad, make us extremely confident in the attractivity of the proposed unit.

3- As for the « *flagship* » concept, we would like to factually recall that a coherent set of instruments is currently and successfully being assembled to cover research and development, education (Master 2 mSSB just graded A+ by AERES), technological platform in cooperation with small industries (recently ranked first in funding), research networking and scientific animation (Epigenomics Project), cooperation with major industries (starting BioIntelligence 43 M€ project), a new building (Genopole®), and a dialogue with the public, the institutions and the stakeholders. We note that the proposed director has simultaneously been proactive on all these frontlines. There are in these recent fields very few examples worldwide of unfolding a comparably coherent set of instruments, and there is obviously none in France. This should favor iSSB visibility.

4- The Committee found that « *there are communication gaps between the teams and collaborations appear thus far a little artificial.* » Let us consider the situation as of the Committee visit in April 2009, nine months before the eventual unit creation. Team 4 is not yet on-site, and academic teams 1, 2 and 5 joined very recently, the last one three months before). The prenatal existence of several formalized scientific cooperations among teams, some financed, could instead be welcome as auguring well of a strong cooperative drive that should facilitate the collective creation of a common, strong vision.

5- It is not clear how the proposed director, with a depicted deficit in leadership and vision, has been able: a) to start multidisciplinary reflections since 1997 on what became known later as Systems Biology, and based on these reflections to become one of the main leaders who gathered since 2000 many scientists in a network whose hub is the Epigenomics Project ; b) to be invited to numerous EC-funded brainstorming sessions to prospectively shape EC FP7; c) to motivate good teams for the iSSB unit project.

In the following, specific observations are provided for some teams.

6- Team 1 would like to thank the review panel for their constructive comments. As far as intertwining with experimental work is concerned, this team is already actively collaborating with team 5 for toxicity measurement (MIC assay) in *E. coli*. Additionally, experimental lab work, especially in regards to metabolic engineering, will start in the near future as this team leader is the recipient of an ANR « Chairs of Excellence » project, which provides funds to set up a molecular biology lab and recruit post-doctoral appointees and technicians.

Regarding the project's goals, team 1 admits these may appear a bit conservative, but as discussed in the impact section, the proposed work has the more ambitious endeavour of determining the fraction of the chemical space that is metabolically accessible. The current proposal is setting up a ground stage for this endeavour through translational research by adapting an approach developed in chemistry to metabolic engineering. Ultimately, team 1 proposes to probe how far can synthetic biology supplement and enhance synthetic chemistry, a challenge with tremendous industrial impacts.

7- Team 2 is involved in creating new computational methodologies in the emergent discipline of Synthetic Biology. This implies the development of novel methods through several scales, which led team 2 to an exploratory research track. To better optimise the efforts, and in agreement with the recommendations that future work should be more focused around selected poles, team 2 research is converging towards the single subject of the design and construction of macromolecular networks. The collaborations arising from the creation of the iSSB will allow team 2 to better shape this pole.

8- Team 3 has hugely invested in novel methodologies in 2006-2008 (bioinformatics detection of gene positional regularities, biophysical model of DNA-protein interactions). Team 3 acknowledges that this methodological investment has led to a transient decrease of its productivity of primary articles on its main project, without affecting the other productivity indices, as documented in « Bilan ». These two original methods are now proving very fruitful: new results were presented during the Committee visit, and a new wave of publications is ensuing. These results also open avenues to iSSB internal collaborations around new concepts of transcriptional regulation.

Besides, we wonder why the last two sentences, in a section devoted to team 3, are repeating a criticism addressed to the proposed director.