RESEARCH CENTER

FIELD
Digital Health, Biology and Earth

Activity Report 2015

Section Highlights of the Team

Edition: 2016-03-21

COMPUTATIONAL BIOLOGY

COMPUTATIONAL NEUROSCIENCE AND MEDECINE

EARTH, ENVIRONMENTAL AND ENERGY SCIENCES

MODELING AND CONTROL FOR LIFE SCIENCES

ABS Project-Team

4. Highlights of the Year

4.1. Highlights of the Year

In 2015, several achievements are worth noticing in three realms, namely in computer science, computational structural biology, and software.

4.1.1. Computer Science

► Beyond Two-sample-tests: Localizing Data Discrepancies in High-dimensional Spaces
Reference: [17]

In a nutshell: A classical problem in statistics is to decide whether two populations exhibit a statistically significant difference—the so-called two-sample test problem (TST). If so, another classical problem is to assess the magnitude of the difference—the so-called effect size calculation. While various effect size calculations were available for univariate data, hardly any existed for multivariate data.

Assessment: In this work, we provide one of the very first (if not the first) effect size calculation for multivariate data. The method combines techniques from machine learning (regression) and computational topology (topological persistence).

4.1.2. Computational Structural Biology

► High Resolution Crystal Structures Leverage Protein Binding Affinity Predictions
Reference: [20]

In a nutshell: The binding affinity of two proteins forming a complex is a key quantity, whose estimation from structural data has remained elusive, a difficulty owing to the variety of protein binding modes. In this work, we present sparse models using up to five variables describing enthalpic and entropic variations upon binding, and a (cross-validation based) model selection procedure identifying the best sparse models built from a subset of these variables.

Assessment: Our estimation method ranks amongst the top two or three known so far, and is possibly the most accurate when applied to high resolution crystal structures. One of its key limitations (similar to contenders) is that the crystal structures of the partners and that of the complex are required. This limitation motivates our work on energy landscapes, see below.

► Unveiling Contacts within Macro-molecular assemblies by solving Minimum Weight Connectivity Inference Problems
Reference: [14]

In a nutshell: Following the 2002 Nobel prize in chemistry of Fenn and Tanaka, and the recent developments led in particular by Carol Robinson (Oxford), native mass spectrometry is about to become a technique of major importance in structural biology, providing information on large assemblies (more than 10 subunits) studied in solution. One key question is to infer pairwise contacts between subunits from native mass spectrometry data.

Assessment: In this work, we provide a method to predict pairwise contacts between subunits of a large assembly, based on the composition of oligomers. The method is based on a mixed linear integer program, and essentially doubles the prediction performances of the method developed by Robinson et al.

► Hybridizing Rapidly Growing Random Trees and Basin Hopping Yields an Improved Exploration of Energy Landscapes
Reference: [22]

In a nutshell: Energy landscapes of biomolecular systems code their emergent thermodynamic and kinetic properties, so that their exploration is a question of paramount importance. This task requires in particular finding (metastable) states and their occupancy probabilities. Landscape exploration methods can be ascribed to two categories: continuous methods related to molecular dynamics, and discrete methods related to Monte Carlo sampling.

Assessment: In this work, we present a discrete sampling method combining features of robotics inspired methods (rapidly expanding random trees), and of biophysics inspired methods (basin hopping). Our hybrid algorithm outperforms contenders significantly. It is possibly one of the most efficient sampling method for energy landscapes known to date, but making such a statement will require testing thoroughly on a variety of systems. The method may strike a major impact if we manage to qualify the conformational ensembles generated from a thermodynamic standpoint.

► **Conformational Ensembles and Sampled Energy Landscapes: Analysis and Comparison**
Reference: [16]

In a nutshell: A paper presenting novel methods to analyze conformational ensembles and sampled energy landscapes, using techniques from optimal transportation theory and computational topology.

Assessment: The method proposed significantly enriches those classically used in biophysics, and triggered a collaboration with David Wales (Cambridge), one of the leading scientists on energy landscapes.

4.1.3. The Structural Bioinformatics Library

We released the Structural Bioinformatics Library, a library whose main features are detailed below.

AMIB Project-Team

4. Highlights of the Year

4.1. Highlights of the Year

4.1.1. Keynote addresses

Y. Ponty delivered one of the 8 plenary addresses at the 5th biennial Canadian Discrete and Algorithmic Mathematics Conference (CanaDAM) in University of Saskatchewan (Saskatoon, Canada). Held every two-years, with ∼300 participants and ∼150 contributed and invited talks, CanaDAM is the foremost event in Discrete Mathematics in Canada.

4.1.2. Awards

Alice Héliou received "Prix Poster École Doctorale Interfaces,Pôle : Science Du Vivant"

BEAGLE Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

We organized the first EvoEvo workshop (York, July 2015) as a satellite meeting of the 2015 ECAL conference (http://www.evoevo.eu).

5.1.1. Awards

Best paper award at the ACM Genetic and Evolutionary Computation Conference GECCO'15, in category Evolutionary Machine Learning, for the following paper: .
BEST PAPERS AWARDS :
[31] **Genetic and Evolutionary Computation Conference (GECCO)**. S. PEIGNIER, C. RIGOTTI, G. BESLON.

BIGS Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

The composition of the team was changed this year : Bruno Scherrer (Inria researcher) and Anne Gégout-Petit (Pr) joined the team (resp in January and in May). Samy Tindel moved to Purdue University as full Professor and Céline Lacaux has been promoted full Professor at Avignon University. Anne Gégout-Petit is temporary team leader since September.

BONSAI Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. MyNorine invents the crowd sourcing for Non Ribosomal Peptides

For ten years, the team has been developing a unique knowledge base, Norine, dedicated to the modeling and analysis of Nonribosomal peptides (NRPs). NRPs are secondary metabolites produced by bacteria and fungi that represent a huge source of natural products with applications in agricultural or health areas. In January 2015, we have released a new version which contains several major advances. MyNorine is a user-friendly service, that allows to submit new NRPs and to edit existing ones [2]. It was tested and validated by a panel of expert users during an international workshop that we organized in Lille in October, and that attracted 32 attendees from 8 countries. Moreover, s2m is an innovative tools to infer the monomeric structure of the peptides [1].

5.1.2. 1,000 white blood cell samples processed by Vidjil

Vidjil is an open-source platform for the analysis of high-throughput sequencing data from lymphocytes developed by the team. In October 2014, we opened a web server to grant everyone an access to Vidjil, our white blood cell analysis software used for leukemia diagnosis and follow-up. For one year, Vidjil analyzed more than 1,000 samples totalling 5 billion DNA sequences. Our users come from about thirty hospitals and labs throughout the world [3]. About fifteen of them regularly submit new samples. In Lille, the hematology department of the hospital uses Vidjil to identify malignant white blood cells at diagnosis on every patient with acute leukemia.

CAPSID Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

Large ANR Grant – Investissements d’Avenirs

Marie-Dominique Devignes and Malika Smaïl-Tabbone (Orpailleur Team) coordinated a work-package on network-based science for the project “FIGHT_HF” (Fight Heart Failure) that was submitted by Nancy University Hospital’s Federation “CARTAGE” (http://www.fhu-cartage.com/) to the ANR “Investissements d’Avenirs” programme. This project aims to discover novel mechanisms for heart failure and to propose decision support for precision medicine. The project has been granted € 9M.

Journal Front Cover

A figure from our article in the *Journal of Chemical Information and Modeling* [15] was used to illustrate the front cover of the August issue of the journal.

DYLISS Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

The main novelty in 2015 was the use of Semantic Web technologies to support the integration and query and investigation of large-scale heterogeneous databases. These technologies were applied in the framework of the MiRNAdapt project (funded by ANR) to design a tool for representing and querying bio-molecular information. The tool Askomics was designed in this perspective. In addition, Semantic Web technologies are currently combined with Formal Concept Analysis, to decipher the main regulators of complex systems, with application in cancer system biology (novel project funded by Plan Cancer).

ERABLE Project-Team (section vide)

GENSCALE Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

Special Issue

Publication of a special issue on Discrete Applied Mathematics. Guest Editors: A. Mucherino, R. de Freitas, C. Lavor [35]

Awards

For the third time in the last three editions of JOBIM (National workshop on Biology, Informatics and Mathematics), PhD students of the GenScale team won the best poster award:

- JOBIM 2015: Simka: fast kmer-based method for estimating the similarity between numerous metagenomic datasets [39] (https://hal.inria.fr/hal-01180603)
- JOBIM 2013 : MINIA on a Raspberry Pi, Assembling a 100 Mbp Genome on a Credit Card Sized Computer (https://hal.inria.fr/hal-00842027)
- JOBIM 2012 : Compareads: comparing huge metagenomic experiments (https://hal.inria.fr/hal-00760332)

In 2014, due to the ECCB conference in Strasbourg, France, there was no specific JOBIM event.

IBIS Project-Team

4. Highlights of the Year

4.1. Highlights of the Year

A paper based on the PhD thesis of Jérôme Izard and the post-doctoral work of Cindy Gomez Balderas was published in *Molecular Systems Biology* this year [18]. The paper describes foundational results for the RESET project (Section 8.2). A paper by Eugenio Cinquemani and colleagues from the LIFEWARE project-team and from the University of Pavia was accepted for *PLoS Computational Biology* this year [20], while a paper based on the PhD thesis of Valentin Zulkower was published in a special issue of *Bioinformatics* associated with the major bioinformatics conference ISMB/ECCB [24].

LIFEWARE Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

Four PhD Theses Defended this Year

Katherine Chiang defended her thesis [1] in three years at National Taiwan University and two internships with us in 2012 and 2013, on the computer-aided design of biomolecular systems, a subject co-supervised by Jie-Hong Jiang and François Fages which is of increasing importance in Lifeware and led to several publications this year [11], [6], [5].

Artemis Llamosi defended his thesis [3] in three years also, on the modeling of cell-to-cell variability, a subject co-supervised by Grégory Batt and Pascal Hersen, which led to a major publication in *PLoS Computational Biology* [8] to appear in 2016, and a cooperation with Marc Lavielle (EP POPIX).

Steven Gay finally defended his thesis [2] on subgraph epimorphisms and model reductions, a subject co-supervised by François Fages and Sylvain Soliman, 18 months after he leaved us for taking a Post Doc position at Univ. Louvain-la-Neuve, Belgium.

Thierry Martinez defended his thesis [4] supervised by François Fages, on a logical kernel for constraint programming, with direct impact on the design of the ClpZinc modeling language and the rewriting of Biocham v4, for which he got engineer positions n the last years.

In addition, François Bertaux has sent to reviewers his thesis on the modeling of cell-to-cell variability and cell apoptosis, co-supervised by Dirk Draso and Grégory Batt. Sylvain Soliman has sent to reviewers his *Habilitation à Diriger des Recherches* on the dynamics of biochemical systems. Pauline Traynard is also finishing her thesis co-supervised by François Fages and Denis Thieffry, on temporal logic patterns and solvers and the modeling of the interactions between the cell cycle and the circadian clock, for a defense in early 2016 in three years and half. Jean-Baptiste Lugagne is also expected to defend his thesis in 2016.

These theses are the foundations of some major themes of Lifeware for the next years.

MORPHEME Project-Team

4. Highlights of the Year

4.1. Highlights of the Year

Prizes and distinctions

L. Blanc-Féraud has been declared Knight of the Legion of Honor september the 25th.

Awards

T. Benseghir and G. Malandain have received a best paper award at the IPCAI conference.

X. Descombes has co-authored of a paper that received the best student paper award at the Workshop on Diff - CV.

BEST PAPERS AWARDS :

[3] **International Conference on Information Processing in Computer-Assisted Interventions, IPCAI 2015**. T. BENSEGHIR, G. MALANDAIN, R. VAILLANT.

[5] **1st iInternational Workshop on Diff - CV: Differential Geometry in Computer Vision for Analysis of Shapes, Images and Trajectories (in conjunction with BMVC)**. A. DUNCAN, E. KLASSEN, X. DESCOMBES, S. ANUJ.

PLEIADE Team (section vide)

SERPICO Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

Publication of overview papers

Publication of two tutorial-style overview papers:

- D. Fortun, P. Bouthemy, C. Kervrann. Optic flow modeling and computation: a survey, Computer Vision and Image Understanding, 134:1-21, 2015.
- C. Kervrann, C.O.S. Sorzano, S.T. Acton, J.-C. Olivo-Marin, M. Unser. A guided tour of selected image processing and analysis methods for fluorescence and electron microscopy, IEEE Journal of Signal Topics in Signal Processing (Special issue on Advanced Signal Processing in Microscopy and Cell Imaging, Lead Guest Editor: C. Kervrann), 10(1):1-25, 2016.

VIRTUAL PLANTS Project-Team

4. Highlights of the Year

4.1. Highlights of the Year

- *Statistical methods*: One of our main activities consists of identifying and characterizing developmental patterns in plant phenotyping data. Phenotyping data are very diverse ranging from the tissular to the whole plant scale but are often highly structured in space, time and scale. We intend to analyse such data using state-of-the-art methods at the crossroad between statistical modelling, machine learning and pattern recognition. This generates regularly new methodological results as illustrated this year by [17] and [22].
- *Scientific Workflows*: Analyzing biological data may involve very complex and interlinked steps where several tools are combined together. Scientific workflow systems have reached a level of maturity that makes them able to support the design and execution of such in-silico experiments, and thus making them increasingly popular in the bioinformatics community. However, in some emerging application domains such as system biology, developmental biology or ecology, the need for data analysis is combined with the need to model complex multi-scale biological systems, possibly involving multiple simulation steps. This requires the scientific workflow to deal with retroaction to understand and predict the relationships between structure and function of these complex systems. In collaboration with the Zenith EPI, we have proposed a conceptualisation of OpenAlea workflows [34] by introducing the concept of higher-order dataflows as a means to uniformly combine classical data analysis with modeling and simulation, in the context of plant phenotyping.
- *Mechanical model of meristem development*: The growth of plant tissues results from the growth of cells that are inflated by turgor pressure. In recent years, different bio-physical processes by which genes regulate locally the rate and the directions of cell growth have been identified. At tissue level, the growth of each region is mechanically constrained by the existence of neighboring regions. This creates stresses within the plant tissues, possibly with differential directional intensities, which in turn, can be sensed locally at the level of each individual cell by genes. Shapes thus results from the complex interplay between genes and growth, mediated by mechanics. In the recent years, we have been developing a model of growth of plant tissues that is able to represent this overall feedback mechanism [13]. This model is the first 3D approach of multicellular plant tissue development based on a tensorial representation of mechanical properties and stresses in cell walls. Its implementation relies on a coupling between OpenAlea and Sofa, two main sofware platforms for modeling in biology developed at Inria.

ARAMIS Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

- Stanley Durrleman has been awarded an ERC Starting Grant by the European Research Council
- The team has been awarded the H2020 project EuroPOND, under societal challenge "Personalizing Health and Care"
- The team has been awarded the ANR-NIH project NETBCI, under the "Collaborative Research in Computational Neuroscience" program (CRCNS)

ASCLEPIOS Project-Team

4. Highlights of the Year

4.1. Highlights of the Year

4.1.1. Awards

- Thomas Benseghir received a Best Paper Award at the 2015 IPCAI conference, Barcelona, Spain, for his paper entitled “A tree-topology preserving pairing for 3D/2D registration”, co-authored by Grégoire Malandain and Régis Vaillant.
- Matthieu Lê received a Young Scientist Award at the 2015 MICCAI conference, Munich, Germany, for his paper entitled “GPSSI: Gaussian Process for Sampling Segmentations of Images” , co-authored by Jan Unkelbach, Nicholas Ayache, and Hervé Delingette.
- Bjorn Menze received the Young Scientist Publication Impact Award at the 2015 MICCAI conference, Munich, Germany, for his article “A generative model for brain tumor segmentation in multimodal images”, co-authored by Koen Van Leemput, Danial Lashkari, Marc-André Weber, Nicholas Ayache and Polina Golland presented at MICCAI 2010 in Beijing, China [100].
- Marco Lorenzi received an honorary mention at the 2015 Cor Baayen Award for his PhD prepared jointly within the Asclepios project team at Inria Sophia Antipolis and the IRCCS San Giovanni di Dio Fatebenefratelli (Italy), and for his post-doctoral research performed at University College London (UCL).
- Hervé Delingette is the co-recipient of the Dirk Bartz First Prize for Visual Computing in Medicine awarded during the 2015 Eurographics conference. The prize was given to a group of 7 Inria researchers who pioneered the development of medical simulators based on the SOFA software platform.
- Nicholas Ayache received a research medal from the University Côte d’Azur on December 10th 2015.

BEST PAPERS AWARDS :

[26] **International Conference on Information Processing in Computer-Assisted Interventions, IPCAI 2015**. T. BENSEGHIR, G. MALANDAIN, R. VAILLANT.

[38] **MICCAI - Medical Image Computing and Computer Assisted Intervention - 2015**. M. LÊ, J. UNKELBACH, N. AYACHE, H. DELINGETTE.

ATHENA Project-Team (section vide)

DEMAR Project-Team (section vide)

GALEN Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Awards

- Pr. Iasonas Kokkinos was appointed associate editor for the Computer Vision and Image Understandin Journal.
- Pr. Pawan Kumar was appointed associate editor for the Computer Vision and Image Understandin Journal.
- Pr. Nikos Paragios was admitted as a senior fellow at the Insitut Universitaire de France in the section of Mathematics.

MIMESIS Team

4. Highlights of the Year

4.1. Highlights of the Year

4.1.1. Translational Simulation: from pre-operative to intra-operative simulation

In recent years, an active development of novel technologies dealing with medical training, planning and guidance has become an increasingly important area of interest in both research and health-care manufacturing. With a combination of advanced physical models, realistic human-computer interaction and growing computational power, the MIMESIS team aims at bringing new solutions in order to help both medical students and experts to achieve a higher degree of accuracy and reliability in surgical interventions [26].

4.1.1.1. Pre-operative planning

In the context of cryoablation, planning the outcome of the procedure is key to ensure an optimal ablation. Cryotherapy is a rapidly growing minimally invasive technique for the treatment of certain tumors. It consists in destroying cancer cells by extreme cold delivered at the tip of a needle-like probe. As the resulting iceball is often smaller than the targeted tumor, a key to the success of cryotherapy is the planning of the position and orientation of the multiple probes required to treat a tumor, while avoiding any damage to the surrounding tissues. In order to provide such a planning tool, a number of challenges need to be addressed such as fast and accurate computation of the freezing process or interactive positioning of the virtual cryoprobes in the pre-operative image volume. To address these challenges, we developed a thermal model using the finite-element method and implemented on GPU. Our thermal model was intensively validated and specific solvers were built. From these simulations, we developed a prototype for cryotherapy planning.

4.1.1.2. Towards intra-operative guidance

Not only does the simulation bring a pre-operative support to the radiologist, but computational models can also be used intra-operatively. During the minimally-invasive liver surgery, only the partial surface view of the liver is usually provided to the surgeon via the laparoscopic camera. Therefore, it is necessary to estimate the actual position of the internal structures such as tumors and vessels from the pre-operative images. Nevertheless, such task can be highly challenging since during the intervention, the abdominal organs undergo significant deformations due to the pneumoperitoneum, respiratory and cardiac motion and the interaction with the surgical tools. Therefore, a reliable automatic system for intra-operative guidance requires fast and reliable registration of the pre- and intra-operative data. This year, we presented a complete pipeline for the registration of pre-operative patient-specific image data to the sparse and incomplete intra-operative data [21]. While the intra-operative data is represented by a point cloud extracted from the stereo-endoscopic images, the pre-operative data is used to reconstruct a biomechanical model which is necessary for accurate estimation of the position of the internal structures, considering the actual deformations. This model takes into account the patient-specific liver anatomy composed of parenchyma, vascularization and capsule, and is enriched with anatomical boundary conditions transferred from an atlas. The registration process employs the iterative closest point technique together with a penalty-based method. Following this work, we performed a quantitative assessment based on the evaluation of the target registration error on synthetic data as well as a qualitative assessment on real patient data. We demonstrated that the proposed registration method provides good results in terms of both accuracy and robustness w. r. t. the quality of the intra-operative data

4.1.2. Eurographics Award

In recent years, an active development of novel technologies dealing with medical training, planning and guidance has become an increasingly important area of interest in both research and health-care manufacturing. A combination of advanced physical models, realistic human-computer interaction and growing computational power is bringing new solutions in order to help both medical students and experts to achieve a higher degree of accuracy and reliability in surgical interventions. In our work entitled "Surgery Training, Planning, and Guidance using the SOFA Framework" [26], we presented three different examples of medical physically-based simulations implemented in a common software platform called SOFA. Each example represented a different application: training for cardiac electrophysiology, pre-operative planning of cryosurgery and per-operative guidance for laparoscopy. This paper assessed the realism, accuracy and efficiency of the simulations, as well as the potential and flexibility of the SOFA platform.

EUROGRAPHICS MEDICAL PRIZE

Dirk Bartz Prize
for Visual Computing in Medicine 2015
1st Prize
Hugo Talbot
"Surgery Training, Planning and Guidance Using the SOFA Framework"

Eurographics Medical Pri
Dirk Bartz Prize
for Visual Computing in
Medicine 2015

1st Prize

Hugo Talbot
Nazim Haouchine
Igor Peterlik
Jeremie Dequidt
Christian Duriez
Herve Delingette
Stéphane Cotin

Surgery Training, Planning and Guidance Using

Figure 6. First Dirk Medical Prize at Eurographics 2015

This work has been awarded at the Eurographics conference in Zurich and won the **1st prize of the Dirk Bartz Medical Prize**.

4.1.3. SOFA Consortium

After ten years of development, a Consortium around the simulation platform SOFA was founded by Inria in November 2015. The MIMESIS team intensively participated in the creation of this Consortium. The objectives of this Consortium are to make the SOFA community grow and encourage contributions from new SOFA users. The Consortium should also be a way to better answer to the needs of academic or industrial partners.

A member of the MIMESIS team is now in charge of the coordination of this Consortium. A new engineer was also hired to manage the support on the SOFA forum, handle the SOFA events and communicate about SOFA Consortium. The activity of the SOFA Consortium is expected to significantly grow in the coming years.

4.1.4. Evaluation by IHU Strasbourg

Every year, research done at IHU is evaluated by a group of 15 international experts, scientists and clinicians. The 2015 report highlighted our work in the field of modeling and augmented reality: "Interestingly, besides its numerous applications for computer assisted surgery, it paves the way to build a new science of anatomy, with the establishment of innovative, "big data" based organ atlases. The program truly shows the most disruptive results. It is scientifically impressive and potentially very practical. There is no doubt that this is the domain where IHU is close to be the leading group. The program has a real strategy beyond distinct projects, and clear synergies have been identified." This report attests to our involvement within the IHU Strasbourg.

4.1.5. Science & You

Science & You is an international event about scientific mediation in the field of digital technologies. In 2015, Science & You took place in Nancy from the 1st until the 6th June 2015. Inria co-organized the event with

INS2I and SIF. At this occasion, the MIMESIS team presented the results and prototypes developed in the team. This event drew a crowd and was a real success.

MNEMOSYNE Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. ReScience journal

Nicolas Rougier has co-founded the ReScience journal (http://rescience.github.io/) with Konrad Hinsen and is one the Editor-in-chief. ReScience is a peer-reviewed journal that target computational research and encourage the explicit replication of already published research promoting new and open-source implementations in order to ensure the original research is replicable.

5.1.2. Most viewed and downloaded article

Our paper [4] is in the spotlight of the Frontiers blog (cf. http://blog.frontiersin.org/2015/12/22/spotlight100/): among the 100 articles the most viewed and downloaded among over 12,500 articles published by Frontiers in 2015.

5.1.3. Awards

Our paper was given the Best Paper Award at the 2015 International Conference on Neural Computation Theory and Applications, cf. http://www.ncta.ijcci.org/PreviousAwards.aspx
BEST PAPERS AWARDS :
[11] **International Joint Conference on Computational Intelligence**. R. KASSAB, F. ALEXANDRE.

NEUROMATHCOMP Project-Team

4. Highlights of the Year

4.1. Highlights of the Year

Awards

Olivier Faugeras received the Okawa Foundation Prize for "Pioneering contributions for computer vision and for computational neuroscience". The prize was awarded to him in Tokyo, Japan, in March 2015. He received the PAMI Azriel Rosenfeld Lifetime Achievement Award in December 2015 at the ICCV 2015 in Santiago, Chile. This award is given to researchers in Computer Vision who have made major contributions to the field over their career and who have influenced the field in an extraordinary way.

Habilitation à Diriger des Recherches (HDR) Mathieu Desroches has defended an habilitation thesis on the 11th December 2015 at the Université Pierre et Marie Curie - Paris 6. The title of his habilitation thesis is *Complex oscillations with multiple timescales - Application to neuronal dynamics* [15]. The reviewer of this HDR were: Eusebius J. Doedel (Concordia University, Canada), Christopher K. R. T. Jones (University of North Carolina at Chapel Hill, USA) and Daniel Panazzolo (Université de Haute-Alsace, France). The jury was formed by : Stephen Coombes (University of Nottingham, UK), Peter De Maesschalck (Hasselt University, Belgium), Olivier Faugeras (Inria Sophia Antipolis, France), Jean-Pierre Françoise (President of the Jury, Université Pierre et Marie Curie - Paris 6, France), Christopher K. R. T. Jones (University of North Carolina at Chapel Hill, USA) and Daniel Panazzolo (Université de Haute-Alsace, France).

NEUROSYS Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

- Laurent Bougrain co-organized an **international Brain-Computer Interfaces competition** on *Error Potential Detection with Cross-subject Generalization* with Maureen Clerc, Fabien Lotte, Emmanuel Maby, Jérémie Mattout and Théodore Papadopoulo. **311 participants of 260 different teams** in the world participated to the competition. Gao Shangkai and Bin He were in the advisory board. IEEE EMBS, Inria, and Institute for Engineering in Medicine at University of Minnesota were sponsors of this event. The prizes have been presented to winners during the IEEE EMBS Neural Engineering conference, April 22-24, 2015. The winner has been invited to publish a manuscript at IEEE Transactions on Biomedical Engineering.
  https://www.kaggle.com/c/inria-bci-challenge
- **We stepped up our collaboration with the department of anesthesia of the university hospital in Nancy** (Dr. Denis Schmartz and Pr. Claude Meistelmann) leading to a **PhD thesis co-funded** by the school of medicine of the university of Lorraine, Inria, the Lorraine laboratory for research in computer science (LORIA), the Lorraine Region and the urban community of Nancy. The PhD will start in January 2016 on the study of the dynamics of cerebral motor patterns during general anesthesia with Sébastien Rimbert under the supervision of Axel Hutt and Laurent Bougrain.

PARIETAL Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

Michael Eickenberg got an oral presentation at the OHBM 2015 conference(success rate $< 1\%$). Elvis Dohmatob got an oral presentation at the OHBM 2015 conference(success rate $< 1\%$).

POPIX Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Awards

Marc Lavielle received the 2015 ISoP (International Society of Pharmacometrics) Innovation award

Marc Lavielle received the 2015 Inria – French Académie des Sciences – Dassault Systèmes Innovation Award

SISTM Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Time-Course Gene Set Analysis for Longitudinal Gene Expression Data

A work in collaboration with J. Skinner has been published in *PLoS Computational Biology* : [10]

Gene set analysis methods, which consider predefined groups of genes in the analysis of genomic data, have been successfully applied for analyzing gene expression data in cross- sectional studies. The time-course gene set analysis (TcGSA) introduced here is an exten- sion of gene set analysis to longitudinal data. The proposed method relies on random effects modeling with maximum likelihood estimates. It allows to use all available repeated measurements while dealing with unbalanced data due to missing at random (MAR) mea- surements. TcGSA is a hypothesis driven method that identifies a priori defined gene sets with significant expression variations over time, taking into account the potential heteroge- neity of expression within gene sets. When biological conditions are compared, the method indicates if the time patterns of gene sets significantly differ according to these conditions. The interest of the method is illustrated by its application to two real life datasets: an HIV therapeutic vaccine trial (DALIA-1 trial), and data from a recent study on influenza and pneumococcal vaccines. In the DALIA-1 trial TcGSA revealed a significant change in gene expression over time within 69 gene sets during vaccination, while a standard univariate individual gene analysis corrected for multiple testing as well as a standard a Gene Set Enrichment Analysis (GSEA) for time series both failed to detect any significant pattern change over time. When applied to the second illustrative data set, TcGSA allowed the identification of 4 gene sets finally found to be linked with the influenza vaccine too although they were found to be associated to the pneumococcal vaccine only in previous analyses. In our simulation study TcGSA exhibits good statistical properties, and an increased power compared to other approaches for analyzing time-course expression patterns of gene sets. The method is made available for the community through an R package.

5.1.2. Two new books

DC is co-editor and RT is co-author of the two following books :

- Daniel Commenges and Héléne Jacqmin-Gadda (2015), Dynamical Biostatistical Models, Chapman & Hall.
- Daniel Commenges and Hélène Jacqmin-Gadda (2015), Modèles biostatistiques pour l'épidémiologie. De Boeck.

VISAGES Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Awards

- In 2015, the Neurinfo platform obtained the IBISA label. The IBISA label is a national label for technological platforms awarded by the GIS IBISA on an annual basis.
- In 2015, Edan G was elected Fellow of the European Academy of Neurologie.

AIRSEA Team

5. Highlights of the Year

5.1. Highlights of the Year

Early 2015 AIRSEA team succeed MOISE in developing of *mathematical and computational methods for the modeling of oceanic and atmospheric flows*.

The substantial changes compared to the scientific objectives of the MOISE team include a redefinition of the domains of applications now centered on oceanic and atmospheric modeling (the latter is a new target application for the team), the increased focus on statistical methods and hybrid deterministic/statistical approaches, as well as an emphasis on the development of numerical algorithms for high performance computing.

5.1.1. Awards

Clémentine Prieur was awarded by the Prix Blaise Pascal of GAMNI-SMAI.

Jose R. Leon was granted by an International Inria Chair.

ANGE Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

Contracts and cooperations

- ANR project Hyflo-Eflu accepted
- Industrial contract with SAUR/Agence de l'eau Loire-Bretagne concerning the Vilaine River
- IPL Algae In Silico

Involvment of the team in a large popularisation process

In 2015, members of the team got involved in many popularisation events on behalf of Inria to emphasize the scope of research for the advantages of citizens, whether they be average people, entrepreneurs, decision-makers or students.

CASTOR Project-Team (section vide)

CLIME Project-Team (section vide)

COFFEE Project-Team (section vide)

FLUMINANCE Project-Team (section vide)

LEMON Team

5. Highlights of the Year

5.1. Highlights of the Year

- In 2015, the *Marine Energies Research International Center* (MERIC) was launched in Chile. Antoine ROUSSEAU will be the scientific coordinator for Inria, and several members of LEMON, CARDAMOM and TOSCA research teams will be involved in this 8 years project in partnership with DCNS and Enel.
- Antoine ROUSSEAU co-organized the CEMRACS 2015, in Marseilles: 6 weeks with more than 100 participants.
- Fabien MARCHE and Antoine ROUSSEAU co-organized the workshop Numerical Models for Coastal Hazards in Montpellier.

5.1.1. Awards

- Carole Delenne's project **Cart'Eaux** was selected in the Languedoc Roussillon *Chercheur d'avenir* competition.
- The GERIMU project has earned a distinction from the local Scientific Advisory Committee ("Coup de coeur du COSTI").

MAGIQUE-3D Project-Team (section vide)

SAGE Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

The team SAGE ended in December 2015.

N. Nassif, J. Erhel and B. Philippe published a book entitled "introduction to computational linear algebra" [23]. E. Gallopoulos, B. Philippe and A. Sameh published a book entitled "Parallelism in Matrix Computations".

SERENA Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Awards

Martin Vohralík obtained the ERC consolidator grant in the 2015 campaign with his project GATIPOR “Guaranteed fully adaptive algorithms with tailored inexact solvers for complex porous media flows”.

Jérôme Jaffré was awarded the 2015 SIAM Geosciences Senior Career Prize.

STEEP Project-Team

4. Highlights of the Year

4.1. Highlights of the Year

The adventure continues!

The start of STEEP as an exploratory action in 2010 constituted a significant thematic change for all its members. This risky adventure was successfully consolidated in 2015, with the acceptance of STEEP as a full project-team. The adventure continues!

Various significant contributions

In other respects, two important results have been obtained this year on the ecological accounting front. First, a generic method of evaluation of environmental pressures from material flows has been developed and published (paper in press at the time of writing). Second, the errors associated to the national transport database which is heavily used in material flow analysis have been quantified; this work will be published in 2016 but is eagerly awaited by a number of researchers and agencies, as the disaggregated error is not evaluated in the database itself.

As a by-product of its investment in the ESNET project (Ecosystem Services Network), the team has developed an important expertise on the methodological aspects of LUCC modelling. This expertise has turned into a theoretical analysis of the foundations of LUCC theory itself, as important methodological flaws and their theoretical cures have been identified in the course of the project. These methodological and theoretical advances will be submitted to publication within the coming year.

Finally, our benchmarking tools designed for climate negotiations have been used by the "*Groupe Interdisciplinaire sur les Contributions Nationales*" (GICN) which has been mandated by french ministry of Sustainable Development to prepare the **climate change conference COP21** at Paris. Some contributions have been presented at the Side Events of COP 21, the 2nd of December 2015. Contributions have been published in a special working paper [11].

TONUS Team

5. Highlights of the Year

5.1. Highlights of the Year

We have launched the SCHNAPS project: http://schnaps.gforge.inria.fr/. Its goal is to develop a high performance software for plasma simulations. It is based on the runtime tool StarPU developed at Inria Bordeaux. The objective is to perform asynchronous hybrid CPU/GPU computations on HPC computers.

BIOCORE Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

- Metabolic mathematical models are required to fully understand and optimize the microalgae lipid metabolism and finally maximize biofuel production. However, unlike heterotrophic microorganisms that use the same substrate as sources of energy and carbon, photoautotrophic microorganisms require light for energy and CO2 as carbon source. Furthermore, they are submitted to permanent fluctuating light environments due to outdoor cultivation or mixing inducing a flashing effect. Modelling these nonstandard organisms is therefore a major challenge for which classical tools are often inadequate. This year, the work consisted in assessing and comparing the potential of several approaches for modelling microalgae. As a conclusion, the DRUM approach developed within Biocore seems highly promising since it requires a lowest number of parameters while it can predict internal accumulation during transients [14].
- We study the occurrence of periodic solutions in an n-dimensional class of negative feedback systems defined by smooth vector fields. By circumscribing the smooth system by two piecewise linear ones, we show that there exists an invariant toroidal region which contains a periodic orbit of the original smooth system [37]. The strong point of this work is is that it makes a link between hybrid piecewise linear systems (where computations are easier) and smooth classical systems.
- We developed a plant epidemic model to address the epidemiological and evolutionary management of plant virus epidemics in agricultural landscapes using resistant cultivars. Based on the principles of cultivar mixtures and cultivar rotations, we explored different resistance deployment strategies and their impact on disease prevalence and pathogen evolution. Overall, combining cultivar mixtures and rotations provided most efficient and durable pathogen control [25].

CARMEN Team

5. Highlights of the Year

5.1. Highlights of the Year

A large part of the newly-constructed LIRYC building, hosting researchers' offices, has been taken in use. The extra space greatly facilitates collaboration between Carmen and LIRYC researchers.

The *service de cardiologie-électrophysiologie et stimulation cardiaque* of the CHU Haut-Leveque, the clinical partner in LIRYC, was ranked first in the classification 2015–2016 of Hospitals and Clinics published by the news magazine *L'Express*, while its director, professor M. Haissaguerre, has been awarded the Gold Medal of the European Society of Cardiology.

M. Potse published a high-profile paper with a group of internationally renowned researchers on terminology and criteria for the diagnosis of a rare but potentially fatal ECG abnormality named Early repolarisation syndrome [37].

In silico assessment of drugs effects on human embryonic stem cells derived cardiomyocytes electrical activity Computational modeling and simulation is extensively used to investigate diseases in cardiac electrophysiological activity and also drug effects, side effects and interactions. Human embryonic stem cell-derived cardiomyocytes (hESC-CMs) have been recently considered as a promising tool in regenerative medicine: their major role in repairing damaged tissue is due to pluripotency and ability to differentiate. These pluripotent cells are also used in early stages of drugs development. Pharmaceutical companies use the MultiElectrode Array (MEA) device in order to perform many in vitro experiments on hESC-CMs. The goal of our study is to derive a mathematical model and to simulate these in vitro experiments. Sensitivity of the Electrocardiography Inverse Solution to the Torso Conductivity Uncertainties Electrocardiography imaging (ECGI) is a new non invasive technology used for heart diagnosis. It allows to construct the electrical potential on the heart surface only from measurement on the body surface and some geometrical informations of the torso. The purpose of this work is twofold: First, we propose a new formulation to calculate the distribution of the electric potential on the heart, from measurements on the torso surface. Second, we study the influence of the errors and uncertainties on the conductivity parameters, on the ECGI solution. We use an optimal control formulation for the mathematical formulation of the problem with a stochastic diffusion equation as a constraint. The descretization is done using stochastic Galerkin method allowing to separate random and de-terministic variables. The optimal control problem is solved using a conjugate gradient method where the gradient of the cost function is computed with an ad-joint technique. The efficiency of this approach to solve the inverse problem and the usability to quantify the effect of conductivity uncertainties in the torso are demonstrated through a number of numerical simulations on a 2D geometrical model. Our results show that adding ±50alter the inverse solution, whereas adding ±50lung conductivity affects the reconstructed heart potential by almost 50

Inverse Localization of Ischemia in a 3D Realistic Geometry: A Level Set Approach The reconstruction of cardiac ischemic regions from body surface potential measurements (BSPMs) is usually performed at a single time instant which corresponds to the plateau or resting phase of the cardiac action potential. Using a different approach, we previously proposed a level set formulation that incorporates the knowledge of the cardiac excitation process in the inverse procedure, thus exploiting the spatio-temporal correlations contained in the BSPMs. In this study, we extend our inverse level-set formulation for the reconstruction of ischemic regions to 3D realistic geometries, and analyze its performance in different noisy scenarios. Our method is benchmarked against zero-order Tikhonov regularization. The inverse reconstruction of the ischemic region is evaluated using the correlation coefficient (CC), the sensitive error ratio (SN), and the specificity error ratio (SP). Our algorithm outperforms zero-order Tikhonov regularization, specially in highly noisy scenarios.

Inverse problem in electrocardography via the factorization method of boundary value problems We present a new mathematical approach for solving the inverse problem in electrocardiography. This approach is based on the factorization of boundary value problems method. In this paper we derive the mathematical equations and test this method on synthetical data generated on realistic heart and torso geometries using the state-of-the-art bidomain model in the heart coupled to the Laplace equation in the torso. We measure the accuracy of the inverse solution using spatial Relative Error (RE) and Correlation Coefficient (CC).

It is now possible for all Carmen members to go to the IHU LIRYC since the construction of the new building. This aims for the Carmen teams to follow doctors and researchers at Xavier Arnozan hospital.

DRACULA Project-Team (section vide)

M3DISIM Team

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Awards

A. Collin (who did her PhD in the team) received the SMAI-GAMNI award 2015 for Best PhD thesis and the ECCOMAS PhD award 2015.

A. Aalto received the award for the best doctoral thesis in Aalto University School of Science during 2014.

MAMBA Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

Awards

Benoît Perthame is the 2015 laureate of the Inria - French Académie des Sciences Grand Prize: http://www.inria.fr/en/institute/inria-in-brief/inria-awards/2015-prize-winners/benoit-perthame-grand-prize.

MODEMIC Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

The project Soil$\mu 3D$, which Modemic is a partner, has been selected and funded by the ANR (French National Research Agency) for the 2015-2019 period.

Alain Rapaport has been invited to give a plenary session at the next CMPDE'16 [0] (Conference in Mathematical Population Dynamics and Epidemiology), Marseille, 5–9 September 2016.

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[0] http://mpde16.mio.univ-amu.fr/

Monc Team

5. Highlights of the Year

5.1. Highlights of the Year

Awards

Perrine Berment won the third price of *Ma thèse en 180 secondes* of the Aquitaine region.

MYCENAE Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

- HDR defense of Jonathan Touboul : Contribution to the theoretical study of large neuronal ensembles. June 5th 2015, ED3C
- Co-organization of founding events to federate the national scientific communities in Reproduction: Reprosciences 2015, and in Modeling for cell and developmental biology: 2015 ITMO BCDE workshop on Modeling in Cell and Developmental Biology

NUMED Project-Team (section vide)

REO Project-Team

5. Highlights of the Year

5.1. Highlights of the Year

Irène Vignon-Clementel: Article [16] selected for journal cover in Cardiovascular Engineering and Technology.

5.1.1. Awards

Jessica Oakes was awarded an American Lung Association Senior Research Training Grant for salary support for 1-2 years.