Bioémergences

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on the unit:

Multiscale Dynamics in Morphogenesis

BioEmergences

Under the supervision the following institution and research bodie:

Centre National de la Recherche Scientifique - CNRS

April 2014

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

Department for the evaluation of research units

On behalf of AERES, pursuant to the Decree of 3 november 2006[1]*,*

- Mr. Didier HOUSSIN, president
- Mr. Pierre GLAUDES, head of the evaluation of research units department

On behalf of the expert committee,

- Mr. Roeland MERKS, chair of the committee

[1] The AERES President "signs [...], the evaluation reports, [...] countersigned for each department by the director concerned" (Article 9, paragraph 3 of the Decree n ° 2006-1334 of 3 November 2006, as amended).

Evaluation report

This report is the resultof the evaluation by the experts committee, the composition of which is specified below.

The assessments contained herein are the expression of an independent and collegial deliberation of the committee.

Unit name:	Multiscale Dynamics in Morphogenesis
Unit acronym:	BioEmergences
Label requested:	URS
Present no.:	UPS 3674
Name of Director (2010-2014):	Ms Nadine PEYRIERAS
Name of Project Leader (2015-2019):	Ms Nadine PEYRIERAS

Expert committee members

Chair:	Mr Roeland MERKS, Centrum Wiskunde & Informatica, Netherlands
Experts:	Mr Tristan PIOLOT, Institut Curie, Paris (representative of the CoNRS)

Scientific delegate representing the AERES:

Mr Pierre COUBLE

Representative of the unit's supervising institutions and bodies:

Mr Daniel BOUJARD, CNRS

1 • Introduction

History and geographical location of the unit

The BioEmergences USR originated from the European project of the same name co-coordinated by a mathematician, and a developmental biologist (future director of the platform) from 2006-2009. The mathematician was at the time director of the CREA (Research Center in Applied Epistemology, UMR 7656 CNRS École Polytechnique). The BioEmergence future director was leading the Genetic Networks and cell morphodynamics team at the DEPSN (Development and Evolution of the Nervous System, UPS CNRS). The platform was labelled by the GIS IBISA in 2009 and created UPS 3674 by the CNRS in January 2014.

The current location of BioEmergences is in the Gif-sur-Yvette campus were it occupies 250 m^2 principally in the INAF building (wet lab, offices, systems, storage, servers) and secondarily in the IMAGIF building (storage, servers, clusters, and office and lab dedicated to the PharmaTox project). The strong connection between BioEmergence and the institute for Complex Systems has led to the creation of a space of 80-100 m^2 dedicated to BioEmergences in this institute. A strong collaboration between BioEmergences and Banyuls biology station should drive to some technological transfer to this station and will be therefore associated to BioEmergence dedicated space on this site.

Management team

BioEmergences will gather a team and a platform. They will be supervised by a director assisted by three PIs.

AERES nomenclature

Domaine principal:	SVE1_LS3 Biologie cellulaire, Biologie du développement animal
Domaines secondaires:	ST1 Mathématiques
	ST6 Sciences et technologies de l'information et de la communication

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent researchers from Institutions and similar positions	5	4
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	2	2
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	8	5
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**17**	**13**

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	6	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit*	3	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	5	5

2 • Overall assessment of the unit

The *BioEmergences* unit has been tremendously successful in visualizing, analysing and reconstructing the collective behaviour of individual cells in developing embryos, with the aim of getting more insight into the mechanisms of development. Focusing primarily on solving this biological question, the unit has brought together an thriving and enthusiastic, interdisciplinary team of biologists, physicists, computer scientists, mathematicians, and technicians. Over the years, the team has developed new imaging technology, new algorithms for identifying and tracking individual cells in large volumes of data, data presentation and visualization technology, data integration methodology and computational and mathematical modelling techniques. As a result, the work has led to a number of high-impact publications to present the technology (e.g. Science, 2010) and to contribute to solving biological questions (e.g. Development, 2013). The experts committee was particularly impressed by the width of technologies "spinning off" from one ambitious (yet feasible) goal of reconstructing embryonic development at cellular detail. Despite the much more modest size of the *BioEmergences* project, the structure is reminiscent of "big science" projects as e.g. in particle physics. The results and technologies have already positively impacted developmental biology, and will likely have a much wider impact on studies of multicellular systems involving large scale data analysis.

Strengths and opportunities related to the context

- innovative technology;

- whole pipeline – not only image acquisition, also data analysis, data structuring, modelling and simulation;

- strong biological collaborators with relevant questions-> impact on developmental biology;

- looking for additional applications (e.g. toxicology);

- many developmental biologists will be interested in collaborating with the team;

- setting the "standard" for data formats, etc. in the field.

Weaknesses and threats related to the context

- width of technologies may lead to lack of coherence, especially further from data;

- continuity: know-how may get lost if students graduate, postdocs move on, etc.;

- modelling and simulation, needed to interpret data ('reconstruction') move away from project;

- scientific and technological credits not always given to bioemergences by collaborators, not all output is visible.

Recommendations

- develop generic technologies, starting from specific, real-world questions – helps investigators further from data focus their efforts. specific technology can then be generalized;

- spread know-how over multiple persons in the team, create overlapping terms of positions such that one postdoc can train the next;

- reinvest in modelling & simulation efforts;

- in collaborative projects, to ensure that proper scientific and technological credits are given to the bioemergences project, state the expectations (re: co-authorships, author positions, etc.) to collaborators formally and in advance. More prominent authorships (e.g., shared senior author) may be appropriate in cases where new scientific results are due to a large extent to results from the BioEmergences project.

3 • Detailed assessments

Assessment of scientific quality and outputs

The BioEmergences project analyses embryogenesis at single cell level using advanced microscopy, and uses this data to reconstruct it using computational modelling. The team's philosophy is that to build accurate explanatory models of biological development, we cannot rely on hypothetical models that will be overturned by data later on. It is much better to collect accurate data right from the start. The team applies a strict multiscale and cell-based philosophy: biological development is the result of cross-scale interactions, including the molecular, cellular, tissue levels, in which the cellular level is the central scale. To this end, the team has developed a series of imaging pipelines in which cell behaviour can be followed at individual cells and often subcellular resolution, generating datasets that contain the trajectories of cells over time, and more recently the cell membranes, cell shapes, and additional attributes of the cells. In this way the fate of cell clones can be followed in unprecedented detail, generating datasets that would hitherto require tagging of individual cells or cell clones in many individual embryos. The fact that such datasets can now be collected in individual embryos has the added advantage that now variations between individual specimens can be assessed.

The project has the potential of bringing the "data deluge" of biology to a next scale, that of individual cells and tissues, in interaction with gene expression. This is a key step with that may change the main approaches in biology and bioinformatics, which is still overly focused on the molecular scale because of the easy availability of molecular data. The methods that are further developed and applied to generate and analyse this data, breach a wide range of scientific fields in biophysics, informatics, and the mathematical sciences. They range from optics and bio-sensor development, to image analysis and machine learning, to topology, stochastics, and cell-based modelling methodology.

The team has already contributed to new insights into a range of biological questions, both as proof of concept of the prototypes, and in their role as service provider. For example, the cell lineage reconstruction software Mov-IT was applied to the reconstruction the first 10 cell divisions (producing 2^10=1024 cells) of the early zebrafish embryo. These results showed a progressive loss of synchrony of the cell division cycles and a number of apparent division waves. Follow-up work is precisely characterizing the cell behaviour during gastrulation and has yielded a dynamic atlas of gene expression during zebrafish development (submitted). The framework has also played a key role in identifying a unique, specialized vertebrate progenitor population in the zebrafish peripheral midbrain. The output has been impressive so far: by contributing detailed lineage traces this work is yielding surprising new insights and unveiling causalities into basic questions of developmental questions.

This work has resulted in five publications in high-impact factor biological journals, including Nature, Science, and Development, and in eight publications in high-ranking computational and methodological journals, including Bioinformatics and IEEE Transactions in Image Processing. In addition the work has resulted in five papers in the top conference EMBC (Annual International Conference of the IEEE Engineering in Medicine and Biology Society), which is listed among the top conferences by Microsoft Academic Search (note that in computer science top conferences have status comparable to the top biological journals). Also the team has written six reviews and book chapters. In at least two of those contributions (including the one in Science) the team and PI were the leading authors.

Despite these top contributions, the experts committee understands that a challenge for the team is to not be perceived as a "mere technological contributor", but indeed as a key contributor to scientific results in which the BioEmergences members have played a driving, or even the main role. For example, middle co-authorships for mere "running" of datasets, whereas more prominent authorships would be appropriate if the data analysis plays a more steering, intellectual role in collaborative projects. Achieving this would defitely help the team to stabilize their scientific success and allows securing funding strongly needed to allows set-up maintenance, renew and recruitment.

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

The work of the team is resulting in interesting social, scientific and potential economic valorisation. Notable examples include:

- the use of serious gaming to correct and validate cell lineage trees, which is currently tested in an old people's home in Aveyron, France;

- application of the research strategies to drug discovery and toxicology (REACH);

- contributions to the construction and roll-out of the UNESCO UNITWIN Complex Systems Digital Campus;

- dissemination and sharing of automated cell-lineage reconstruction pipelines as a service provider.

Assessment of the unit's organisation and life:

The experts committee appreciated the very positive comments and opinions of researchers, PhD students, postdoctoral fellows, engineers, collaborators from different laboratories on the site (and from collaborators coming from European countries who were present), about the governance and atmosphere at BioEmergences. A scientific life well organized with weekly seminars and specific discussions within working groups and strong interactions between the personnel keeps a spirit of BioEmergence membership.

The surface allocated to BioEmergences is at present a little constrained, but it is expected that the unit finds new premises on the Gif-sur-Yvette campus in the coming years.

Assessment of the unit's involvement in training through research

The team has trained 7 PhD students and many postdocs over the years, who have found excellent next positions, e.g., at Université de Versailles, and the Institut Curie.

Assessment of the strategy and the five-year plan

The BioEmergences project has gained significant momentum since its inception in 2006. It is currently gearing up for its consolidation into a service provider of established pipelines and a developer of new prototypes of microscopy pipelines, with many new opportunities. A range of collaborations have been set up, both nationally and internationally, and ranging from methodological collaborations (e.g. development of new cell tracking algorithms) to biological collaborations (application of the pipelines to biological problems, e.g. notochord formation). Also it is bringing the technology to additional institutes, e.g. the Laboratory Arago, Banyuls biology station. A number of new innovative microscopy technologies are being set up, e.g. multi-photon microscopy, single plane illumination microscopy, Digital Scanned Laser Light-sheet Microscopy, second harmonic generation microscopy, etc). Also, a large number of qualified scientific and technological personnel has been trained over the last years (see section personnel above).

In this light, in the opinion of the evaluators, a potential threat is that coherence and continuity of the project is lost during the coming years. Without long term job security and persistent assignment of personnel to the project, a major threat is that specialized know-how gets lost, for example where it concerns the persons in charge of image acquisition, new applications microscopy development and running microscopy pipelines. With respect to the cell-based modelling and simulation of collective cell behaviour, some personnel have recently moved on to new positions. As modelling and simulation technology are essential for 'closing the loop' from data collection to finding causative developmental mechanisms that are analysed in the project, it is recommended to either support new efforts on modelling and simulation, or refocus efforts on data collection and analysis.

In relation to this point, the experts committee notes the width of the five-year plan, from data collection and mathematical methods for image analysis and data integration, to building knowledge maps and topological inference schemes to analyse the data. Indeed it is important to develop of such tools and techniques in conjunction with the data collection, such that they the algorithms are well adapted to the collected data and vice versa. The evaluators encourage the team to ensure that these components of the project remain closely knit to the rest of the project.

4 • Conduct of the visit

Visit dates:

Start: Monday 14th April 2014 at 09:00 am

End: Monday 14th April 2014 at 03:00 pm

Visit site:

Institution: CNRS

Address: Bâtiment INAF - Avenue de la Terrasse

91190, Gif-sur-Yvette

Conduct or programme of visit:

Monday 14th April 2014

09:15 am – 09:30 am	Welcome to BioEmergences
09:30 am – 09:45 am	Closed-door meeting of the AERES experts committee
09:45 am – 10:00 am	Presentation of AERES evaluation by the Scientific Delegate
10:00 am – 11:00 am	Presentation of BioEmergences by the director and PIs
11:00 am – 11:30 am	Meeting with the personal
11:30 am – 12:00 am	Meeting with the CNRS representative
12:00 pm – 12:30 pm	Lab tour and visit of the platform
12:30 pm – 01:30 pm	Lunch
01:30 pm - 03:00 pm	Closed-door meeting of the experts committee
03:00 pm	End of the visit

5 • Supervising bodies general comments

Paris, le 15 MAI 2014

Note à l'attention du comité d'évaluation de l'AERES
UPS3674 Nadine Peyriéras

Référence S2PUR150008891-BioEmergences-0753639Y

Institut des sciences biologiques

www.cnrs.fr

Campus Gérard-Mégie
3 rue Michel-Ange Auteuil
75794 Paris cedex 16

T. 01 44 96 40 00
F. 01 44 96 53 90

Directrice adjointe administrative
Marie-Thérèse Dorin-Gérald

Objet : Vague E – Volet d'observations

Faisant suite à la visite du 14 avril 2014, le CNRS n'a aucune observation à apporter sur le rapport d'évaluation de l'UPS 3674 intitulée « BioEmergences » dirigée par Madame Nadine Peyriéras.

Catherine Jessus
Directrice de l'Institut des sciences biologiques