RESEARCH CENTER

FIELD
Digital Health, Biology and Earth

Activity Report 2018

Section Partnerships and Cooperations

Edition: 2019-03-07

ABS Project-Team

6. Partnerships and Cooperations

6.1. International Research Visitors

6.1.1. Visits of International Scientists

6.1.1.1. Internships

- Internship of Maria Guramare, Harvard University, Cambridge, Massachusetts. Supervision: Frédéric Cazals and Dorian Mazauric. *Shortest Paths under Constraints Problem with Application for Structural Alignments.*
- Internship of Xuchun Zhang, École Polytechnique de l'Université Nice Sophia Antipolis, filière Mathématiques Appliquées et Modélisation, year 4 (Master 1). Supervision: Jean-Baptiste Caillau (Inria project-team McTao), Enzo Giusti (startup Oui!Greens), Dorian Mazauric, and Joanna Moulierac (Inria/I3S project-team Coati). *Problèmes d'affectations d'annonces dans un réseau anti gaspillage !*
- Project of Ruiqing Chang and Xuchun Zhang, École Polytechnique de l'Université Nice Sophia Antipolis, Filière Mathématiques Appliquées et Modélisation, year 4 (Master 1). Supervision: Jean-Baptiste Caillau (Inria project-team McTao), Enzo Giusti (startup Oui!Greens), Dorian Mazauric, and Joanna Moulierac (Inria/I3S project-team Coati). *Problèmes d'affectations d'annonces dans un réseau anti gaspillage !*
- Internship of Nguyen Thi Viet Ha, Master 2 Fundamental Computer Science, École Normale Supérieure de Lyon. Supervision: Frédéric Havet (Inria/I3S project-team Coati), Dorian Mazauric, and Rémi Watrigant (École Normale Supérieure de Lyon and Université Claude Bernard Lyon 1). *Graph Algorithms for low resolution model of large protein assemblies.*
- Internship of Timothée O'Donnell, Master 2 University Paris Saclay, Master bioinformatique. *Structural modeling of FMRP dimers in solution*. Supervision: F. Cazals.

BEAGLE Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

- Lipuscale (2018-2019): Hybrid simulation of lipid digestion and absorption, a two-year project funded by the Rhône-Alpes Institute for Complex Systems (IXXI). With Marie-Caroline Michalski (CarMeN, INSERM U1060, INRA U1397) and Samuel Bernard (Institut Camille Jordan and Inria Dracula team). Participant: Carole Knibbe.

8.2. National Initiatives

8.2.1. ANR

Dopaciumcity (2014-2018): Dopamine modulation of calcium influx underlying synaptic plasticity, a 4-year project funded by a grant from the ANR-NSF-NIH Call for French-US Projects in Computational Neuroscience. With L. Venance, College de France, CIRB, CNRS/UMR 7241 - INSERM U1050, Paris, France and K Blackwell, Krasnow Institute of Advanced Studies, George Mason University, Fairfax, VA, USA. Supervisor: L Venance (for France) and K.L. Blackwell (for US). Participants: H Berry, I Prokin, A Foncelle

Dallish (2016-2020): Data Assimilation and Lattice LIght SHeet imaging for endocytosis/exocytosis pathway modeling in the whole cell, Call AAPG ANR 2016. With C. Kervrann (Inria Rennes), J. Salamero (Institute Curie, Paris), B. Laroche (INRA, Jouy-en-Josas). Participants: H. Berry.

Storiz (2018-2020): Horizontal transfers as documents from extinct or unknown species. Call ANR JCJC 2018. Leaded by Damien de Vienne (LBBE, Lyon) Participant: Eric Tannier

LncEvoSys (2017-2019): An evolutionary systems approach to understand long non-coding RNA functionality, Call ANR JCJC 2017. Leaded by Anamaria Necsulea (LBBE, Lyon). Participant: Eric Tannier

8.2.2. Inria

ADT Phylophile (2016-2018). Participants: E Tannier, in collaboration with D Parsons, Inria, V Daubin, B Boussau, CNRS, Université de Lyon 1. This project aims at producing an easy to use software integrating modern algorithmic methods to build gene trees. It has been funded by Inria by a 24 month software engineer.

Naviscope (Inria Project Lab, 2018-2022): image-guided Navigation and VIsualization of large data sets in live cell imaging and microSCOPy. Nowadays, the detection and visualization of important localized events and process in multidimensional and multi-valued images, especially in cell and tissue imaging, is tedious and inefficient. Specialized scientists can miss key events due to complexity of the data and the lack of computer guidance. In Naviscope we develop original and cutting-edge visualization and navigation methods to assist scientists, enabling semi-automatic analysis, manipulation, and investigation of temporal series of multi-valued volumetric images, with a strong focus on live cell imaging and microscopy application domains. We build Naviscope upon the strength of scientific visualization and machine learning methods in order to provide systems capable to assist the scientist to obtain a better understanding of massive amounts of information. Such systems will be able to recognize and highlight the most informative regions of the dataset by reducing the amount of information displayed and guiding the observer attention. Head: C. Kervrann (Serpico), other EPIs: Aviz, Beagle, Hybrid, Morpheme, Mosaic, Parietal, and MaIage (INRA unit).

8.3. International Initiatives

8.3.1. Inria International Partners

8.3.1.1. Informal International Partners

- Anton Crombach collaborates with Dr. Alexander Fleischmann, who moved this year from CIRB, College de France (Paris), to Brown University, USA.
- Carole Knibbe collaborates with Kirsty Spalding and Peter Arner from Karolinska University Hospital in Stockholm, Sweden.
- Eric Tannier collaborates with Gergerly Szollosi, Eotvos University, Budapest, Cedric Chauve, SFU, Vancouver, Igor Sharakov, from Virginia Tech, Rob Waterhous, Univ Lausanne, Tom Williams, Univ Bristol, ...
- Eric Tannier has leaded the publication of a collaborative paper on a phylogenetic format co-signed by 27 researchers from 10 nationalities.

8.3.2. Participation in Other International Programs

Program: CNRS-Royal society

Project title: Modeling lateral gene transfer on a new bacterial tree

Duration: 2018

Coordinator: Bastien Boussau

Other partners: Eric Tannier (Beagle), LBBE (Lyon), Eotvos University (Budapest), University of Bristol (UK)

Abstract: Bacteria play a major role in human health and in the functioning of all ecosystems. Most of the genomes available in public databases come from Bacteria. However, we understand little of their evolution: both their phylogeny and their timeline of diversification are highly uncertain. This is due in great part to the difficulty of reconstructing events that happened billions of years ago, and also to the fact that individual genes are often transferred across species and therefore have a history that differs from that of the species that contain them. Recently we have proposed novel methods for dealing with the very problems that make reconstructing the bacterial phylogeny challenging. This proposal aims to support a joint project that will reconstruct and date the bacterial phylogeny by combining novel methods (Boussau, Lyon) with existing skills in microbial phylogenetics, genomics and evolution (Williams, Bristol).

8.4. International Research Visitors

8.4.1. Visits to International Teams

Audrey Denizot stayed 4 months in Okinawa, OIST University, Erik de Schutter's team, from june to october 2018

BIGS Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

- GDR 3475 Analyse Multifractale, Funding organism: CNRS, Leader: S. Jaffard (Université Paris-Est), Céline Lacaux
- GDR 3477 Géométrie stochastic, Funding organism: CNRS, Leader: P. Calka (Université Rouen), Céline Lacaux
- FHU CARTAGE (Fédération Hospitalo Universitaire Cardial and ARTerial AGEing ; leader : Pr Athanase Benetos), Jean-Marie Monnez
- RHU Fight HF (Fighting Heart Failure ; leader : Pr Patrick Rossignol), located at the University Hospital of Nancy, Jean-Marie Monnez
- Project "Handle your heart", team responsible for the creation of a drug prescription support software for the treatment of heart failure, head: Jean-Marie Monnez
- A. Gégout-Petit, N. Sahki, S. Mézières are involved in the learning aspect of the clinical protocol "EOLEVAL" with Assistance Publique des Hopitaux de Paris (APHP)
- "ITMO Physics, mathematics applied to Cancer" (2017-2019): "Modeling ctDNA dynamics for detecting targeted therapy", Funding organisms: ITMO Cancer, ITMO Technologies pour la santé de l'alliance nationale pour les sciences de la vie et de la santé (AVIESAN), INCa, Leader: N. Champagnat (Inria TOSCA), Participants: A. Gégout-Petit, A. Muller-Gueudin, P. Vallois.
- PEPS AMIES (2018-2019), Etude Biométrique en foetopathologie et développement de l'enfant, Collaboration Institut Elie Cartan avec le CRESS INSERM, S. Ferrigno.
- Modular, multivalent and multiplexed tools for dual molecular imaging (2017-2020), Funding organism: ANR, Leader: B Kuhnast (CEA). Participant: T. Bastogne.
- Sophie Mézières belongs to GDR 720 ISIS, Funding organism: CNRS, leader: Laure Blanc-Féraud.

8.2. European Initiatives

8.2.1. Collaborations in European Programs, Except FP7 & H2020

T. Bastogne participates to the ASCATIM Project (project FEDER), leaded by N. Tran and J.-P. Jehl (2018-2021).

BONSAI Project-Team

7. Partnerships and Cooperations

7.1. National Initiatives

7.1.1. ANR

- ANR Transipedia: The purpose of Transipedia is to provide means of identifying relevant transcriptomic events within thousands of RNA sequencing experiments. This project will be achieved in collaboration with I2BC (principal investigator) in Paris Saclay and IRMB in Montpellier.
- ANR ASTER: ASTER is a national project that aims at developing algorithms and software for analyzing third-generation sequencing data, and more specifically RNA sequencing. BONSAI is the principal investigator in this ANR. Other partners are Erable (LBBE in Lyon) and two sequencing and analysis platforms that have been very active in the MinION Access Program (Genoscope and Institut Pasteur de Lille).
- PIA France Génomique: National funding from "Investissements d'Avenir" (call *Infrastructures en Biologie-Santé*). France Génomique is a shared infrastructure, whose goal is to support sequencing, genotyping and associated computational analysis, and increases French capacities in genome and bioinformatics data analysis. It gathers 9 sequencing and 8 bioinformatics platforms. Within this consortium, we are responsible for the work package devoted to the computational analysis of sRNA-seq data, in coordination with the bioinformatics platform of Génopole Toulouse-Midi-Pyrénées.

7.1.2. ADT

- ADT SeedLib (2017–2019): The SeedLib ADT aims to consolidate existing software developments in Bonsai, into an existing and well-engineered framework. Bonsai has published several new results on spaced seeds and developed several tools that integrate custom implementations of spaced seeds. In parallel, the GATB project is a C++ software library that facilitates the development of next-generation sequencing analysis tools. It is currently maintained by a collaboration between the GenScale team at Inria Rennes and the Bonsai team. Many users from other institutions (including the Erable team at Inria Rhones-Alpes) actively develop tools using GATB. The core object in GATB is k-mers, which can be seen as the predecessor of spaced seeds. The goal of this ADT is to integrate existing space seeds formalisms into GATB, therefore further expanding the features offered by the library, and at the same time provide visibility for tools and results in the Bonsai team.

7.2. European Initiatives

7.2.1. Collaborations in European Programs, Except FP7 & H2020

- International ANR RNAlands (2014-2018): National funding from the French Agency Research (call *International call*). Our objective is the fast and efficient sampling of structures in RNA Folding Landscapes. The project gathers three partners: Amib from Inria Saclay, the Theoretical Biochemistry Group from Universität Wien and BONSAI.
- Interreg Va (France-Wallonie-Vlaanderen): Portfolio "SmartBioControl", including 5 constitutive projects and 25 partners working together towards sustainable agriculture.

7.3. International Research Visitors

7.3.1. Visits of International Scientists

7.3.1.1. Internships

- Inria MITACS 3-month internship of D. Martchenko (PhD student, Trent University)

CAPSID Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. CPER – IT2MP

Participants: Marie-Dominique Devignes [contact person], Malika Smaïl-Tabbone, David Ritchie.

Project title: *Innovations Technologiques, Modélisation et Médecine Personnalisée*; PI: Faiez Zannad, Univ Lorraine (Inserm-CHU-UL). Value: 14.4 M€ ("SMEC" platform – Simulation, Modélisation, Extraction de Connaissances – coordinated by Capsid and Orpailleur teams for Inria Nancy – Grand Est, with IECL and CHRU Nancy: 860 k€, approx); Duration: 2015–2020. Description: The IT2MP project encompasses four interdisciplinary platforms that support several scientific pôles of the university whose research involves human health. The SMEC platform supports research projects ranging from molecular modeling and dynamical simulation to biological data mining and patient cohort studies.

8.1.2. LUE-FEDER – CITRAM

Participants: Marie-Dominique Devignes [contact person], Isaure Chauvot de Beauchêne, Bernard Maigret, Philippe Noël, David Ritchie.

Project title: *Conception d'Inhibiteurs du Transfert de Résistances aux agents Anti-Microbiens: bio-ingénierie assistée par des approches virtuelles et numériques, et appliquée à une relaxase d'élément conjugatif intégratif*; PI: N. Leblond, Univ Lorraine (DynAMic, UMR 1128); Other partners: Chris Chipot, CNRS (SRSMSC, UMR 7565); Value: 200 k€ (Capsid: 80 k€); Duration: 2017–2018. Description: This project follows on from the 2016 PEPS project "MODEL-ICE". The aim is to investigate protein-protein interactions required for initiating the transfer of an ICE (Integrated Conjugative Element) from one bacterial cell to another one, and to develop small-molecule inhibitors of these interactions.

8.1.3. PEPS – DynaCriGalT

Participants: Isaure Chauvot de Beauchêne [contact person], Bernard Maigret, David Ritchie.

Project title: *Criblage virtuel et dynamique moléculaire pour la recherche de bio-actifs ciblant la β4GalT7, une enzyme de biosynthèse des glycosaminoglycanes*; PI: I. Chauvot de Beauchêne, Capsid (Inria Nancy – Grand Est); Partners: Sylvie Fournel-Gigleux, INSERM (IMoPA, UMR 7365); Value: 15 k€; Duration: 2017–2018. Description: The β4GalT7 glycosyltransferase initiates the biosynthesis of glycosaminoglycans (GAGs), and is a therapeutical target for small molecules which might correct a defect in the synthesis and degradation of GAGs in rare genetic diseases. Classical approaches to propose active molecules have failed for this target. The DynaCriGalT project combines molecular dynamics modelling of the GAG active site with virtual screening in order to propose a diverse set of small molecules for *in vitro* compound testing.

8.1.4. PEPS – InterANRIL

Participant: Isaure Chauvot de Beauchêne [contact person].

Project title: *TBA* Duration: 2017–2018. Description: *TBA*

Project title: *Identification et modélisation des interactions nécessaires à l'activité du long ARN non-codant ANRIL dans la régulation épigénétique des gènes*; PI: Sylvain Maenner, Univ Lorraine (IMoPA, UMR 7365); Value: 20 k€; Duration: 2017–2018. Description: ANRIL is a long non-coding RNA (lncRNA) which has been identified as an important factor in the susceptibility cardiovascular diseases. ANRIL is involved in the epigenetic regulation of the expression of a network of genes via mechanisms that are still largely unknown. This project aims to identify and model the protein-RNA and/or DNA-RNA interactions that ANRIL establishes within the eukaryotic genome.

8.1.5. GlycoEst

Participant: Isaure Chauvot de Beauchêne [contact person].

GlycoEst is an informal working group which was recently created to develop an interdisciplinary regional network of Glyco-scientists. Isaure Chauvot de Beauchêne gave a talk on her protein-GAG docking method at the first meeting of this group in March 2018.

8.2. National Initiatives

8.2.1. FEDER – SB-Server

Participants: David Ritchie [contact person], Bernard Maigret, Isaure Chauvot de Beauchêne, Sabeur Aridhi, Marie-Dominique Devignes.

Project title: *Structural bioinformatics server*; PI: David Ritchie, Capsid (Inria Nancy – Grand Est); Value: 24 k€; Duration: 2015–2020. Description: This funding provides a small high performance computing server for structural bioinformatics research at the Inria Nancy – Grand Est centre.

8.2.2. ANR

8.2.2.1. Fight-HF

Participants: Marie-Dominique Devignes [contact person], Malika Smaïl-Tabbone [contact person], Bernard Maigret, Sabeur Aridhi, Kévin Dalleau, Claire Lacomblez, David Ritchie.

Project title: *Combattre l'insuffisance cardiaque*; PI: Patrick Rossignol, Univ Lorraine (FHU-Cartage); Partners: multiple; Value: 9 m€ (Capsid and Orpailleur: 450 k€, approx); Duration: 2015–2019. Description: This "Investissements d'Avenir" project aims to discover novel mechanisms for heart failure and to propose decision support for precision medicine. The project has been granted € 9M, and involves many participants from Nancy University Hospital's Federation "CARTAGE" (http://www.fhu-cartage.com/). In collaboration with the Orpailleur Team, Marie-Dominique Devignes is coordinating a work-package on network-based science and drug discovery for this project.

8.2.2.2. IFB

Participants: Marie-Dominique Devignes [contact person], Sabeur Aridhi, Isaure Chauvot de Beauchêne, David Ritchie.

Project title: *Institut Français de Bioinformatique*; PI: Claudine Médigue and Jacques van Helden (CNRS UMS 3601); Partners: multiple; Value: 20 M€ (Capsid: 126 k€); Duration: 2014–2021. Description: The Capsid team is a research node of the IFB (Institut Français de Bioinformatique), the French national network of bioinformatics platforms (http://www.france-bioinformatique.fr). The principal aim is to make bioinformatics skills and resources more accessible to French biology laboratories.

8.2.3. Collaborations with Major European Organizations

EBI: European Bioinformatics Institute, Maria Martin team (UK). We are working with the EBI team to validate and improve our graph-based approaches for protein function annotation.

8.2.4. PEPS-INS2I – ORCA 3D

Participants: Isaure Chauvot de Beauchêne [contact person], Agnibha Chandra, Rohit Roy.

Protect Title: *Oligo-RNA Combinatorial Assembly for 3D modeling of protein-RNA complexes.* PI: Isaure Chauvot de Beauchêne. Value: 8k€. Description: The project aimed at improving our fragment-based ssRNA docking method, of which we already provided a proof of principle. It mainly provided grants for two internship students to work on (i) a new ssRNA-protein scoring function and (ii) docking with constraints specific to the geometry of ssRNA in RNA loops.

8.3. International Initiatives

8.3.1. TempoGraphs

Participants: Sabeur Aridhi [contact person], Marie-Dominique Devignes, Malika Smaïl-Tabbone, David Ritchie, Bishnu Sarker, Wissem Inoubli.

Project title: *Analyzing big data with temporal graphs and machine learning: application to urban traffic analysis and protein function annotation.* PI: Sabeur Aridhi; Partners: LORIA/Inria NGE, Federal University of Ceará (UFC); Value: 20 k€; Duration: 2017–2020. Description: This project aims to investigate and propose solutions for both urban traffic-related problems and protein annotation problems. In the case of urban traffic analysis, problems such as traffic speed prediction, travel time prediction, traffic congestion identification and nearest neighbors identification will be tackled. In the case of protein annotation problem, protein graphs and/or protein–protein interaction (PPI) networks will be modeled using dynamic time-dependent graph representations.

8.3.1.1. Informal International Partners

Participant: David Ritchie; Project: *Integrative Modeling of 3D Protein Structures and Interactions;* Partner: Rocasolano Institute of Physical Chemistry, Spain. Funding: Inria Nancy – Grand Est ("Nancy Emerging Associate Team").

Participant: Bernard Maigret; Project: *Characterization, expression and molecular modeling of TRR1 and ALS3 proteins of Candida spp., as a strategy to obtain new drugs with action on yeasts involved in nosocomial infections;* Partner: State University of Maringá, Brazil.

Participant: Bernard Maigret; Project: *Fusarium graminearum target selection;* Partner: Embrapa Recursos Geneticos e Biotecnologia, Brazil.

Participant: Bernard Maigret; Project: *The thermal shock HSP90 protein as a target for new drugs against paracoccidioidomicose;* Partner: Brasília University, Brazil.

Participant: Bernard Maigret; Project: *Protein-protein interactions for the development of new drugs;* Partner: Federal University of Goias, Brazil.

8.4. International Research Visitors

8.4.1. Visits of International Scientists

Ghania Khensous from the University of Sciences and Technologies in Oman visited the team to develop a tabu-based search algorithm for flexible protein-ligand docking, under the supervision of Bernard Maigret.

Patricia Alves from the University of Brasilia is visiting the team to carry out drug repositioning on several target fungus proteins under the supervision of Bernard Maigret.

8.4.1.1. Internships

Agnibha Chandra from the Indian Institute of Engineering Science & Technology visited the team to optimize a force-field for ssRNA-protein docking, under the supervision of Isaure Chauvot de Beauchêne.

Ismail El Fadli from the Mohammed V University of Rabat visited the team to adapt our RNA-protein docking method to DNA-protein systems, under the supervision of Isaure Chauvot de Beauchêne.

Aichata Niang from the University of Paris Diderot visited the team to to apply modeling and virtual screening of a galactosyl-transferase enzyme in order to find new inhibitors, under the supervision of Isaure Chauvot de Beauchêne.

Rohit Roy from the Indian Institute of Technology at Kharagpur visited the team in order to include geometric constrains in our docking algorithm for docking RNA loops, under the supervision of Isaure Chauvot de Beauchêne.

Giammarco Mastronardi from the University of Lorraine visited the team to carry out a virtual screening study of small-molecule inhibitors of a bacterial polyketide synthase module, under the supervision of Bernard Maigret and David Ritchie.

Wissem Inoubli from the University of Tunis El Manar visited the team to work on his PhD thesis on distributed graph processing under the supervision of Sabeur Aridhi.

Damien Vantourout from the University of Lorraine visited the team to develop a tool for protein function annotation using semantic protein networks and deep neural networks under the supervision of Sabeur Aridhi.

Xavier Farchetto from the University of Lorraine visited the team to work on the segmentation of images in Crohn's disease under the supervision of Malika Smaïl-Tabbone and Chedy Raissy (Orpailleur team).

Maxime Guyot from the University of Lorraine (Telecom Nancy stage 2A) visited the team to perform statistical analyses on KBDock and to develop a scoring function for protein-protein interaction subgraphs extracted from a knowledge graph database.

DYLISS Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. Ecosyst (Brittany region)

Participants: Marie Chevallier, Clémence Frioux, Anne Siegel.

This project aims at creating a regional research network related to the emerging topic of *systems ecology*, together with the development of tools to be shared by the researchers. It is co-leaded by OSUR (environmental lab) and Dyliss. 2016-2018. Total grant: 100k€

9.1.2. Ph.D. fundings from Université, Inria Rennes and Inserm

The team benefits from the funding of Ph.D. theses by Univ. Rennes (L. Bourneuf, 2016-2019 – H. Talibart, 2017-2020 – N. Guillaudeux, 2018-2021), by Inria (C. Frioux, 2015-2018), by Inserm (M. Louarn, 2017-2019, Inria-Inserm PhD Grant program), and by our collaborators from IRSET (M. Conan, 2017-2020 - P. Vignet, 2018-2020).

9.2. National Initiatives

9.2.1. IDEALG (ANR/PIA-Biotechnology and Bioresource)

Participants: Meziane Aite, Arnaud Belcour, Marie Chevallier, François Coste, Clémence Frioux, Jeanne Got, Jacques Nicolas, Anne Siegel.

The project gathers 18 partners from Station Biologique de Roscoff (coordinator), CNRS, IFREMER, UEB, UBO, UBS, ENSCR, University of Nantes, INRA, AgroCampus, and the industrial field in order to foster biotechnology applications within the seaweed field. Dyliss is co-leader of the WP related to the establishment of a virtual platform for integrating omics studies on seaweed and the integrative analysis of seaweed metabolism. Major objectives are the building of brown algae metabolic maps, metabolic flux analysis and the selection of symbiotic bacteria for brown algae. We will also contribute to the prediction of specific enzymes (sulfatases and haloacid dehalogenase) [More details]. 2012-20. Total grant: 11M€. Dyliss grant: 534k€.

9.2.2. PEPS: a platform for supporting studies in pharmaco-epidemiology using medico-administrative databases (ANSM)

Participants: Olivier Dameron, Yann Rivault.

The project involves EHESP (coordinator) (public health, Rennes), Univ. Rennes 1 (including the Dyliss), INSERM, CESP and CHU Rennes. The project goal is to develop generic methods supporting efficient and semantically-rich queries for pharmaco-epidemiology studies on medico-administrative databases. 2015-2018. Total grant: 3,6M€. Lacodam & Dyliss grant: 145k€.

9.2.3. TGFSysBio (ITMO Cancer)

Participants: Olivier Dameron, Maxime Folschette, Vijay Ingalalli, Jacques Nicolas, Anne Siegel, Nathalie Théret, Pierre Vignet.

Partners are INSERM (coordinator) (IRSET, Univ. Rennes 1) CNRS (Dyliss team) and Inria (Antique, Paris). The TGFSYSBIO project aims at developing the first model of extracellular and intracellular TGF-beta system by combining a ruled-based modelling approach (kappa) and a Petri net modelling approach (cadbiom). 2015-18. Total grant: 418k€. Dyliss grant: 129k€.

9.2.4. Programs funded by Inria

9.2.4.1. IPL Algae in silico

Participants: Meziane Aite, Arnaud Belcour, François Coste, Jeanne Got, Anne Siegel.

This project involves mainly the inria teams BIOCORE (coordinator), ANGE and DYLISS. Microalgae are recognized for the extraordinary diversity of molecules they can contain: proteins, lipids (for biofuel or long chain polyunsaturated fatty acids for human health), vitamins, antioxidants, pigments. The project aims at predicting and optimizing the productivity of microalgae. Dyliss is in charge of the identification of physiological functions for microalgae based on their proteomes, which is undergone through the reconstruction of the metabolic network of the *T. lutea* microalgae. Dyliss is also working with the the inria team PLEIADE on learning and predicting the specificities of desaturase enzymes in *Ostreococcus tauri* green algae. 2014-18.

9.2.4.2. IPL Neuromarkers

Participants: Olivier Dameron, Anne Siegel.

This project involves mainly the inria teams Aramis (coordinator) Dyliss, Genscale and Bonsai. The project aims at identifying the main markers of neurodegenerative pathologies through the production and the integration of imaging and bioinformatics data. Dyliss is in charge of facilitating the interoperability of imaging and bioinformatics data. 2017-20.

9.2.4.3. FederatedQueryScaler (Exploratory Research Action)

Participants: Olivier Dameron, Xavier Garnier, Vijay Ingalalli.

This project is coordinated by Dyliss and is a common project with the WIMMICS Inria team. This project aims at developing automatic generation of abstractions for biological data and knowledge in order to scale federated queries in the context of semantic web technologies. 2017-2018.

9.2.4.4. Askomics (ADT)

Participants: Olivier Dameron, Xavier Garnier, Guillaume Alviset, Anne Siegel.

AskOmics [url] is a visual SPARQL query interface supporting both intuitive data integration and querying while avoiding the user to face most of the technical difficulties underlying RDF and SPARQL. The underlying motivation is that even though Linked (Open) Data now provide the infrastructure for accessing large corpora of data and knowledge, life science end-users seldom use them, nor contribute back their data to the LOD cloud by lack of technical expertise. AskOmics aims at bridging the gap between end users and the LOD cloud. 2018-2020.

9.3. European Initiatives

9.3.1. Collaborations in European Programs, Except FP7 & H2020

Program: Polish National Science Center

Project acronym: NCN 2016/21/B/ST6/02158

Project title: Grammatical inference methods in classification of amyloidogenic proteins

Duration: January 2017 - January 2020

Coordinator: Olgierd Unold, Politechnika Wroclawska

Other partners: Politechnika Wroclawska (Polland)

Abstract: The objective is to develop the methods for induction of context-free and probabilistic grammars to describe a language matching amyloidogenic protein sequences.

9.3.2. Collaborations with Major European Organizations

Partner: University of Potsdam, Computer science department (Germany)

Title: Modeling combinatorial and hybrid problems with Answer Set Programming

9.4. International Initiatives

9.4.1. IIL projects

We have a cooperation with Univ. of Chile (MATHomics, A. Maass) on methods for the identification of biomarkers and software for biochip design. It aims at combining automatic reasoning on biological sequences and networks with probabilistic approaches to produce biomarkers of extremophile bacteria. In this context, IntegrativeBioChile was an Associate Team between Dyliss and the Laboratory of Bioinformatics and Mathematics of the Genome hosted at Univ. of Chile funded from 2011 to 2016. The collaboration is now supported by Chilean programs.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- **Niger**. University of Maradi [O. Abdou-Arbi]
- **Poland**. Politechnika Wroclawska [W. Dyrka]

9.5.2. Visits to International Teams

- **Chile**. University of Chile [A. Siegel, C. Frioux, M. Aite, M. Louarn]
- **Poland**. Politechnika Wroclawska [F. Coste]

9.5.2.1. Research Stays Abroad

- **Germany**. University of Potsdam [L. Bourneuf, 3 months (nov 2017 - jan 2018)]

ERABLE Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Muse

- Title: Multi-Omics and Metabolic models iNtegration to study growth Transition in *Escherichia coli*
- Coordinators: Delphine Ropers (EPI Ibis) and Marie-France Sagot
- ERABLE participants: Marie-France Sagot and Arnaud Mary.
- Type: IXXI Project (2018-2019).
- Web page: none for now.

8.2. National Initiatives

8.2.1. ANR

8.2.1.1. Aster

- Title: Algorithms and Software for Third gEneration Rna sequencing
- Coordinator: Hélène Touzet, University of Lille and CNRS.
- ERABLE participants: Vincent Lacroix (ERABLE coordinator), Clara Benoît-Pilven, Audric Cologne, Alex di Genova, Leandro I. S. de Lima, Arnaud Mary, Marie-France Sagot, Camille Sessegolo, Blerina Sinaimeri.
- Type: ANR (2016-2020).
- Web page: http://bioinfo.cristal.univ-lille.fr/aster/.

8.2.1.2. ExHyb

- Title: Exploring genomic stability in hybrids
- Coordinator: C. Vieira
- ERABLE participant(s): C. Vieira
- Type: ANR (2014-2018)
- Web page: Not available

8.2.1.3. GraphEn

- Title: Enumération dans les graphes et les hypergraphes : Algorithmes et complexité
- Coordinator: D. Kratsch
- ERABLE participant(s): A. Mary
- Type: ANR (2015-2019)
- Web page: http://graphen.isima.fr/

8.2.1.4. GrR

- Title: Graph Reconfiguration
- Coordinator: N. Bousquet
- ERABLE participant(s): A. Mary
- Type: ANR JCJC (2019-2021)
- Web page: Not available

8.2.1.5. Green

- Title: Deciphering host immune gene regulation and function to target symbiosis disturbance and endosymbiont control in insect pests
- Coordinator: A. Heddi
- ERABLE participant(s): M.-F. Sagot, C. Vieira
- Type: ANR (2018-2021)
- Web page: Not yet available

8.2.1.6. Hmicmac

- Title: Host-microbiota co-adaptations: mechanisms and consequences
- Coordinator: F. Vavre
- ERABLE participant(s): F. Vavre
- Type: ANR PRC (2017-2020)
- Web page: Not available

8.2.1.7. IMetSym

- Title: Immune and Metabolic Control in Intracellular Symbiosis of Insects
- Coordinator: A. Heddi
- ERABLE participant(s): H. Charles, S. Colella
- Type: ANR Blanc (2014-2017)
- Web page: Not available

8.2.1.8. Resist

- Title: Rapid Evolution of Symbiotic Interactions in response to STress: processes and mechanisms
- Coordinator: N. Kremer
- ERABLE participant(s): F. Vavre
- Type: ANR JCJC (2017-2020)
- Web page: Not available

8.2.1.9. Suzukill

- Title: Managing cold tolerance and quality of mass-produced *Drosophila suzukii* flies to facilitate the application of biocontrol through incompatible and sterile insect techniques
- Coordinator: H. Colinet
- ERABLE participant(s): F. Vavre
- Type: ANR PCRI (2015-2018)
- Web page: Not available

8.2.1.10. Swing

- Title: Worldwide invasion of the Spotted WING Drosophila: Genetics, plasticity and evolutionary potential
- Coordinator: P. Gibert
- ERABLE participant(s): C. Vieira
- Type: ANR PCR (2016-2020)
- Web page: Not available

8.2.1.11. U4atac-brain

- Title: Rôle de l'épissage mineur dans le développement cérébral
- Coordinator: Patrick Edery, Centre de Recherche en Neurosciences de Lyon.

- ERABLE participants: Vincent Lacroix (ERABLE coordinator), Clara Benoît-Pilven, Audric Cologne.
- Type: ANR (2018-2021).
- Web page: Not available.

8.2.2. Idex

8.2.2.1. Micro-be-have

- Title: Microbial Impact on insect behaviour: from niche and partner selection to the development of new control methods for pests and disease vectors
- Coordinator: F. Vavre
- ERABLE participant(s): F. Vavre
- Type: AO Scientific Breakthrough (2018-2021)
- Web page: Not available

8.2.3. ADT Inria

8.2.3.1. ADT Inria Kirikomics

- Main objective: Development of a portal to increase the visibility of the tools and resources elaborated by ERABLE around the analysis – using omics data – of metabolic networks modelled by hypergraphs, and enable to visualise the results. (the web page is for now private, it will be made public later in the project).
- Duration: 2016-2017, renewable one more year.
- Person responsible for ADT: Arnaud Mary with David Parsons (Inria).
- Beneficiary of ADT: Martin Wannagat.
- Funds received: Salary for engineer.

8.2.4. Others

Notice that were included here national projects of our members from Italy and the Netherlands when these have no other partners than researchers from the same country.

8.2.4.1. Advanced computational methodologies for the analysis of biomedical data

- Title: Advanced computational methodologies for the analysis of biomedical data
- Coordinator: P. Milazzo
- ERABLE participant(s): R. Grossi, N. Pisanti
- Type: PRA, MIUR PRIN, Italian Ministery of Research National Projects (2017-2018)
- Web page: Not available

8.2.4.2. Advanced Tools and Techniques for the analysis of criminal networks

- Title: Advanced Tools and Techniques for the analysis of criminal networks
- Coordinator: G. Italiano
- ERABLE participant(s): G. Italiano
- Type: LEONARDO SpA (2015-2018)
- Web page: Not available

8.2.4.3. Open Innovation: Digital Innovation for Driving

- Title: Open Innovation: Digital Innovation for Driving
- Coordinator: G. Italiano
- ERABLE participant(s): G. Italiano
- Type: Bridgestone (2018-2019)

- Web page: Not available

8.2.4.4. CMACBioSeq

- Title: Combinatorial Methods for analysis and compression of biological sequences
- Coordinator: G. Rosone
- ERABLE participant(s): N. Pisanti
- Type: SIR, MIUR PRIN, Italian Ministery of Research National Projects (2015-2019)
- Web page: http://pages.di.unipi.it/rosone/CMACBioSeq.html

8.2.4.5. Statistical Models for Structural Genetic Variants in the Genome of the Netherlands

- Title: Statistical Models for Structural Genetic Variants in the Genome of the Netherlands
- Coordinator: A. Schönhuth
- ERABLE participant(s): A. Schönhuth
- Type: Nederlandse Wetenschappelijke Organisatie (NWO) (2013-2018)
- Web page: Not available

8.2.4.6. TALS and splicing

- Title: Development of bioinformatic methods for the analysis of splicing events in patients with the Taybi-Linder Syndrome (TALS)
- Coordinator: P. Edery
- ERABLE participant(s): C. Benoît-Pilven, Audric Cologne, V. Lacroix
- Type: INSERM
- Web page: Not available

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

8.3.1.1. MicroWine

- Title: Microbial metagenomics and the modern wine industry
- Duration: January 2015 - January 2019
- Coordinator: Lars Hestbjerg Hansen, University of Copenhagen
- ERABLE participant(s): A. Marchetti-Spaccamela, A. Mary, H. T. Pusa, M.-F. Sagot, L. Stougie
- Type: H2020-MSCA-ETN-2014
- Web page: https://team.inria.fr/erable/en/microwine/ and http://www.microwine.eu/

8.3.2. Collaborations in European Programs, Except FP7 & H2020

8.3.2.1. Combinatorics of co-evolution

- Title: The combinatorics of co-evolution
- Duration: 2015 - 2018
- Coordinator: Katharina Huber, University of Warwick, UK
- ERABLE participant(s): M.-F. Sagot, B. Sinaimeri
- Type: The Royal Society
- Web page: not available

8.3.3. Collaborations with Major European Organizations

By itself, ERABLE is built from what initially were collaborations with some major European Organisations (CWI, Sapienza University of Rome, Universities of Florence and Pisa, Free University of Amsterdam) and now has become a European Inria Team.

8.4. International Initiatives

8.4.1. Inria Associate Teams Not Involved in an Inria International Labs

Compasso

- Title: COMmunity Perspective in the health sciences: Algorithms and Statistical approacheS for explOring it
- Duration: 2018, renewable from 2 to 5 years more
- Coordinator: On the Portuguese side, Susana Vinga, IST, Lisbon, Portugal; on the French side, Marie-France Sagot
- ERABLE participant(s): R. Andrade, M. Ferrarini, G. Italiano, A. Marchetti-Spaccamela, A. Mary, H. T. Pusa, M.-F. Sagot, B. Sinaimeri, L. Stougie, A. Viari, I. Ziska
- Web page: http://team.inria.fr/erable/en/projects/inria-associated-team-compasso/

8.4.2. Participation in International Programs

ERABLE is coordinator of a CNRS-UCBL-Inria Laboratoire International Associé (LIA) with the Laboratório Nacional de Computação Científica (LNCC), Petrópolis, Brazil. The LIA has for acronym LIRIO ("Laboratoire International de Recherche en bIOinformatique") and is coordinated by Ana Tereza Vasconcelos from the LNCC and Marie-France Sagot from BAOBAB-ERABLE. The LIA was created in January 2012 for 4 years, renewable once for 4 more years. A web page for the LIA LIRIO is available at this address: http://team.inria.fr/erable/en/cnrs-lia-laboratoire-international-associe-lirio/.

ERABLE also participated to the BASIS project. This was funded by the European Community Seventh Framework Programme (Grant 242006 - 2010-2015). It was led by Dr. Mike Stratton and involved six European countries. It was primarily focused on ER+/HER2- breast cancers, but during the course of the project, was merged with the HER2+ French-ICGC and triple negative UK-ICGC projects, resulting in the analysis of the whole spectrum of breast cancers. The French group was initiated by Dr. Gilles Thomas and was pursued by Alain Viari after the loss of Dr. Thomas in 2014. The project resulted in the sequencing and thorough analysis of 560 breast cancer whole genomes (Nik-Zainai *et al.*, *Nature*, 534:47-54, 2016), including 75 HER2+ performed by the French working group (Ferrari *et al.*, *Nature Communications*, 7, 2016) and funded by the Institut National du Cancer and by Inserm.

Finally, Marie-France Sagot participates in a Portuguese FCT project, Perseids for "Personalizing cancer therapy through integrated modeling and decision" (2016-2019), with Susana Vinga and a number of other Portuguese researchers. The budget of Perseids is managed exclusively by the other Portuguese partner.

8.5. International Research Visitors

8.5.1. Visits of International Scientists

In 2018, ERABLE greeted the following International scientists:

- In France: Alexander Stuart Ralph (University of Melbourne), Katharina Huber and Vincent Moulton (University of Warwick, UK), Ifigeneia Kyrkou (Aarhus University, Danemark), Ana Tereza Vasconcelos from the LNCC, Brazil), Nuno Mira (IST Portugal), May Alzamel and Costas Iliopoulos (King's College, London, UK), Simona Rombo (University of Palermo, Italy).
- In Italy: Loukas Georgiadis (University of Ioannina, Greece), Matthias Mnich (University of Bonn, Germany), Adam Karczmarcz (University of Warsaw, Poland).
- In the Netherlands: Solon Pissis (King's College, UK).

8.5.1.1. Internships

In 2018, ERABLE in France greeted the following Internships:

- Gabriela Paludo, Federal University of Mato Grosso do Sul, Brazil, from Dec 1st 2017 to June 30 2018, funds for 6 months from Capes, Brazil, and for the last month from ERABLE;
- Rafael Nahat, University of São Paulo, Brazil, from June 1st 2018 to Dec 15, 2018.

In the Netherlands, ERABLE greeted the following Internship: Luca Denti, University Bicocca of Milano, Italy, from October 1 to January 2019.

8.5.2. Visits to International Teams

8.5.2.1. Research Stays Abroad

In 2018, two members of ERABLE from France did research stays at Sapienza University of Rome. These were Marie-France Sagot and Blerina Sinaimeri, both funded by Sapienza, M.-F. Sagot as senior scientist for a visit of one month, and B. Sinaimeri as a junior scientist for a visit of three months. The visits took place at the beginning of 2018, Jan-Feb for M.-F. Sagot, and Jan-Apr for B. Sinaimeri. In the context of her visit to Sapienza, Blerina furthermore gave a mini-course (9h) at the University.

GENSCALE Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. Project Thermin: Differential characterization of strains of a bacterial species, Streptococcus thermophilus, with a Nanopore Minion

Participants: Jacques Nicolas, Emeline Roux, Gregoire Siekaniec, Dominique Lavenier.

Coordinator: J. Nicolas (Inria/Irisa, GenScale, Rennes)
Duration: 36 months (Oct. 2018 – Sept. 2021)
Partners: INRA (STLO, Agrocampus Rennes, E. Guédon and Y. Le Loir).

The Thermin project aims at exploring the capacities of a low cost third generation sequencing device, the Nanopore Minion, for rapid and robust pan-genome dicrimination of bacterial strains and their phenotypes. It has started at the end of this year with the recruitment (délégation Inria) of E. Roux, a biochemist from Lorraine University and G. Siekaniec (INRA -Inria collaboration, INRA grant), a new PhD student. We will study pan-genomic representations of multiple genomes and the production of characteristic signatures of each genome in this context.

9.2. National Initiatives

9.2.1. ANR

9.2.1.1. Project HydroGen: Metagenomic applied to ocean life study

Participants: Dominique Lavenier, Pierre Peterlongo, Claire Lemaitre.

Coordinator: P. Peterlongo (Inria/Irisa, GenScale, Rennes)
Duration: 42 months (Nov. 2014 – Apr. 2018)
Partners: CEA (Genoscope, Evry), INRA (AgroParisTech, Paris – MIG, Jouy-en-Jossas).

The HydroGen project aims to design new statistical and computational tools to measure and analyze biodiversity through comparative metagenomic approaches. The support application is the study of ocean biodiversity based on the analysis of seawater samples available from the Tara Oceans expedition.

9.2.1.2. Project SpeCrep: speciation processes in butterflies

Participants: Dominique Lavenier, Jeremy Gauthier, Fabrice Legeai, Claire Lemaitre, Pierre Peterlongo.

Coordinator: M. Elias (Museum National d'Histoire Naturelle, Institut de Systématique et d'Evolution de la Biodiversité, Paris)
Duration: 48 months (Jan. 2015 – Dec. 2018)
Partners: MNHN (Paris), INRA (Versailles-Grignon), Genscale Inria/IRISA Rennes.

The SpeCrep project aims at better understanding the speciation processes, in particular by comparing natural replicates from several butterfly species in a suture zone system. GenScale's task is to develop new efficient methods for the assembly of reference genomes and the evaluation of the genetic diversity in several butterfly populations.

9.2.1.3. Project Supergene: The consequences of supergene evolution.

Participants: Dominique Lavenier, Fabrice Legeai, Claire Lemaitre, Pierre Peterlongo.

Coordinator: M. Joron (Centre d'Ecologie Fonctionnelle et Evolutive (CEFE) UMR CNRS 5175, Montpellier)
Duration: 48 months (Nov. 2018 – Oct. 2022)
Partners: CEFE (Montpellier), MNHN (Paris), Genscale Inria/IRISA Rennes.

The Supergene project aims at better understanding the contributions of chromosomal rearrangements to adaptive evolution. Using the supergene controlling adaptive mimicry in a polymorphic, ubiquitous butterfly from the Amazon basin (H. numata), the project will investigate the evolution of inversions involved in adaptive polymorphism and their consequences on population biology. GenScale's task is to develop new efficient methods for the detection and genotyping of inversion polymorphism with several types of re-sequencing data.

9.2.2. PIA: Programme Investissement d'Avenir

9.2.2.1. RAPSODYN: Optimization of the rapeseed oil content under low nitrogen

Participants: Dominique Lavenier, Claire Lemaitre, Sebastien Letort, Pierre Peterlongo, Guendal Virlet.

Coordinator: N. Nesi (Inra, IGEPP, Rennes)
Duration: 99 months (2012-2020)
Partners: 5 companies, 9 academic research labs.

The objective of the Rapsodyn project is the optimization of the rapeseed oil content and yield under low nitrogen input. GenScale is involved in the bioinformatics work package to elaborate advanced tools dedicated to polymorphism and application to the rapeseed plant. (http://www.rapsodyn.fr)

9.2.3. Programs from research institutions

9.2.3.1. Inria Project Lab: Neuromarkers

Participants: Dominique Lavenier, Pierre Peterlongo, Claire Lemaitre, Celine Le Beguec.

Coordinator: O. Colliot (Inria, Aramis, Paris)
Duration: 4 years (2017-2020)
Partners: Inria (Aramis, Bonsai, Dyliss, GenScale, XPOP), ICM

The IPL Neuromarkers aims to design imaging bio-markers of neuro-degenerative diseases for clinical trials and study of their genetic associations. In this project, GenScale bring its expertise in the genomics field. More precisely, given a case-control population, a first step is to locate small genetic variations (SNPs, small indels) from their genomes. Then, having these variations together with brain images (also partitioned into case-control data sets), the challenge is to select variants that present potential correlation with brain images.

9.3. European Initiatives

9.3.1. Collaborations in European Programs

Program: ITN (Initiative Training Network)

Project acronym: IGNITE

Project title: Comparative Genomics of Non-Model Invertebrates

Duration: 48 months (April 2018, March 2022)

Coordinator: Gert Woerheide

Partners: Ludwig-Maximilians-Universität München (Germany), Centro Interdisciplinar de Investigação Marinha e Ambiental (Portugal), European Molecular Biology Laboratory (Germany), Université Libre de Bruxelles (Belgium), University of Bergen (Norway), National University of Ireland Galway (Ireland), University of Bristol (United Kingdom), Heidelberg Institute for Theoretical Studies (Germany), Staatliche Naturwissenschaftliche Sammlungen Bayerns (Germany), INRA Rennes (France), University College London (UK), University of Zagreb (Croatia), Era7 Bioinformatics (Spain), Pensoft Publishers (Bulgaria), Queensland Museum (Australia), Inria, GenScale (France), Institut Pasteur (France), Leibniz Supercomputing Centre of the Bayerische Akademie der Wissenschaften (Germany), Alphabiotoxine (Belgium)

Abstract: Invertebrates, i.e., animals without a backbone, represent 95 per cent of animal diversity on earth but are a surprisingly underexplored reservoir of genetic resources. The content and architecture of their genomes remain poorly characterised, but such knowledge is needed to fully appreciate their evolutionary, ecological and socio-economic importance, as well as to leverage the benefits they can provide to human well-being, for example as a source for novel drugs and biomimetic materials. IGNITE will considerably enhance our knowledge and understanding of animal genome knowledge by generating and analyzing novel data from undersampled invertebrate lineages and by developing innovative new tools for high-quality genome assembly and analysis.

9.4. International Initiatives

9.4.1. Inria Associate Teams

9.4.1.1. HipcoGen

Title: High-Performance Combinatorial Optimization for Computational Genomics

International Partner (Institution - Laboratory - Researcher):

LANL (United States)

Information Science department

Hristo Djidjev

Start year: 2017

See also: https://team.inria.fr/genscale/presentation/associated-team/

Genome sequencing and assembly, the determination of the DNA sequences of a genome, is a core experiment in computational biology. During the last decade, the cost of sequencing has decreased dramatically and a huge amount of new genomes have been sequenced. Nevertheless, most of recent genome projects stay unfinished and nowadays the databases contain much more incompletely assembled genomes than whole stable reference genomes. The main reason is that producing a complete genome, or an as-complete-as-possible-genome, is an extremely difficult computational task (an NP-hard problem) and, in spite of the efforts and the progress done by the bioinformatics community, no satisfactory solution is available today. New sequencing technologies (such as PacBio or Oxford Nanopore) are being developed that tend to produce longer DNA sequences and offer new opportunities, but also bring significant new challenges. The goal of this joint project–a cooperation between Los Alamos National Laboratory, US and Inria, is to develop a new methodology and tools based on novel optimization techniques and massive parallelism suited to these emerging technologies and able to tackle the complete assembly of large genomes.

9.4.1.2. Informal International Partners

- Free University of Brussels, Belgium: Genome assembly [P. Perterlongo, D. Lavenier]

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- Visit of Hristo Djidjev from Los Alamos National Laboratory, USA, June 2018.
- Visit of Bernardo Clavijo from the Earlham Institute, United Kingdom, February 2018.
- Visit of Nicole Van Dam from Institute of Ecology, Jena university, June 2018.

9.5.2. Visits to International Teams

9.5.2.1. Research Stays Abroad

- Visit of R. Andonov at Los Alamos National Laboratory, USA, from March 23 to April 30th, 2018.
- Visit of S. Francois at Los Alamos National Laboratory, USA, from March 23 to April 23th, 2018.

IBIS Project-Team

7. Partnerships and Cooperations

7.1. Regional Initiatives

Project name	MuSE: MUlti-Omics and Metabolic models integration to study growth transition in Escherichia coli
Coordinator IBIS participants Type Web page	D. Ropers D. Ropers, T. Etienne IXXI/BioSyl project (2018-2020) http://www.biosyl.org/news/muse-2013-multi-omics-and-metabolic-models-integration-to-study-growth-transition-in-escherichia-coli

Project name	RNAfluo: Quantification d'ARN régulateurs *in vivo*
Coordinator IBIS participants Type	S. Lacour S. Lacour AGIR project Univ Grenoble Alpes (2016-2019)

7.2. National Initiatives

Project name	MEMIP – Modèles à effets mixtes de processus intracellulaires : méthodes, outils et applications
Coordinator IBIS participants Type	G. Batt E. Cinquemani, A. Marguet, D. Ropers ANR project (2016-2020)

Project name	ENZINVIVO – Détermination in vivo des paramètres enzymatiques dans une voie métabolique synthétique
Coordinator IBIS participants Type	G. Truan J. Geiselmann, H. de Jong ANR project (2016-2020)

Project name	MAXIMIC: Optimal control of microbial cells by natural and synthetic strategies
Coordinator IBIS participants Type Web page	H. de Jong C. Boyat, E. Cinquemani, J. Geiselmann, H. de Jong, A. Pavlou, C. Pinel, D. Ropers ANR project (2017-2021) https://project.inria.fr/maximic

Project name	RIBECO (RIBonucleotide ECOnomy): Engineering RNA life cycle to optimize economy of microbial energy
Coordinator	M. Cocaign-Bousquet
IBIS participants	E. Cinquemani, T. Etienne, D. Ropers
Type	ANR project (2018-2022)
Web page	https://project.inria.fr/ribeco/

Project name	COSY: real-time COntrol of SYnthetic microbial communities
Coordinator	E. Cinquemani
IBIS participants	E. Cinquemani, H. de Jong, J. Geiselmann, M. Mauri, T. Muszbek, C. Pinel, D. Ropers
Type	Inria Project Lab (2017-2021)
Web page	https://project.inria.fr/iplcosy/

Project name	CoSoft: Control software for a system of mini-bioreactors
Coordinator	E. Cinquemani
IBIS participants	E. Cinquemani, H. de Jong, J. Geiselmann, T. Muszbek
Type	Inria Hub (2017-2018)

Project name	AlgeaInSilico: Prédire et optimiser la productivité des microalgues en fonction de leur milieu de croissance
Coordinator	O. Bernard
IBIS participants	H. de Jong, N. Giordano
Type	Inria Project Lab (2015-2019)
Web page	https://project.inria.fr/iplalgaeinsilico/

Project name	Analyse intégrative de la coordination entre stabilité des ARNm et physiologie cellulaire chez Escherichia coli
Coordinators	D. Ropers, M. Cocaign-Bousquet (Inra, LISBP)
IBIS participants	T. Etienne, D. Ropers
Type	Contrat Jeune Scientifique Inra-Inria (2016-2019)

7.3. European Initiatives

7.3.1. Collaborations with Major European Organizations

Systems biotechnology department at Technische Universität Münich (Germany), Andreas Kremling

Modeling of carbon metabolism in bacteria

Automatic control laboratory at ETH Zürich (Switzerland), John Lygeros, and Cell cycle laboratory, School of Medicine, University of Patras (Greece), Zoe Lygeros

Control theory and systems identification with applications to single-cell systems biology

LIFEWARE Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANR Projects

- ANR-FWF CyberCircuits (2018-2022): "Cybergenetic circuits to test composability of gene networks", co-coordinated by C. Guet (IST Austria, Klosterneuburg, Austria) and J. Ruess (Inria EPI Lifeware);
- ANR-DFG SYMBIONT (2018-2021) on "Symbolic Methods for Biological Systems", coordinated by T. Sturm (CNRS, LORIA, Nancy, France) and A. Weber (Univ. Bonn, Germany) with F. Fages and F. Boulier (U. Lille), O. Radulescu (U. Montpellier), A. Schuppert (RWTH Aachen), S. Walcher (RWTH Aachen), W. Seiler (U. Kassel);
- ANR-MOST BIOPSY (2016-2020) on "Biochemical Programming System", coordinated by F. Molina (CNRS, Sys2diag, Montpellier) and J.H. Jiang (National Taiwan University), with F. Fages;
- ANR MEMIP (2016-2020) on "Mixed-Effects Models of Intracellular Processes", coordinated by G. Batt, with P. Hersen, (CNRS/Paris7), E. Cinquemani (Inria EPI IBIS) and M. Lavielle (Inria/CNRS/Polytechnique, EPI XPOP);
- ANR COGEX (2016-2019) on "Computer Aided Control of Gene Expression" coordinated by P. Hersen (MSC lab, CNRS/Paris7), with G. Batt and G. Truan (LISBP, CNRS/INSA);
- ANR Blanc HYCLOCK (2014-2018) on "Hybrid modeling of time for Circadian Clock Biology and Chronopharmacology", coordinated by F. Delaunay (CNRS, Nice), with F. Lévi (INSERM Paris-Sud), G. Bernot (CNRS I3S, Nice), O. Roux (Ecole Centrale Nantes), F. Fages and S. Soliman;
- ANR Blanc STOCH-MC (2014-2018) on "Stochastic Models: Scalable Model Checking", coordinated by Blaise Genest (Inria Rennes), with Grégory Batt, Wieslaw Zielonka (LIAFA), and Hugo Gimbert (LaBRI).

8.1.2. Inria Project Lab

- IPL COSY (2017-2021) "real-time control of synthetic microbial communities", coordinated by Eugenio Cinquemani (Ibis, Inria), with Jean-Luc Gouzé (Biocore, Inria), Gregory Batt, Frédéric Bonnans (Commands, Inria), Efimov Denis (Non-A, Inria), and Hans Geiselmann (BIOP, Université Grenoble-Alpes), Beatrice Laroche (Maiage, Inra Jouy-en-Josas).

8.2. European Initiatives

8.2.1. H2020 Projects

- H2020 FET-OPEN COSY-BIO (2017-2020), "Control Engineering of Biological Systems for Reliable Synthetic Biology Applications", coordinated by Diego di Bernardo (Tigem), with Filippo Menolascina (Edinburgh U), Mario di Bernardo (Naples U), Pascal Hersen (Paris7 U), Mustafa Khammash (ETHZ), Gregory Batt, Guy-Bart Stan (Imperial College), and Lucia Marucci (Bristol U).

8.3. International Research Visitors

8.3.1. Visits of International Scientists

The following researchers have been invited for short visits

- Carlo Spaccasassi, Microsoft Research Cambridge, UK
- Debdas Paul, Univ. Stuttgart, Germany

8.3.1.1. Internships

Lucia Nasti, PhD candidate at the Universita of Pisa, Italy, is visiting our group for 4 months.

8.3.2. Visits to International Teams

8.3.2.1. Research Stays Abroad

Jakob Ruess stayed at IST Austria twice a week in Feb and Nov 2018.

MORPHEME Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Labex Signalife

The MORPHEME team is member of the SIGNALIFE Laboratory of Excellence.

Florence Besse and Xavier Descombes are members of the Scientific Committee.

8.1.2. Idex UCA Jedi

Florence Besse is a member of the scientific council of the IDEX JEDI Academy 2.

Laure Blanc-Féraud is chair of the scientific council of Academy 1 of Idex UCA JEDI.

A number of projects has been partially funded by the Idex.

- Artificial intelligence application to the identification of functional traits of zooplankton from high-resolution images (ARTIFACTZ) collaboration with Laval University, Québec / UCA Coll. with : F. Maps (ULaval), D. Laurandeau (ULaval),L. Guidi (LOV), S. Ayata (LOV), J.-O. Irisson (LOV) Participants : E. Debreuve
- Biological Image Super-resolution Enhanced with Tensor (Biset) supported by Académie 1 RISE Coll. with G. Favier (I3S), G. Sandoz (iBV) Participants : E. Debreuve, L. Blanc-Féraud, S. Schaub
- Quantitative analysis of exovesicle transport dynamics in the zebrafish Left/Right organizer. supported by Academy 2 "Complex Systems" Coll. with M. Furthauer (PI, iBV), T. Juan (iBV) Participants: R. Pages, X. Descombes
- Study of a complex biological system pf prostate organoid: applications in biomedical research. supported by Academy 2 "Complex Systems" Coll. with F. Bost (PI, C3M), S. Clavel (C3M), R.F. Roustan (C3M), S. Torrino (C3M). Participants: C. Girard-Riboulleau, X. Descombes
- Imaging analysis for mitochondrial network tracking and recgnition. supported by Academy 1 "Living Sciences" Coll. with M. Chami (IPMC), C. Badot (IPMC), F. Bost (C3M), S. Clavel (C3M), A. Charezac (C3M) Participants: G. Lavisse, X. Descombes.

8.1.3. 3AI Côte d'Azur

Laure Blanc-Féraud is a member of the scientific committee of the 3IA proposal of Nice.

8.2. National Initiatives

8.2.1. ANR RNAGRIMP

Participants: Florence Besse [PI], Fabienne de Graeve, Xavier Descombes, Eric Debreuve.

Here, we propose to study the molecular bases underlying the assembly and regulation of RNA granules, using the highly conserved IMP-containing granules as a paradigm. Specifically, we propose to perform an unbiased genome-wide RNAi screen on Drosophila cultured cells to identify mutant conditions in which the organization and/or distribution of IMP-containing granules is altered. To quantitatively and statistically analyze mutant conditions, and to define precise and coherent classes of mutants, we will combine high throughput microscopy with the development of a computational pipeline optimized for automatic analysis and classification of images. The function of positive hits isolated in the screen will then be validated in vivo in Drosophila neurons using fly genetics and imaging techniques, and characterized at the molecular and cellular levels using biochemical assays, in vitro phase transition experiments and live-imaging. Finally, the functional conservation of identified regulators will be tested in zebrafish embryos combining gene inactivation and live-imaging techniques. This integrative study will provide the first comprehensive analysis of the functional network that regulates the properties of the conserved IMP RNA granules. Our characterization of the identified regulators in vivo in neuronal cells will be of particular significance in the light of recent evidence linking the progression of several degenerative human diseases to the accumulation of non-functional RNA/protein aggregates.

This 4-years project started january, 2016 and is leaded by F. Besse (iBV, Nice). Participants are iBV, institut de biologie Paris Seine (IBPS, Paris), and Morpheme.

8.2.2. ANR HMOVE

Participants: Xavier Descombes, Eric Debreuve.

Among the signaling molecules involved in animal morphogenesis are the Hedgehog (Hh) family proteins which act at distance to direct cell fate decisions in invertebrate and vertebrate tissues. To study the underlying process we will develop accurate tracking algorithm to compare trajectories of different Hh pools transportation in live animals. This will allow us to analyze the contribution of the different carriers in the establishment of the Hh gradient. Moreover, we will develop new methods to modify the spatio-temporal and dynamical properties of the extra-cellular Hh gradient and separate the contribution of the apical versus basal Hh pools. We will complete this study with a genome-wide screen to identify genes and related cellular processes responsible for Hh release. The particular interest of this collaboration lies in the combination of development of tracking algorithm to analyze Hh distribution and trajectories with extremely powerful genetics, ease of in vivo manipulation and lack of genetic redundancy of Drosophila.

This 4-years project started january, 2016 and is leaded by P. Thérond (iBV, Nice). Participants are iBV and Morpheme.

8.2.3. ANR DIG-EM

Participants: Grégoire Malandain, Xavier Descombes, Gaël Michelin.

Morphogenesis controls the proper spatial organization of the various cell types. While the comparatively simple process of patterning and cell differentiation has received considerable attention, the genetic and evolutionary drivers of morphogenesis are much less understood. In particular, we very poorly understand why some morphogenetic processes evolve very rapidly, while others show remarkable evolutionary stability.

This research program aims at developing a high-throughput computational framework to analyze and formalize high-throughput 4D imaging data, in order to quantify and formally represent with cellular resolution the average development of an organism and its variations within and between species. In addition to its biological interest, a major output of the project will thus be the development of robust general computational methods for the analysis, visualization and representation of massive high-throughput light-sheet data sets.

This 4-years project started october the 1st, 2014 and is leaded by P. Lemaire (CRBM, Montpellier). Participants are the CRBM, and two Inria project-team, Morpheme and Virtual Plants.

8.2.4. ANR PhaseQuant

Participants: Grégoire Malandain, Eric Debreuve, Kevin Giulietti, Sarah Laroui.

The PhaseQuantHD project aims at developing a high-content imaging system using quadriwave lateral shearing interferometry as a quantitative phase imaging modality. Automated analysis methods will be developed and optimized for this modality. Finally an open biological study question will be treated with the system.

This 3-years project started october the 1st, 2014 and is leaded by B. Wattelier (Phasics, Palaiseau). Participants are Phasics, and three academic teams TIRO (UNS/CEA/CAL), Nice, Mediacoding (I3S, Sophia-Antipolis), and Morpheme.

8.2.5. Inria Large-scale initiative Naviscope

Participant: Grégoire Malandain.

This action gathers the expertise of seven Inria research teams (Aviz, Beagle, Hybrid, Morpheme, Parietal, Serpico and Mosaic) and other groups (MaIAGE, INRA, Jouy-en-Josas and UMR 144, Institut Curie Paris) and aimed at developing original and cutting-edge visualization and navigation methods to assist scientists, enabling semi-automatic analysis, manipulation, and investigation of temporal series of multi-valued volumetric images, with a strong focus on live cell imaging and microscopy application domains. More precisely, the three following challenges will be addressed:

- Novel machine learning methods able to detect the main regions of interest, and automatic quantification of sparse sets of molecular interactions and cell processes during navigation to save memory and computational resources.
- Novel visualization methods able to encode 3D motion/deformation vectors and dynamics features with color/texture-based and non-sub-resolved representations, abstractions, and discretization, as used to show 2D motion and deformation vectors and patterns.
- Effective machine learning-driven navigation and interaction techniques for complex functional 3D+Time data enabling the analysis of sparse sets of localized intra-cellular events and cell processes (migration, division, etc.).

8.2.6. Octopus Project

Participant: Eric Debreuve.

The Octopus project deals with automatic classification of images of zooplankton. It is conducted in collaboration with the Laboratoire d'Océanographie de Villefranche-sur-mer (LOV) et l'ENSTA Paris. The kickoff meeting took place in May 2015 and a 3-day *brainstorming* meeting on Deep Learning took place in December 2015. Participants are I3S (Frédéric Precioso and Mélanie Ducoffe), LOV (Marc Picheral and Jean-Olivier Irisson), and ENSTA Paris (Antoine Manzanera).

MOSAIC Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. ENS de Lyon projets Emergents - Phyllo (2018 - 2019)

Participants: Christophe Godin, Bruno Leggio, Teva Vernoux [External Collaborator].

The aim in this project is to develop a model of phyllotaxis that would be compatible with the recent detailed and quantitative observations made by our group of the distribution of auxin in space and time at the SAM. In particular the work will seek at using the new quantitative data to estimate the parameters of the stochastic model previously developed of organ patterning.

8.1.2. IDEX Lyon Impulsion - MecaField (2019 - 2020

Participants: Christophe Godin, Teva Vernoux [External Collaborator].

In a previous work, we have shown that the coupling of mechanical and hydraulical descriptions in a 2D model of multicellular tissue growth induces the emergence of remarkable phenomena at tissue level. In particular, we have shown that the growth of an organ may induce a lateral inhibition surrounding the organ that prevents other organs to grow in its vicinity. The goal of this project is to estimate the hydraulic and mechanical parameters of such a model from confocal images of a growing SAM and to compare observations with the order of magnitude of the predicted inhibitory zones and of their amplitude at cellular resolution.

8.2. National Initiatives

8.2.1. Inria ADT - Gnomon

Participants: Olivier Ali, Romain Azaïs, Guillaume Cerutti, Florian Gacon, Christophe Godin, Jonathan Legrand, Grégoire Malandain [External Collaborator], Teva Vernoux [External Collaborator].

Gnomon is a user-friendly computer platform developed by the Mosaic team for seamless simulation of form development in silico. It is intended to be a major tool for the team members to develop, integrate and share their models, algorithms and tools. Flexible components (plugins) make it possible to up-load or to create such data-structures, to program their development, to analyze, visualize them and interact with them in 3D+time.

Based on the past experience of the team with the OpenAlea platform, the goal of this ADT is to develop a more scalable software engineering solution based on the dtk kernel developed by the group of software engineers (SED) from the Sophia-Antipolis Inria Center.

Partners:

- SED Sophia Antipolis Inria Research Centre
- Morpheme Inria projec-team, Sophia Antipolis, France

8.2.2. Inria IPL - Naviscope

Participants: Guillaume Cerutti, Emmanuel Faure [External Collaborator], Christophe Godin, Jonathan Legrand, Grégoire Malandain [External Collaborator].

In this project, we plan to develop original and cutting-edge visualization and navigation methods to assist scientists, enabling semi-automatic analysis, manipulation, and investigation of temporal series of multi-valued volumetric images, with a strong focus on live cell imaging and microscopy application domains. We will build Naviscope upon the strength of scientific visualization and machine learning methods in order to provide systems capable to assist the scientist to obtain a better understanding of massive amounts of information. Such systems will be able to recognize and highlight the most informative regions of the dataset by reducing the amount of information displayed and guiding the observer attention. Finally, we will overcome the technological challenge of gathering up the software developed in each team to provide a unique original tool for users in biological imaging, and potentially in medical imaging.

8.2.3. ANR - ReVeRIES

Participant: Guillaume Cerutti.

The aim of ReVeRIES (Reconnaissance de Végétaux Récréative, Interactive et Educative sur Smartphone) is to make use of mobile technologies to transmit general knowledge and identification skills on the plant world to an urban audience who has little to no botanical background. Following the work of the ReVeS project and the development of the Folia mobile application, a major objective is to recognize automatically the species of trees and shrubs encountered in France using photographs of their leaves, fruits, flowers and barks, while providing the user the botanical vocabulary and the keys to learn how to identify species.

Partners:

- EVS Laboratoire Environnement Ville et Société, Saint-Etienne
- IRHS Institut de Recherches en Horticulture et Semences, Angers
- LIRIS Laboratoire d'Informatique en Image et Système d'Information, Lyon
- LISTIC Laboratoire d'Informatique, Système, Traitement de l'Information et de la Connaissance, Annecy
- LIUM Laboratoire d'Informatique de l'Université du Maine, Le Mans

8.2.4. ANR - Imago (2016 - 2019)

Participants: Guillaume Cerutti, Christophe Godin, Jonathan Legrand.

The goal of this project is to investigate the role of ovule growth constraints on germ cell fate establishment. This project is motivated by recent findings from the partners' groups suggesting that disturbances in cell divisions and expansion in early (pre-meiotic) ovules are sufficient to induce ectopic germ cells. These observations suggest novel routes to engineer apomixis in plants but remains poorly understood. Recent developments in high-resolution 3D imaging, image processing, and modeling offer a powerful combination of approaches to investigate this question. IMAGO proposes to elucidate patterning rules governing ovule growth, and their contribution to female germ cell fate acquisition. We use a combination of high-resolution static and real-time 3D imaging, quantitative image processing, cell-based growth models and functional approaches to (1) define cellular growth patterns in the ovule primordium using quantitative imaging (2) test patterning rules in silico by cell-based growth models (3) validate patterning rules in vivo using genetic, pharmacological and mechanical perturbations.

Partners:

- UMR DIADE, IRD, Montpellier, France
- Department of Plant and Microbial Biology, Zurich, Swisszerland
- RDP, ENS de Lyon, France

8.2.5. ANR DigEM (2015 - 2019)

Participants: Christophe Godin, Bruno Leggio, Patrick Lemaire [External Collaborator], Grégoire Malandain [External Collaborator].

In this project, we will use advanced ligh-sheet imaging of live embryos to quantitatively describe embryonic morphogenesis in ascidians, a class of animals that undergo very rapid genomic divergence, yet show an extraordinary stasis of embryonic morphologies, based on invariant early cell lineages shared by all studied species. The global aims of the proposal, which will bridge micro- and macroevolutionary scales of analysis, are: i) to provide a global systems-level description at cellular resolution of an animal embryonic program; ii) to use this description to characterize intra-specific and inter-specific patterns of morphogenetic variations; iii) to analyze possible molecular mechanisms explaining the unusual robustness of this program to environmental and genetic perturbations. To achieve these aims, we will combine advanced live light-sheet microscopy, computational biology, functional gene assays and evolutionary approaches.

Partners:

- UMR CRBM, CNRS Montpellier, France
- Morpheme Inria projec-team, Sophia Antipolis, France

8.2.6. ERA-CAPS Genes2shape (2018 - 2021)

Participants: Olivier Ali, Guillaume Cerutti, Christophe Godin, Bruno Leggio, Jan Traas [External Collaborator].

This project is aimed at understanding how molecular regulation integrates with mechanics to control overall plant shape, an unresolved problem with wide implications for both fundamental and applied biology. We will address this issue in the Arabidopsis flower, which, besides their obvious importance as reproductive structures, are amongst the best characterised systems in plant developmental biology. From a mechanistic point of view, it is widely accepted that regulatory molecular networks interfere with the properties of the structural cellular elements (cell wall, cytoskeleton) to induce particular growth patterns. How this occurs and how this is coordinated in space is not known. To obtain a mechanistic understanding of such a complex process, information from multiple scales, from molecular networks to physical properties and geometry have to be combined into a single picture. An integrated tool to do so is currently not available. Building on our complementary experience in interdisciplinary research on plant development, we will therefore develop a tool, called the "Computable Flower" that permits (i) integration of data on geometry, gene expression and biomechanics and (ii) the user to explore, interpret and generate hypotheses based on data supported by mechanistic modelling approaches. The tool therefore provides an integrated description in the form of a 3D dynamic template of the growing flower bud.

Partners:

- University of Cambridge (Sainsbury Lab.)
- California Institute of Technology
- MaxPlanck Institutes of Molecular Plant Physiology

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

Program: H2020

Project acronym: ROMI

Project title: RObotics for MIcrofarms

Duration: November 2017 - October 2021

Coordinator: Sony

Other partners: Iaac, (Spain), FEI (France), Inria (France), CNRS (France), UBER (Germany), Chatelain (France)

Abstract: All over Europe, young farmers are starting small market farms and direct sales businesses. These farms can be found both in rural, peri-urban and urban areas. They grow a large variety of crops (up to 100 different varieties of vegetables per year) on small surfaces (0.01 to 5 ha) using organic farming practices. These farms have proven to be highly productive, sustainable and economically viable. However, a lot of work is done manually, resulting in physically challenging work conditions. ROMI will develop an open and lightweight robotics platform for these microfarms. We will assist these farms in weed reduction and crop monitoring. This will reduce manual labour and increase the productivity through advanced planning tools. Thanks to ROMI's weeding robot, farmers will save 25 percents of their time. This land robot will also acquire detailed information on sample plants and will be coupled with a drone that acquires more global information at crop level. Together, they will produce an integrated, multi-scale picture of the crop development that will help the farmer monitor the crops to increase efficient harvesting. For this, ROMI will have to adapt

and extend state-of-the-art land-based and air-borne monitoring tools to handle small fields with complex layouts and mixed crops. To achieve this, we will: (i) develop and bring to the market an affordable, multi-purpose, land-based robot, (ii) develop a weeding app for this robot that is adapted for organic microfarms, (iii) apply advanced 3D plant analysis and modelling techniques to in-field data acquisition, (iv) integrate these analysis techniques in the robot for detailed plant monitoring, (iv) integrate these techniques also in the aerial drone N-E-R-O for multi-scale crop monitoring, (v) extend the robot with novel, adaptive learning techniques to improve sensorimotor control of the plant monitoring app, and (vii) test the effectiveness of our solution in real-world field conditions.

8.3.2. Inria International Partners

8.3.2.1. Informal International Partners

8.3.2.1.1. Laboratoire International Associé (LIA): Computing Plant Morphogenesis

The focus of this LIA headed by Teva Vernoux (RDP) and Ottoline Leyser (SLCU) is on plant morphogenesis i.e. the mechanisms allowing the generation of plant shapes at different scales. Both the RDP and SLCU Laboratories are leaders of this field. The scenario for morphogenesis that has recently emerged is that chemical signals controlling cell identities lead to changes in mechanical properties of cells, triggering changes in shapes feeding back on the gene regulatory network. This in turn affects the distribution of chemical signals and mechanical forces, thus channeling morphogenesis. However, our understanding of the molecular and physical basis of morphogenesis in plants or in any other eukaryotic system is still in its infancy due to the complexity and non-linearity of processes involved in morphogenesis dynamics (or Morphodynamics). Understanding morphodynamics requires a modeling environment for the explicit representation of forms at multiple scales and for incorporating complex data from different origins and nature (chemical, mechanical, geometrical). In addition to creating a unique scientific environment, this LIA will gather the critical mass and interdisciplinary expertise required to create such a computational platform and to generate the data to produce an integrated vision of how chemical and mechanical signals interaction drive morphogenesis.

Partners:

- Sainsbury Lab. University of Cambridge (SLCU)

8.4. International Research Visitors

8.4.1. Visits of International Scientists

8.4.1.1. Internships

Farah Ben Naoum, associate professor at the University of Sidi Bel Abbes, paid a one-month visit (July 2018) in the Mosaic group to work with Romain Azaïs and Christophe Godin on algorithms to compute incrementally tree-edit distances based on their directed acyclic graph representation. This visit was funded by Inria and will be followed by another one month visit in March 2019 to complete the writing a related paper.

PLEIADE Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. High-performance computing and metabarcoding

PLEIADE is member of two projects, one funded by the Région Nouvelle Aquitaine and one funded as Inria ADT Gordon, connecting Chameleon, StartPU and NewMadeleine, where the use case of metabarcoding (questions, data sets) hase been selected to link these layers together. This will permit us to address unsupervised clustering of one million reads next year. These projects are in collaboration with the HiePACS, TADAAM, and STORM project-teams.

8.1.2. COTE – Continental to Coastal Ecosystems

The Labex cluster of excellence COTE (Continental To coastal Ecosystems: evolution, adaptability and governance) develops tools to understand and predict ecosystem responses to human-induced changes as well as methods of adaptative management and governance to ensure their sustainability. The LabEx includes nine laboratories of the University of Bordeaux and major national research institutes involved in research on terrestrial and aquatic ecosystems (INRA, CNRS, IFREMER and IRSTEA). PLEIADE is a partner in two projects funded by COTE:

- *Malabar: Métabarcoding appliqué à la biodiversté des communauéts algales du Bassin d'Arcachon*
- *Aerobarcoding: détection de pollens allergenisants*. 2017-18.

8.2. National Initiatives

8.2.1. Biocontamination in aircraft reservoirs

ANTICOR is an industrial-academic research and development working group coordinated by Dassault Aviation, investigating the causes of microbial contamination in aircraft reservoirs and aimed at developing mitigating procedures and equipment. Previous results have shown that this contamination forms biofilms at the fuel-water interface and is comprised of complex communities of hundreds of bacterial and fungal species. PLEIADE is particularly interested in measuring and modeling these communities, especially as concerns understanding how they change based on environmental conditions and on reservoir geometry.

This working group continues work started in CAER – Alternative Fuels for Aeronautics, a 6 M-Euro contract with the Civil Aviation Directorate (Direction Générale de l'Aviation Civile, DGAC), coordinated by the French Petroleum Institute (Institut français de pétrole-énergies nouvelles, IFPEN) on behalf of a large consortium of industrial (EADS, Dassault, Snecma, Turbomeca, Airbus, Air France, Total) and academic (CNRS, INRA, Inria) partners to explore different technologies for alternative fuels for aviation.

8.2.2. Agence Française pour la Biodiversité

The AFB is a public law agency of the French Ministry of Ecology that supports public policy in the domains of knowledge, preservation, management, and restoration of biodiversity in terrestrial, aquatic, and marine environments. PLEIADE is a partner in two AFB projects developed with the former ONEMA:

- *Methods for metabarcoding*. 2017-18.
- *Molecular diagnosis of freshwater quality*. 2014-present.

8.2.3. Inria Projet Lab in silico Algae

In 2017 PLEIADE joined the IPL "In silico Algae" coordinated by Olivier Bernard. The IPL addresses challenges in modeling and optimizing microalgae growth for industrial applications. PLEIADE worked this year on comparative genomic analysis of genes implicated in lipid production by the picoalgae *Ostreococcus tauri*, in collaboration with Florence Corellou of the CNRS UMR 5200 (Laboratoire de Biogénèse Membranaire). The goal of this work is the production of long-chain polyunsaturated fatty acids, developed as nutritional additives. Mercia Ngoma Komb's two-month internship in PLEIADE contributed to this work.

8.3. European Initiatives

8.3.1. Collaborations in European Programs, Except FP7 & H2020

Alain Franc is co-chair of Working Group 4 (Data Analysis and Storage) of COST DNAqua.net [0], with the main task of developing contact with HPC and metabarcoding for serving the whole community. He chaired the meeting of this groups in Pécs in 2018. The goal of DNAqua-Net is to nucleate a group of researchers across disciplines with the task to identify gold-standard genomic tools and novel eco-genomic indices and metrics for routine application for biodiversity assessments and biomonitoring of European water bodies.

8.4. International Initiatives

8.4.1. Vitapalm – Food and nutrition security and sustainable agriculture in Africa

PLEIADE has joined the Vitapalm program financed by LEAP-Agri [0], the joint Europe Africa Research and Innovation (R&I) initiative related to Food and Nutrition Security and Sustainable Agriculture. Vitapalm will use genomics and selection to improve the nutritional quality and the stability of palm oil produced by Africa smallholdings for local consumption. Project partners are from Cameroon, France, Germany, and Ghana.

8.4.2. Simulation of metacommunities

In collaboration with the Pasteur Institute in Cayenne and the INRA MIA Research Team in Toulouse, PLEIADE is developing a stochastic model for simulation of metacommunities, in the framework of patch occupancy models. The objective is a better understanding of zoonose propagation, namely rabies through bat hosts in connection with disturbances of pristine forests in French Guiana, which have an impact on the exposure of human populations to wildlife that act as reservoirs of zoonoses.

8.4.3. CEBA – Center for the study of biodiversity in Amazonia

The Laboratoire of excellence CEBA promotes innovation in research on tropical biodiversity. It brings together a network of internationally-recognized French research teams, contributes to university education, and encourages scientific collaboration with South American countries. PLEIADE participates in three current international projects funded by CEBA:

- *MicroBIOMES: Microbial Biodiversities*. 2017-19.
- *Neutrophyl: Inferring the drivers of Neotropical diversification*. 2017-19.
- *Phyloguianas: Biogeography and pace of diversification in the Guiana Shield*. 2015-present

[0] http://dnaqua.net/
[0] http://www.leap-agri.com/

SERPICO Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

Région Bretagne: Identification, localization and enumeration of ribosomes within a tomogram by combining state-of-the-art denoising methods and object descriptor-based recognition (CATLAS, see Section 8.2.1) (PhD thesis of Emmnuel Moebel); motion saliency in video sequences (PhD thesis of Léo Maczyta).

BioGenOuest: Collaboration with S. Prigent (engineer) in charge of the organization of image processing services for Biogenouest bio-imaging facilities.

IGDR: Collaboration with J. Pecreaux, Y. Le Cunff (co-supervision of PhD thesis of A. Caranfil).

9.2. National Initiatives

9.2.1. France-BioImaging project

Participants: Charles Kervrann, Patrick Bouthemy.

The goal of the France-BioImaging project (http://france-bioimaging.org/) is to build a distributed coordinated French infrastructure for photonic and electronic cellular bioimaging, dedicated to innovation, training and technology transfer. High-computing capacities are needed to exhaustively analyse image flows. Serpico is co-head of the IPDM (Image Processing and Data Management) node of the FBI network composed of 6 nodes. In this context, we address the following scientific problems: i/ exhaustive analysis of bioimaging data sets; ii/ deciphering of key steps of biological mechanisms at organ, tissular, cellular and molecular levels through the systematic use of time-lapse 3D microscopy and image processing methods; iii/ storage and indexing of extracted and associated data and metadata through an intelligent data management system. Serpico recruited R&D engineers (2011-2016) to disseminate image processing software, to build the Mobyle@Serpico web portal and to manage the IGRIDA-Serpico cluster (200 nodes; batch scheduler: OAR; File management: Puppet/Git/Capistrano; OS: Linux Debian 7; User connexion: public ssh key) opened for end-users and dedicated to large scale computing and data sets processing (storage: 200 TeraBytes).

- **Coordinator:** CNRS (Jean Salamero, UMR 144 CNRS-Institut Curie).
- **Partners:** University of Paris-Diderot-Paris 7, Aix-Marseille University, University of Bordeaux, University of Montpellier, Institut Pasteur, Institut Curie, Inria, ENS Ulm, University of Paris Descartes, UPMC, Ecole Polytechnique, Inserm.
- **Funding:** Investissement d'Avenir Infrastructures Nationales en Biologie et Santé, ANR INBS-PIA 2011.
- **Total amount:** 26 000 Keuros (Inria Serpico: 606 Keuros).

9.2.2. ANR DALLISH project (2016-2020): Data Assimilation and Lattice LIght SHeet imaging for endocytosis/exocytosis pathway modeling in the whole cell

Participants: Charles Kervrann, Ancageorgiana Caranfil, Antoine Salomon.

Cutting-edge LLS microscopy represents the novel generation of 3D fluorescence microscopes dedicated to single cell analysis, generating extraordinarily high resolved and sharp, but huge 3D images and videos. One single live cell experiment in one single biological condition can result into up to one terabyte of data.The goal of the project is to develop new paradigms and computational strategies for image reconstruction and 3D molecule tracking/motion estimation. Furthermore, establishing correspondences between image-based measurements and features, stochastic motion models, and underlying biological and biophysical information remains a challenging task. In a larger perspective, the quantitative description of image data corresponding to protein transport will be a prerequisite for understanding the functioning of a cell in normal and pathological situations including cancer, viral infection and neurodegenerative diseases.

- **Coordinator:** Inria (Charles Kervrann)
- **Partners:** Inria (Serpico, Beagle, Fluminance teams), INRA MaIAGE Unit Jouy-en-Josas, Institut Curie (UMR 144 CNRS & U1143 Inserm UMR 3666) Paris
- **Funding:** ANR (Agence Nationale de la Recherche) PRC (Collaborative Research Project)
- **Total amount:** 440 Keuros (Inria Serpico: 170 Keuros).

9.2.3. Inria Project Labs, Exploratory Research Actions and Technological Development Actions

Participants: Charles Kervrann, Patrick Bouthemy.

In the frame of the "Naviscope" IPL project, we plan to develop original and cutting-edge visualization and navigation methods to assist scientists, enabling semi-automatic analysis, manipulation, and investigation of temporal series of multi-valued volumetric images, with a strong focus on live cell imaging and microscopy application domains. We will build Naviscope upon the strength of scientific visualization and machine learning methods in order to provide systems capable to assist the scientist to obtain a better understanding of massive amounts of information. Such systems will be able to recognize and highlight the most informative regions of the dataset by reducing the amount of information displayed and guiding the observer attention. We will address the three following challenges and issues:

- Novel machine learning methods able to detect the main regions of interest, and automatic quantification of sparse sets of molecular interactions and cell processes during navigation to save memory and computational resources.
- Novel visualization methods able to encode 3D motion/deformation vectors and dynamics features with color/texture-based and non-sub-resolved representations, abstractions, and discretization, as used to show 2D motion and deformation vectors and patterns.
- Effective machine learning-driven navigation and interaction techniques for complex functional 3D+Time data enabling the analysis of sparse sets of localized intra-cellular events and cell processes (migration, division, etc.).

Finally, we will have also to overcome the technological challenge of gathering up the software developed in each team to provide a unique original tool for users in biological imaging, and potentially in medical imaging.

- **Coordinator:** Serpico Inria team (Charles Kervrann)
- **Partners:** Aviz Inria team (Saclay); Beagle Inria team (Lyon), Morpheme Inria team (Sophia-Antipolis); Parietal Inria team (Saclay); Mosaic Inria team (Lyon); MaIAGE INRA Unit (Jouy-en-Josas); Institut Curie CNRS-UMR 144 (Paris).
- **Funding:** Inria Project Lab (from 2018-2022)

9.3. European Initiatives

9.3.1. Major European Organizations with which the Team have followed Collaborations

ESFRI Euro-BioImaging initiative: SERPICO is involved in the ESFRI Euro-BioImaging project, one of the four new biomedical science projects in the roadmap of the European Strategic Forum on Research

Infrastructures (ESFRI). The mission of Euro-BioImaging is to provide access, service and training to state-of-the-art imaging technologies and foster the cooperation and networking at the national and European level including multidisciplinary scientists, industry, regional, national and European authorities. SERPICO also is involved in the French initiative, the so-called "France-BioImaging" (FBI) network which gathers several outstanding cellular imaging centers (microscopy, spectroscopy, probe engineering and signal processing) as described in Section 9.2.1 .

- **Coordinator:** EMBL (Jan Ellenberg, Heideldberg, Germany)
- **Partners:** 15 european countries in 2017
- **Funding:** Member states of the European Union

9.4. International Initiatives

9.4.1. Informal International Partners

Collaboration with Max-Planck Institute, Martinsried (Germany), Dr. Julio Ortiz and Antonio Martinez: Detection and segmentation of macromolecules in cryo-electron tomography (project in progress with Emmanuel Moebel and Charles Kervrann).

9.4.2. Inria Associate Teams Not Involved in an Inria International Labs

9.4.2.1. CytoDI Inria Associated-Team

Title: Quantitative Imaging of Cytoskeleton Dynamics in 3D

International Partner:

University of Texas, SouthWestern Medical Center, Dallas (United States) - Gaudenz Danuser

Start year: 2016

See also: http://serpico.rennes.inria.fr/doku.php?id=research:cytodi

Participants: Sandeep Manandhar, Patrick Bouthemy, Charles Kervrann.

The main scientific goal of the Associated-Team is the spatiotemporal characterization and comparison of cytoskeleton networks involved in cell migration and observed through live cell imaging in three dimensions (3D). Those networks include the cytoskeleton, i.e., microtubules (MT), intermediate filaments (IF), dynamically resolvable by Bessel Beam Light Sheet fluorescent microscopy. The goal will be achieved through the design of local and global descriptors of the spatial conformation and deformation of the cytoskeleton. Subsequently, general metrics to compare and classify the MT and IF networks will be investigated. This study will be carried out on oncogenically transformed lung cancer epithelial cells.

In 2018, the objective of the visit of Sandeep Manandhar (PhD student) at UTSW Dallas (March 1-31, 2018) was to i) get a deeper understanding of bioimaging capacities and limitations in the context of biological studies, 2) to refine the design and validation of his approaches in this context and 3) returning from his visit with a clear vision for biologically relevant tools. For the Danuser lab, the objective was 1) to evaluate the breakpoint of path-match-based approach toward heterogeneous motion 2) to fill the gap between object tracking and generic motion estimation for studies such as actin speckle or collagen.

9.5. International Research Visitors

9.5.1. Visits to International Teams

Leo Maczyta attended a summer school (one week): ICVSS 2018 (International Computer Vision Summer School), July, 8-14, Sicily, Italy.

ARAMIS Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

9.1.1.1. ANR-NIH-NSF NETBCI

Participants: Fabrizio de Vico Fallani [Correspondant], Mario Chavez, Denis Schwartz.

Project acronym: NETBCI

Project title: Modeling and predicting brain-computer interface learning from dynamic networks

Duration: Avr 2016 - Avr 2020

Amount: 322k€

Coordinator: Fabrizio De Vico Fallani

Other partners: Complex system group, UPenn, USA

Abstract: This project will bring together expertise in computational and experimental neuroscience, signal processing and network science, statistics, modeling and simulation, to establish innovative methods to model and analyze temporally dynamic brain networks, and to apply these tools to develop predictive models of brain-computer interface (BCI) skill acquisition that can be used to improve performance. Leveraging experimental data and interdisciplinary theoretical techniques, this project will characterize brain networks at multiple temporal and spatial scales, and will develop models to predict the ability to control the BCI as well as methods to engineer BCI frameworks for adapting to neural plasticity. This project will enable a comprehensive understanding of the neural mechanisms of BCI learning, and will foster the design of viable BCI frameworks that improve usability and performance.

9.1.1.2. ANR-NIH-NSF HIPLAY7

Participants: Olivier Colliot [Correspondant], Marie Chupin, Stanley Durrleman, Anne Bertrand.

Project acronym: HIPLAY7

Project title: Hippocampal layers: advanced computational anatomy using very high resolution MRI at 7 Tesla in humans

Duration: Jan 2017 - Jan 2020

Amount: 770k€

Coordinator: Olivier Colliot and Pierre-François Van de Moortele

Other partners: University of Minnesota, Neurospin

Abstract: The overall goal of this proposal is to develop a coherent mathematical framework for computational anatomy of the internal structures of the hippocampus based on cutting edge MRI acquisition techniques at 7 Tesla. These mathematical and computational approaches are expected to significantly advance the field of computational anatomy of the human brain, breaking down the millimeter barrier of conventional brain morphometry and providing a coherent analysis framework for anatomical data at ultra-high spatial resolution.

9.1.1.3. ANR PREV-DEMALS

Participants: Olivier Colliot [Correspondant], Marie Chupin, Stanley Durrleman, Anne Bertrand.

Project acronym: PREV-DEMALS

Project title: Predict to prevent frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS)

Duration: Avr 2015 - Avr 2019

Amount: 487k€

Coordinator: Isabelle Le Ber

Other partners: ICM, AP-HP, CHR de Lille, CHU Limoges, CHU Rouen, Laboratory of Biomedical Imaging

Abstract: The project focuses on C9ORF72, the most frequent genetic form of frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS). Since 2006, major discoveries have helped elucidate the pathological bases and linked FTLD and ALS: 1) TDP-43 aggregates in neurons and 2) C9ORF72 mutations in both disorders. Two major pathological subtypes are now defined in FTLD, FTLD-TDP and FTLD-TAU. C9ORF72 mutations (associated to FTLD-TDP) are the most frequent genetic causes of FTLD (15%), FTLD-ALS (65%) and ALS (40%). No curative treatment actually exists, but therapeutics emerged against tau aggregation. The objectives of the project are to develop appropriate cognitive, brain imaging markers and peripheral biomarkers of the early phase of FTLD, to follow disease progression and to guide future targeted therapeutic trials. To address this questions, we will conduct a multimodal study (cognition, brain structural MRI, brain metabolism - FDG-PET) in C9ORF72 families. The cohort will be followed at 3-time points (M0, M18, M36). Longitudinal analyses will aim at characterizing the trajectory of decline across time. Brain structural changes will be evaluated by 1) morphometric analysis to assess global brain atrophy, cortical thickness and study of the cortical sulci; 2) functional connectivity analysis of resting-state MR data; 3) structural connectivity analysis of diffusion-weighted MRI. Brain metabolism will be evaluated with FDG-PET. We will use the most recent RNA sequencing technology to detect gene expression and RNA splicing alterations in lymphocytes of patients and presymptomatic carriers. The discovery of new markers involved in FTLD will have practical consequences for early and accurate diagnosis of FLD and ALS disease.

9.1.1.4. ANR IVMRS

Participants: Anne Bertrand [Correspondant], Alexandra Petiet, Mathieu Santin, Francesca Branzoli, Benoit Delatour, Marc Sanson.

Project acronym: IVMRS

Project title: Implantable miniaturized probe for In-vivo Magnetic Resonance Spectroscopy: Application to Murine models of Alzheimer's disease and Gliomas.

Duration: Oct 2016 - Oct 2020

Amount: 633k€

Coordinator: Luc Hebrard

Other partners: ICube - Unistra, Strasbourg; ISA Laboratory, Lyon; NYU School of Medicine, NY, USA.

Abstract: During the development of new therapeutics against brain diseases, the pre-clinical phase, i.e. the validation of treatment delivery, safety and efficacy in animal models of the disease, represents a crucial step. Magnetic Resonance Imaging (MRI) is a method of particular interest at this stage, as it provides non-invasive surrogate endpoints that can help selecting appropriate candidates during the process of drug development. Single Voxel Magnetic Resonance Spectroscopy (SVS) provides non-invasive, in-vivo quantitative measurements of brain metabolites, which reflects functional changes at the cellular and subcellular levels, and can be repeated longitudinally. As high-field MRI has become the benchmark in preclinical research on animal models, it appears possible

to investigate the cerebral metabolomics changes in animals, and to use it as a surrogate marker in preclinical therapeutic trials. However, the number of relevant metabolites is much higher than the low number of measurable metabolites with conventional in-vivo high-field SVS. Moreover, considering also the subtle changes of these metabolites at the early stage of the disease, the use of conventional high-field SVS in preclinical studies remains strongly limited. The high volume of the Voxel-of-Interest (VOI), ranging from 10 to 30mm3, which is required to have a usable signal in conventional SVS, and the inherent variability of longitudinal SVS measurement due to the variable position of the VOI in the successive experiments, remain the two major issues when looking during time for small changes in metabolic concentrations and metabolites ratios in a specific small region of the animal brain. The IvMRS project aims at filling this gap by developing the first chronic implantable MRS micro-probe, minimally invasive, exhibiting very high signal sensitivity, and sharp spectral peaks, from sub-millimetric VOI. Such a probe will allow detecting a much higher number of metabolites than conventional in-vivo SVS. The probe will work at frequencies ranging from 300MHz to 500MHz in ultra-high field Magnetic Resonance Imaging scanners, 7T and 11.7T. It will embed a specific micro-coil antenna, a low-noise signal conditioning circuit designed in CMOS microelectronics technology, as well as an accurate on-chip positioning sensor. It will be dedicated to the study of changes in brain metabolite markers of two major diseases, Alzheimer's disease and cerebral gliomas, and to the assessment of effective therapeutic strategies.

9.1.2. Inria Project Labs

9.1.2.1. IPL Neuromarkers

Participants: Stanley Durrleman [Correspondant], Olivier Colliot [Correspondant], Fabrizio de Vico Fallani, Anne Bertrand, Stéphane Epelbaum.

Project acronym: Neuromarkers

Project title: Design of imaging biomarkers of neurodegenerative diseases for clinical trials and study of their genetic associations

Duration: 2017-2021

Coordinators: Stanley Durrleman and Olivier Colliot

Other partners: Inria GENSCALE, Inria BONSAI, Inria DYLISS, Inria XPOP, ICM, IHU/ICM iConics

Abstract: The Inria Project Lab Neuromarkers aims to develop new statistical and computational approaches to integrate multimodal imaging and omics data and to demonstrate their potential to identify early alterations and predict progression of neurodegenerative diseases. To tackle this challenge, the project brings together multidisciplinary expertise from Inria and ICM (Brain and Spine Institute) in the fields of statistical learning, brain imaging, bioinformatics, knowledge modeling, genomics and neurodegenerative diseases.

9.1.3. IHU

9.1.3.1. General program

Participants: Olivier Colliot, Stanley Durrleman, Didier Dormont, Ninon Burgos, Stéphane Epelbaum, Fabrizio de Vico Fallani.

Project acronym: IHU-A-ICM

Project title: Institute of Translational Neuroscience

Founded in 2011

General Director: Bertrand Fontaine

The IHU-A-ICM program was selected, in 2011, in a highly competitive national call for projects. A 10-year, 55M€ program, has been implemented by a recently created foundation for scientific cooperation. Based on the clinical and scientific strenghts of the ICM and the hospital Department of Nervous System Diseases, it mainly supports neuroscience research, but is also invested in improving care and teaching. ARAMIS is strongly involved in the IHU-A-ICM project, in particular in WP6 (neuroimaging and electrophysiology), WP7 (biostatistics), WP2 (Alzheimer) and WP5 (epilepsy). We have started collaborations with the new bioinformatics/biostatistics platform (IHU WP7, head: Ivan Moszer), in particular through a joint project on the integration of imaging and genomics data.

9.1.3.2. ICM-Internal Research projects

Participants: Anne Bertrand [Correspondant], Takoua Kaaouana, Benoit Delatour, Alexandra Petiet, Olivier Colliot, Arnaud Marcoux.

Project title: The Histo-MRI project: targeting MR signature of tauopathy from micro- to macroscopy

Started in 2014

Coordinator: Anne Bertrand

Identifying morphological MR signatures of brain diseases usually follows a top-down process, which starts by describing a pattern of MR signal changes in patients, hypothesizes an underlying pathological mechanism, and confirms this mechanism by correlating the observed MR signal changes with histological lesions on post-mortem examination. This top-down process, relevant for large, centimetric brain lesions, becomes inappropriate when targeting the MR signal intensity changes associated with microscopic lesions. Our project aims at developing an MR biomarker of NFT using a new bottom-up approach. We will start by identifying the MR signal changes associated with the presence of NFT at the level of the histological slice, and utilize these findings to develop a method of NFT quantification on clinical, millimetric 3D MR images. To achieve this goal, we will develop and implement a 11.7T histological coil dedicated to the scanning of histological slices, which allows both ultra-high resolution MR imaging (up to 33 microns in-plane) and perfect co-registration with histological staining, performed subsequently on the same slice. This method has the potential to provide a novel biomarker of tauopathy that could not have been identified using the usual top-down approach. It also envisions the possibility to describe and understand new MRI contrasts in other neurodegenerative diseases associated with microscopic deposition of various proteins.

9.1.3.3. ICM-Internal Research projects

Participants: Mario Chavez, Fabrizio de Vico Fallani [Correspondant].

Project title: Non-invasive manipulation of brain synchrony to enhance brain function and rehabilitate faulty cognition in humans: A proof of concept

Started in 2014

Coordinator: Antoni Valero Cabre (ICM-team “Dynamiques Cérébrales, Plasticité et Rééducation”)

Other partners: Service des Urgences Cérébro-Vasculaires de l’Hôpital Pitié-Salpêtrière, Paris.

The long-term goal of this project is to develop the use of non-invasive manipulation of abnormal cerebral oscillations underlying cognitive activity to restore brain function in neurological patients. Cognitive functions emerge from large distributed networks organized in space and time. The short-term goal of this application is to study the causal role played by oscillatory activity in visual awareness and test whether their manipulation by non-invasive brain stimulation has the potential to restore its function in stroke patients.

9.1.3.4. ICM BBT Program - project PredictICD

Participants: Olivier Colliot [Correspondant], Jean-Christophe Corvol [Correspondant], Johann Faouzi.

Project title: Predict impulse control disorders in Parkinson’s disease (PREDICT-ICD)

Started in 2018

Coordinators: Olivier Colliot and Jean-Christophe Corvol (ICM)

In Parkinson’s disease (PD), the therapeutic strategy is based on the dopamine replacement therapy. Although available since the 1960s’, it is only relatively recently that behavioral disorders associated with these drugs have been described. Gathered under the term of “behavioral addiction”, they include impulse control disorders (ICDs), dopamine dysregulation syndrome (DDS), and punding. Interestingly, whereas addiction to L-dopa itself occurs quasi exclusively with L-dopa, ICDs appear electively under dopamine agonist (DA) therapy. The objectives of this project are: i) to elucidate the genetic basis of DA induced ICDs in PD patients from several international cohorts; ii) to develop and validate a machine learning model to predict the occurrence of ICDs from the combination of clinical and genetic data.

9.1.3.5. ICM BBT Program - project DYNAMO

Participants: Stanley Durrleman [Correspondant], Harald Hampel [Correspondant], Sabrina Fontanella, Simone Lista, Olivier Colliot, Stephanie Allassonniere, Jean-Baptiste Schiratti, Bruno Dubois, Hovagim Bakardjian, Remi Genthon, Enrica Cavedo, Katrine Rojkowa.

Project title: Dynamic models of disease progression across Alzheimer's disease stages informed by multimodal neuroimaging and biological data

Started in 2016

Coordinator: Stanley Durrleman and Harald Hampel

Other partners: Institut de la Mémoire et de la maladie d'Alzheimer

The estimation of data-driven models of disease progression for neurodegenerative diseases, including Alzheimer's disease (AD), is crucial to confirm, refine and extend the current hypothetical models. The estimation of such quantitative models from longitudinal data sets is notably difficult because of the lack of principled methodological frameworks for the analysis of spatiotemporal data.

The project builds on an innovative mathematical, statistical, and computational framework to automatically align the dynamics and the direction of individual trajectories of the evolving pathology, and then to infer a normative scenario of disease progression across different disease stages. The estimated scenario will combine spatiotemporal maps of lesion propagation, such as maps of amyloid deposition or cortical atrophy, and global measurements such as levels of CSF biomarkers. It will be possible to estimate not only a normative scenario but also the inter-individual variability in the values, dynamics and direction of both topographical and pathophysiological biomarkers changes during the course of the disease.

The application of this technology to publicly available and in-house longitudinal data sets of individuals from the asymptomatic at risk to the prodromal and dementia stages will yield new insights into the pathophysiology of AD from the preclinical to the AD dementia stages. This quantitative data-driven approach will be exploited to assess and refine the current qualitative hypothetical models of AD progression. Notably, it will complement these models with typical pathways of lesion propagation in the brain during disease progression. It will also highlight the effect of the known risk factors of AD such as apolipoprotein E genotype on the disease progression profile.

The project will open up the concrete possibility to derive a computer-aided diagnosis, staging, and prognosis tool for a better recruitment of patients in clinical studies and to assist clinicians in the diagnosis and the monitoring of both disease progression and treatment efficacy.

9.1.3.6. ICM BBT Program - project SEMAPHORE

Participants: Stanley Durrleman [Correspondant], Stéphane Lehéricy [Correspondant], Jean-Christophe Corvol, Marie Vidailhet, Raphael Couronné, Safia Said.

Project title: Personalized progression model of Parkinson's disease

Started in 2018

Coordinator: Stanley Durrleman and Stéphane Lehéricy

Other partners: Neurology and Neuro-radiology departments, Pitié-Salpêtrière Hospital, AP-HP

The aim of this project is to build a personalizable model of Parkinson's disease (PD) progression integrating the complex dynamical interplay between phenotypic, imaging, genetic and metabolic alterations. We will identify and validate markers for monitoring of progression of brain damage in early and prodromal PD and identify conversion markers in subjects at risk of PD (idiopathic rapid eye movement sleep behavior disorders iRBD, PD- related mutation carriers). We will describe the appearance, characterize clinical phenotypes of PD, and identify modifier genes of disease phenotype. To this aim, we will relie on a novel statistical learning method using Bayesian non-linear mixed-effects model allowing to combine and realign short term sequence data to estimate

a long-term scenario of disease progression. This method is able to estimate individual stages of disease progression and to analyze automatically non-linear spatiotemporal patterns of data change. It estimates both a group-average scenario of PD progression as well as the inter-individual variability of this model in terms of age at onset, pace of disease progression and variability in the spatiotemporal trajectory of data changes. We will analyse the effect of genetic variants in the modulation of these non-linear progression patterns, and assess the statistical power of the individual parameters encoding for these patterns. The method will be applied to two sets of longitudinal data from the local prospective NUCLEIPARK (60 PD patients, 20 patients with iRBD, 60 controls) and ICEBERG studies (200 early idiopathic PD, 50 iRBD, 30 GBA and LRRK2 PD-related mutation carriers, 50 controls). Examinations included clinical, biological, and neurophysiological data, and multimodal 3T MRI, DATScan, and skin and salivary gland biopsies. The models of PD progression for each category of subjects will be released to the community, as well as the software for reproducibility purposes.

9.1.3.7. ICM BBT Program - project ATTACK

Participants: Fabrizio de Vico Fallani [Correspondant], Charlotte Rosso [Correspondant], Marie-Constance Corsi, Laurent Hugueville.

Project title: ATTACK Brain Network Models Of Motor Recovery After Stroke

Started in 2018

Coordinator: Fabrizio De Vico Fallani, Charlotte Rosso

Other partners: Neurology and Stroke departments, Pitié-Salpêtrière Hospital, AP-HP

Like in other connected systems, studying the structure of the interactions between different brain regions has profound implications in the comprehension of emergent complex phenomena as, for example, the capability of the human brain to functionally reorganize after cerebrovascular "attacks" or stroke. This dynamic skill, which is known in neuroscience as neural plasticity, is not only interesting from a network science perspective, but it also plays a crucial role in determining the motor/cognitive recovery of patients who survive a stroke. As a critical innovation, this project proposes to develop a systematic and rigorous approach based on neuroimaging techniques, signal processing, and network science for the modeling and analysis of temporally dynamic neural processes that characterize motor recovery after stroke. To achieve these goals, this project is organized around the following objectives: i) acquiring a comprehensive longitudinal dataset of brain and behavioral/clinical data after stroke, ii) developing new analytic tools to characterize and generate temporally dynamic brain networks, iii) building network-based models of motor recovery after stroke, accounting for individual patients. These objectives involve an intensive gathering of heterogeneous mass data, their processing, the subsequent outcome interpretation and statistical simulation, as well as the development of longitudinal models and network-based diagnostics of the patient's motor recovery progress. Results will be first characterized from pure network-theoretic and neuroscience perspectives, so as to highlight fundamental research challenges, and then validated to clarify the importance and the applicability to the clinical scenario. Our results will unveil multiscale properties of dynamic brain networks and identify predictive neuromarkers for motor recovery after stroke. This project has a two-fold impact on the society. On the one hand, it will provide new methods and robust tools to properly characterize and model temporally dynamic networks in neuroscience. On the other hand, it will provide longitudinal models of motor recovery in stroke patients that can potentially unveil the neural substrate that underpins rehabilitation, improve prognosis, and eventually lower cost of hospitalization time. From a broader perspective this interdisciplinary project proposes a transformative approach to analyze large-scale neural systems.

9.1.4. National Networks

- GdR Statistics and Medicine - http://gdr-stat-sante.math.cnrs.fr/spip/
- GdR (MaDICS) Masses de Données, Informations et Connaissances en Sciences Big Data - Data ScienceStatistics and Medicine - http://www.madics.fr/reseaux/

- F. De Vico Fallani participated to the GdR (HANDICAP) in the framework of the future strategy of Inria
- F. De Vico Fallani was founding member of the CORTICO national network for brain-computer interfaces

9.1.5. Other National Programs

9.1.5.1. Programme Hospitalier de Recherche Clinique (PHRC)

Participants: Olivier Colliot, Stanley Durrleman, Didier Dormont.

- PHRC PredictPGRN, co-funding by Alzheimer Plan, *Caractérisation multimodale prospective de la démence frontotemporale dûe à des mutations du gène PGRN à un stade symptomatique et présymptomatique*. (Coordinator : A. Brice)
- PHRC ImaBio3, co-funding by Roche (pharmaceutical industry), *Rôle des réactions cellulaires sanguines, inflammatoires et immunitaires anti-amyloïde centrales et périphériques dans la maladie d'Alzheimer débutante*. (Coordinator : M. Sarazin)
- PHRC CAPP, *Caractérisation linguistique, anatomique/métabolique et biologique des différentes formes d'aphasie primaire progressive : vers le rationnel pour des essais pharmacologiques et des rééducations du langage ciblées*. (Coordinator: M. Teichmann)

9.1.5.2. Institut Universitaire d'Ingénierie pour la Santé (IUIS)

Participants: Mario Chavez, Xavier Navarro.

Project acronym: DYSPEV

Project title: Dépistage de la dyspnée par potentiels évoqués visuels

Funded in 2014

Amount: 38K€

Coordinator: Thomas Similowski

Other partners: UPMC, Inserm UMR 1158

Abstract: Steady state visual evoked potentials (SSVEP) have been widely utilized in brain computer interfacing (BCI) in last years. In this project, we explore the possibilities of SSVEP to manage the communication between patients suffering from respiratory disorders and health care providers. By imposing different breathing constraints, we use a SSVEP-based brain computer interface to help those subjects to communicate their breathing sensations (breathing well/breathing bad).

9.2. European Initiatives

9.2.1. FP7 & H2020 Projects

9.2.1.1. H2020 - Project EuroPOND

Participants: Olivier Colliot, Stanley Durrleman, Manon Ansart, Igor Koval, Alexandre Bône.

Project acronym: EuroPOND

Project title: Data-driven models for Progression Of Neurological Disease

Duration: Jan 2016 - Dec 2019

Amount: 6M€

Coordinator: Daniel Alexander

Other partners: University College London (UK), EMC Rotterdam (The Netherlands), VUMC (The Netherlands), Fate Bene Fratelli (Italy), Carol Besta Institute (Italy), Université de Genève (Switzerland), Icometrix (Belgium)

Abstract: EuroPOND will develop a data-driven statistical and computational modeling framework for neurological disease progression. This will enable major advances in differential and personalized diagnosis, prognosis, monitoring, and treatment and care decisions, positioning Europe as world leaders in one of the biggest societal challenges of 21st century healthcare. The inherent complexity of neurological disease, the overlap of symptoms and pathologies, and the high comorbidity rate suggests a systems medicine approach, which matches the specific challenge of this call. We take a uniquely holistic approach that, in the spirit of systems medicine, integrates a variety of clinical and biomedical research data including risk factors, biomarkers, and interactions. Our consortium has a multidisciplinary balance of essential expertise in mathematical/statistical/computational modelling; clinical, biomedical and epidemiological expertise; and access to a diverse range of datasets for sporadic and well-phenotyped disease types.The project will devise and implement, as open-source software tools, advanced statistical and computational techniques for reconstructing long-term temporal evolution of disease markers from cross-sectional or short-term longitudinal data. We will apply the techniques to generate new and uniquely detailed pictures of a range of important diseases. This will support the development of new evidence-based treatments in Europe through deeper disease understanding, better patient stratification for clinical trials, and improved accuracy of diagnosis and prognosis. For example, Alzheimer's disease alone costs European citizens around €200B every year in care and loss of productivity. No disease modifying treatments are yet available. Clinical trials repeatedly fail because disease heterogeneity prevents bulk response. Our models enable fine stratification into phenotypes enabling more focussed analysis to identify subgroups that respond to putative treatments.

9.2.1.2. FET Flagship - Human Brain Project

Participants: Olivier Colliot, Stanley Durrleman.

Project acronym: HBP

Project title: Human Brain Project

Sub-project: SP8 - Medical Informatics Platform

Duration: 2016-

Abstract: The Human Brain Project (HBP) is a European Commission Future and Emerging Technologies Flagship. The HBP aims to put in place a cutting-edge, ICT-based scientific Research Infrastructure for brain research, cognitive neuroscience and brain-inspired computing. The Project promotes collaboration across the globe, and is committed to driving forward European industry. Our team is involved in the Subproject SP8 (Medical Informatics Platform). The Medical Informatics Platform (MIP) is an innovative data management system that gives researchers the means to access and analyse large amounts of anonymized clinical neuroscience data. Within that framework, we will develop and implement a method to construct disease progression models from longitudinal biomarkers. The method will use statistical learning techniques to infer a long-term disease progression model from multiple short term data from a series of individuals. The model will account for variability in age at disease onset, pace of disease progression and trajectories of biomarkers changes across individuals in the observed population.

9.2.1.3. ERC - LEASP

Participant: Stanley Durrleman.

Project acronym: LEASP

Project title: Learning Spatiotemporal Patterns in Longitudinal Image Data Sets of the Aging Brain

Duration: 2016-2021

Abstract: Time-series of multimodal medical images offer a unique opportunity to track anatomical and functional alterations of the brain in aging individuals. A collection of such time series for several individuals forms a longitudinal data set, each data being a rich iconic-geometric representation of the brain anatomy and function. These data are already extraordinary complex and variable across individuals. Taking the temporal component into account further adds difficulty, in that each individual follows a different trajectory of changes, and at a different pace. Furthermore, a disease is here a progressive departure from an otherwise normal scenario of aging, so that one could not think of normal and pathologic brain aging as distinct categories, as in the standard case-control paradigm.

Bio-statisticians lack a suitable methodological framework to exhibit from these data the typical trajectories and dynamics of brain alterations, and the effects of a disease on these trajectories, thus limiting the investigation of essential clinical questions. To change this situation, we propose to construct virtual dynamical models of brain aging by learning typical spatiotemporal patterns of alterations propagation from longitudinal iconic-geometric data sets.

By including concepts of the Riemannian geometry into Bayesian mixed effect models, the project will introduce general principles to average complex individual trajectories of iconic-geometric changes and align the pace at which these trajectories are followed. It will estimate a set of elementary spatiotemporal patterns, which combine to yield a personal aging scenario for each individual. Disease-specific patterns will be detected with an increasing likelihood.

This new generation of statistical and computational tools will unveil clusters of patients sharing similar lesion propagation profiles, paving the way to design more specific treatments, and care patients when treatments have the highest chance of success.

9.3. International Initiatives

9.3.1. Informal International Partners

- F. De Vico Fallani has a collaboration with the University Penn, Philadelphia, US (Prof. Danielle Bassett).
- F. De Vico Fallani has a collaboration with the University of Rome, Italy (Prof. Stefania Colonnese).
- O. Colliot has an enduring collaboration with the Center for Magnetic Resonance Research, University of Minnesota, USA (P-F Van de Moortele, T. Henry).
- S. Durrleman and O. Colliot have a collaboration with the Center for Medical Image Computing (CMIC) at University College London (UCL), London, UK (D. Alexander, H. Zhang).

9.4. International Research Visitors

9.4.1. Visits of International Scientists

- Dr. Sarah-Christine Villeneuve spent a year from the 4th of December 2017 to the 30th of November 2018 as a clinical research fellow in Pitié Salpêtrière Hospital under the supervision of Stéphane Epelbaum (Sabbatical program).

ATHENA Project-Team

7. Partnerships and Cooperations

7.1. Regional Initiatives

7.1.1. Université Côte d'Azur projects

7.1.1.1. Tech-ICOPA

Participants: Maureen Clerc, Théodore Papadopoulo, Sofiane Guebba, Marie-Hélène Soriani [CHU Nice], Mariane Bruno [CHU Nice], Violaine Guy [CHU Nice].

Duration: 24 months

Improving autonomy is a main priority for people with disabilities. The goal of this project is to create a version usable by patients at their home of a brain-computer interface (BCI) research prototype system developped in our project-team. Making this technology actually usable in the context of pathology inducing severe disabilities such as ALS (Amyotrophic Lateral Sclerosis) is a challenge. Tackling this challenge would allow both to meet the expectations of dependent people and to envision a more widespread use of this technology. To reach this goal, several technological advances and industrial developments are needed : (i) developing a suitable ergonomic headset, wireless, functional, comfortable, incorporating a miniaturized amplifier (Nice University Hospital Center - ALS Center), (ii) reducing the number of electrodes while maintaining signal quality (Inria - UCA) and (iii) testing the prolonged use of dry electrodes. In addition to these technological advances, the Tech-ICOPA translational project aims at (1) improving the use of BCI in communication, in accessing the digital world, home automation and robotics and (2) enhancing the use of BCI in commercial applications.

7.1.1.2. EPI-ANALYSE

Participants: Fabrice Duprat [IPMC], Théodore Papadopoulo, Massimo Mantegazza [IPMC], Maureen Clerc.

Duration: 12 months

This project aims at developing two complementary analysis softwares dedicated to the detection of epileptic seizures in mice in order to study epileptogenesis and the consequences of spontaneous seizures. The first software will be the adaptation to the mouse EEG of a powerful algorithm based on a dictionary learning method developed by our project-team. We will use video-EEG recordings already made and analyzed at the IPMC to optimize and validate the new software. This will allow a detailed analysis of seizures and events occurring between seizures (e.g., interictal spikes). The second software deals with the analysis of video recordings of 3 models of mice not recordable until now with EEG. The implementation, recordings and the analysis of the 3 models will be carried out during this project. A prototype of this software already exists at IPMC (in Python, with OpenCV) but the analysis algorithm must be optimized. Semi-automatic video analysis will allow an easy identification of temporal segments corresponding to epileptic seizures. This will help the experimenter to classify the behavioral severity of seizures.

7.1.1.3. MICADome

Participants: Maureen Clerc, Michel Pascal [CNR Nice].

Duration: 24 months

The MICA-Dome project (MICA : Musique Interactive Côte d'Azur) initiates collaborative research between arts, science and humanities within a laboratory for exploring the sound spatialization in 3D, and its usage for an immersive music composition. For this MICADome will be equipped with a "Dome" of loudspeakers for 3D spatialization. Our team collaborates in MICADome in order to develop and anlyze EEG experiments to analyze the neural correlates of spatial auditory attention.

7.2. National Initiatives

7.2.1. Inria Project Lab

7.2.1.1. IPL BCI-LIFT

Participants: Maureen Clerc, Théodore Papadopoulo, Nathalie Gayraud, Federica Turi, Romain Lacroix.

Duration: *January 2015 to December 2018*

The Inria Project-Lab BCI-LIFT is an Inria-funded reasearch consortium to foster collaborative research on Brain-Computer Interfaces on the topic of Learning, Interaction, Feedback and Training. It is coordinated by Maureen Clerc. Its members are from 6 Inria teams: ATHENA, CAMIN, HYBRID, MJOLNIR, NEUROSYS, POTIOC, and from Dycog team from CRNL Lyon, and University of Rouen. The goal is to reach a next generation of non-invasive Brain-Computer Interfaces (BCI), more specifically BCI that are easier to appropriate, more efficient, and suit a larger number of people. For more information, refer to the BCI-LIFT website.

7.2.2. ANR

7.2.2.1. ANR NeuroRef

Participants: Demian Wassermann [Inria Parietal], Antonia Machlouziredes, Guillermo Gallardo Diez, Rachid Deriche.

Duration: *October 2016 to September 2019*
Call: *NSF-ANR Program Collaborative Research in Computational Neuroscience 2015*

This project is a collaboration with Pr. S. Bouix and his team at the Psychiatry NeuroImaging Lab, Dept of Radiology, Brigham and Women's Hospital, Harvard Medical School (USA) to build MRI reference atlases to analyze brain trauma and post-traumatic stress. The goal is to develop a robust framework to perform subject-specific neuroimaging analyses of Diffusion MRI (dMRI), as this modality has shown excellent sensitivity to brain injuries and can locate subtle brain abnormalities that are not detected using routine clinical neuroradiological readings.

7.2.2.2. ANR MOSIFAH

Participants: Rachid Deriche, Abib Olushola Yessouffou Alimi, Rutger Fick [TheraPanacea, Paris], Demian Wassermann [Inria Parietal], Théodore Papadopoulo.

Duration: *October 2013 to September 2018*
Call: *ANR Numerical Models 2013*

This ANR project is about multimodal and multiscale modelling and simulation of the fiber architecture of the human heart. It started on October 2013 and involves three partners: Creatis Team, INSA, Lyon (I. Magnin, Y. Zhu); TIMC-IMAG, CNRS, Grenoble (Y. Uson) and the ATHENA project team.

It consists in modelling and simulating the ex vivo and in vivo 3D fiber architectures at various scales using multiphysical data from different imaging modalities working at different spatial resolutions. To this end, the myocardium of the human heart will be imaged using respectively Polarized Light Imaging (PLI) and dMRI.

7.2.2.3. ANR VIBRATIONS

Participants: Théodore Papadopoulo, Maureen Clerc, Rachid Deriche, Demian Wassermann [Inria Parietal].

Duration: *February 2014 to February 2019*
Call:ANR Programme de Recherche Translationnelle en Santé (PRTS) 2013

The VIBRATIONS project proposes to simulate in a biologically realistic way MEG and EEG fields produced by different configurations of brain sources, which will differ in terms of spatial and dynamic characteristics. The research hypothesis is that computational and biophysical models can bring crucial information to clinically interpret the signals measured by MEG and EEG. In particular, they can help to efficiently address some complementary questions faced by epileptologists when analyzing electrophysiological data.

7.2.3. ADT

7.2.3.1. ADT BCI-Browser

Participants: Théodore Papadopoulo, Maureen Clerc.

Duration: 1 year

Most often, BCI techniques are demonstrated in simple toy applications made. The only "few" real BCI applications are specific developments and are not used much as they lack of functionality, maintenance, ... The goal of this development contract is to demonstrate a new approach to BCI, in which BCI interactions are integrated in existing applications. Ideally, the original software is not modified and not even recompiled. It is modified by providing either modified GUI libraries or providing extensions as plugins. As a proof of concept, we aim at modifying C++/Qt applications with a focus on web browsing, by redefining some of its basic interactions (mouse clicks, keyboard, ...) using some BCI components. In this manner, it might be possible to drive standard and state-of-the-art application using BCI and at a limited maintenance cost.

This contract is part of the AMDT initiative.

7.2.3.2. ADT BOLIS 2

Participants: Théodore Papadopoulo, Juliette Leblond [FACTAS project-team], Jean-Paul Marmorat [CMA Ecole des Mines Paritech].

Duration: *6 months.*

This contract is a follow-up of ADT BOLIS which aimed at building a sofware platform dedicated to inverse source localisation, building upon the elements of software found in FindSources3D. The platform is modular, ergonomic, accessible and interactive and offers a detailed visualisation of the processing steps and the results. Its goal is to provide a convenient graphical interface and a tool that can be easily distributed and used by professionals (target audience: clinicians and researchers). BOLIS 2 aims at simplifying some maintenance aspects of the software.

This contract is part of the AMDT initiative.

7.2.3.3. ADT OpenMEEG

Participants: Théodore Papadopoulo, Maureen Clerc, Kostiantyn Maksymenko, Alexandre Gramfort [PARIETAL], Joan Massich [PARIETAL].

Duration: *24 months.*

The OpenMEEG ADT aims at improving OpenMEEG along 3 main directions:

1. Offer a user interface for the creation and verification of head models most importantly for a simpler management of non-nested head models.
2. Improve the Python interface (extension and reliability). This will also be useful to develop new research axes (in connection with point 3).
3. Enrich the available operators and refactor the code to offer new possibilities in OpenMEEG and reduce the cost of maintenance.

In addition to the expected gains in code maintenance, these improvements will allow a number of new – more sophisticated – applications as well as open OpenMEEG to a larger audience with a simplified interface for classical use-cases.

This contract is part of the AMDT initiative.

7.3. European Initiatives

7.3.1. FP7 & H2020 Projects

7.3.1.1. ERC AdG CoBCoM

Program: H2020-EU.1.1. (ERC-ADG-2015 - ERC Advanced Grant)

Project acronym: CoBCoM - **ID:** 694665

Project title: *Computational Brain Connectivity Mapping*

Start date: 2016-09-01, End date: 2021-08-31

P.I. : R. Deriche

Partners: ATHENA project-team

Abstract:

One third of the burden of all the diseases in Europe is due to problems caused by diseases affecting brain. Although exceptional progress has been obtained for exploring it during the past decades, **the brain is still terra-incognita** and calls for specific research efforts to better understand its architecture and functioning.

CoBCoM is our response to this great challenge of modern science with the overall goal to **develop a joint Dynamical Structural-Functional Brain Connectivity Network** (DSF-BCN) solidly grounded on advanced and integrated methods for diffusion Magnetic Resonance Imaging (dMRI) and Electro & Magneto-Encephalography (EEG & MEG).

To take up this grand challenge and achieve new frontiers for brain connectivity mapping, we will develop a new generation of computational models and methods for identifying and characterizing the structural and functional connectivities that will be at the heart of the DSF-BCN. Our strategy is to break with the tradition to incrementally and separately contributing to structure or function and develop **a global approach involving strong interactions between structural and functional connectivities.** To solve the limited view of the brain provided just by one imaging modality, our models will be developed under a rigorous computational framework integrating complementary non invasive imaging modalities: dMRI, EEG and MEG.

CoBCoM will push far forward the state-of-the-art in these modalities, developing **innovative models and ground-breaking processing tools** to provide in-fine a joint DSF-BCN solidly grounded on a detailed mapping of the brain connectivity, both in space and time.

Capitalizing on the strengths of dMRI, MEG & EEG methodologies and building on the **bio-physical and mathematical foundations** of our new generation of computational models, CoBCoM will be applied to high-impact diseases, and its **ground-breaking computational nature and added clinical value** will open new perspectives in neuroimaging.

7.3.1.2. ChildBrain ETN

ATHENA is an Associated Partner in the ChildBrain European Training Network: the team participates in training workshops and receive PhD students in secondments.

Program: European Training Network

Project acronym: ChildBrain

Project title: Advancing brain research in children's developmental neurocognitive disorders

Duration: March 2015 to March 2019

Coordinator: Prof. Paavo Leppänen, University of Jyväskylä, Finland

Other partners: University of Leuven (Belgium), University of Münster (Germany), Rabboud University (The Netherlands), Aston University (United Kingdom), IcoMetrix (Belgium), Elekta (Finland), BESA (Germany)

Abstract: The purpose of the ChildBrain ETN is to train young scientists, i.e. Early Stage Researchers (ESRs), to utilise evidence-based neuroscientific knowledge for helping children, especially those at high risk for dropout due to neurocognitive disorders, to meet future educational and societal demands.

7.4. International Initiatives

7.4.1. Inria International Partners

7.4.1.1. Declared Inria International Partners

- Sherbrooke University, CA (M. Descoteaux)
- CMRR, University of Minnesota, USA (C. Lenglet)
- Verona University, It (G. Menegaz)
- Department of CISE, the University of Florida, Gainesville, USA (B. C. Vemuri)
- Centre for Medical Image Computing (CMIC), Dept. Computer Science, UCL, UK (D. Alexander)
- SBIA, University of Pennsylvania Medical School, USA (R. Verma).
- EEMagine company on EEG/MEG hardware.

7.4.1.2. Informal International Partners

- University Houari Boumedienne (USTHB, Algiers) (L. Boumghar) and University of Boumerdes, (D. Cherifi), Algeria.

7.5. International Research Visitors

7.5.1. Visits of International Scientists

- Dr. Ragini Verma, Section of Biomedical Image Analysis, Center for Biomedical Image Computing and Analytics, Department of Radiology, University of Pennsylvania, USA (Oct 1st, 2018 - Dec 21st, 2018)
- Dr. Moo K. Chung, Waisman Laboratory for Brain Imaging and Behavior, University of Wisconsin-Madison, From Sept.10 to 14, 2018

7.5.1.1. Internships

- Rebecca Bonham-Carter - Queen's University, Kingston, Canada, From early May to late July, 2918.
- Max Amatsuji-Berry - Queen's University, Kingston, Canada, From early May to late July, 2918.
- Etienne Saint-Onge - Sherbrooke University, From Early Feb. to early June 2018.

BIOVISION Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Modélisation Théorique et Computationnelle en Neurosciences et Sciences Cognitives

The Biovision team is a member of this "Axe Interdisciplinaire de Recherche de l'Université de Nice – Sophia Antipolis" and of the Institute Neuromod of neuroscience modelling . Biovision team has participated to the Rencontre C@UCA 2018 in Fréjus (June 2018). This axe is partly funding our work on retinal waves.

8.2. National Initiatives

8.2.1. ANR

8.2.1.1. Trajectory

Title: Encoding and predicting motion trajectories in early visual networks

Programme: ANR

Duration: October 2015 - September 2020

Coordinator: Invibe Team, Institut des Neurosciences de la Timone, Frédéric Chavane,

Partners:

Institut de Neurosciences de la Timone (CNRS and Aix-Marseille Université, France)

Institut de la Vision (Paris, France)

Universidad Tecnico Federico Santa María (Electronics Engineering Department, Valparaíso, Chile)

Inria contact: Bruno Cessac

Global motion processing is a major computational task of biological visual systems. When an object moves across the visual field, the sequence of visited positions is strongly correlated in space and time, forming a trajectory. These correlated images generate a sequence of local activation of the feed-forward stream. Local properties such as position, direction and orientation can be extracted at each time step by a feed-forward cascade of linear filters and static non-linearities. However such local, piecewise, analysis ignores the recent history of motion and faces several difficulties, such as systematic delays, ambiguous information processing (e.g., aperture and correspondence problems) high sensitivity to noise and segmentation problems when several objects are present. Indeed, two main aspects of visual processing have been largely ignored by the dominant, classical feed-forward scheme. First, natural inputs are often ambiguous, dynamic and non-stationary as, e.g., objects moving along complex trajectories. To process them, the visual system must segment them from the scene, estimate their position and direction over time and predict their future location and velocity. Second, each of these processing steps, from the retina to the highest cortical areas, is implemented by an intricate interplay of feed-forward, feedback and horizontal interactions. Thus, at each stage, a moving object will not only be processed locally, but also generate a lateral propagation of information. Despite decades of motion processing research, it is still unclear how the early visual system processes motion trajectories. We, among others, have proposed that anisotropic diffusion of motion information in retinotopic maps can contribute resolving many of these difficulties. Under this perspective, motion integration, anticipation and prediction would be jointly achieved through the interactions between feed-forward, lateral and feedback propagations within a common spatial reference frame, the retinotopic maps. Addressing this question is particularly challenging, as it requires to probe these sequences of events at multiple

scales (from individual cells to large networks) and multiple stages (retina, primary visual cortex (V1)). “TRAJECTORY” proposes such an integrated approach. Using state-of-the-art micro- and mesoscopic recording techniques combined with modeling approaches, we aim at dissecting, for the first time, the population responses at two key stages of visual motion encoding: the retina and V1. Preliminary experiments and previous computational studies demonstrate the feasibility of our work. We plan three coordinated physiology and modeling work-packages aimed to explore two crucial early visual stages in order to answer the following questions: How is a translating bar represented and encoded within a hierarchy of visual networks and for which condition does it elicit anticipatory responses? How is visual processing shaped by the recent history of motion along a more or less predictable trajectory? How much processing happens in V1 as opposed to simply reflecting transformations occurring already in the retina? The project is timely because partners master new tools such as multi-electrode arrays and voltage-sensitive dye imaging for investigating the dynamics of neuronal populations covering a large segment of the motion trajectory, both in retina and V1. Second, it is strategic: motion trajectories are a fundamental aspect of visual processing that is also a technological obstacle in computer vision and neuroprostheses design. Third, this project is unique by proposing to jointly investigate retinal and V1 levels within a single experimental and theoretical framework. Lastly, it is mature being grounded on (i) preliminary data paving the way of the three different aims and (ii) a history of strong interactions between the different groups that have decided to join their efforts.

8.3. European Initiatives

- Program: Leverhulme Trust
- Project acronym:
- Project title: A novel approach to functional classification of retinal ganglion cells
- Duration: 2017-2020
- Coordinator: Evelyne Sernagor, Institute of Neuroscience (ION, Newcastle, UK)
- Inria contact: Bruno Cessac
- Other partners:

  Melissa Bateson Institute of Neuroscience (ION, Newcastle, UK)

  Matthias Hennig Institute for Adaptive and Neural Computation (ANC, School of Informatics University of Edinburgh, UK)
- Abstract: Vision begins with photoreceptors converting light from different parts of the visual scene into electrical signals, compressing our visual world into a parsimonious code of impulses at the retinal output level, the retinal ganglion cells (RGCs). This information is sent to the brain via only $\approx$1m RGCs (45,000 in mouse). Amazingly, the brain can recreate images from interpreting these “barcodes” or trains of impulses. This ability is partly due to the astonishing functional diversity of RGCs, each interpreting a different feature of the visual scene. It is all these parallel streams of information that impart the complexity of visual scenes to our brain visual areas. At present, at least 30 RGC subtypes have been identified. Classification is typically based on common anatomical features, or on basic functions (e.g. whether cells respond to the onset or offset of the light, or whether they are sensitive to motion direction) and it has recently progressed to include molecular markers. Recent studies have successfully characterised common physiological properties between RGCs sharing gene expression, suggesting that their molecular signature may indeed be a good indicator of function. However, according to mouse genetics repositories (e.g., the Allen Brain Project) many genes are expressed in subpopulations of RGCs for which we have no phenotype yet. Genes that are expressed in most RGCs probably do not reflect specific functional populations, but some other genes are expressed only in sparse RGC groups. Each gene-specific class exhibits a distinct spatial mosaic pattern across the retina, suggesting that the cells belong to a common group. Many classes, even sparse, exhibit asymmetric distributions across the retina, e.g., with larger

numbers on the ventral or dorsal side, suggesting specific roles in ecological vision, e.g., specialised in detecting moving objects in the sky (ventral) or on the ground (dorsal).

We propose to develop a multidisciplinary approach to functionally phenotype "new" RGC subclasses sharing gene expression. Rather than inferring knowledge about the entire population from studying individual cells, we will take a global approach based on large-scale, high-density pan-retinal recordings, pharmacogenetics (allowing us to selectively silence defined cell populations at will) and high-resolution imaging combined with computational approaches and behaviour. This novel approach necessitates collaboration between retinal neurophysiologists, animal behaviour specialists (Newcastle) and modellers (Inria) who specialise in visual processing and have sophisticated mathematical tools and software to handle and interpret the encoding of visual information at the pan-retinal level.

8.4. International Initiatives

8.4.1. International Research Network to Study Predictive Coding in the Retina

Program: CHILEAN SUPPORT OF INTERNATIONAL NETWORKING BETWEEN RESEARCH CENTRES

Project title: International Research Network to Study Predictive Coding in the Retina

Duration: 2018-2020

Coordinator: Maria-José Escobar, Advanced Center for Electrical and Electronic Engineering, Universidad Técnica Federico Santa María, Chile

Other partners:

Advanced Center for Electrical and Electronic Engineering (Valparaiso, Chili)

Centro Interdisciplinario de Neurociencia de Valparaíso (CINV, Valparaíso, Chile)

Abstract: The retina, a well-structured multilayer neural system, encodes the visual information of the environment from an input of photon flux to a series of electrical pulses that are ultimately readout by the brain to create perception and program motor actions. The retina, from an engineering point of view, can be seen as a series of circuits computing visual features from the visual world in parallel encoding only informative inputs that are then sent to the brain. Regarding all the visual features that can be detected from the outer world, motion processing represents a fundamental visual computation ruling many visuomotor behaviours. Motion sensitive neurons have been early reported in the retina, but recently additional features have been added to the pool of capabilities present in this organ: especially motion direction selectivity and predictive coding. Motion processing presents predictive coding characteristics, in the sense that there is an anticipatory response of the visual system when an object in motion follows a trajectory in the visual field. Motion anticipation is fundamental for survival. Interestingly, this mechanism, observed in the visual cortex, has been also reported in the retina. Understanding how the visual system accumulates information along a certain trajectory raises fundamental questions about neural computation, its dynamics, and implementation. This understanding could be also extended to new algorithms to image/video processing, and also, autonomous navigation of robots.

In this project, we propose the formal establishment of a collaborative network between the AC3E Biomedical System group (AC3E-UTFSM), Centro Interdisciplinario de Neurociencia de Valparaíso (CINV -UV) and Biovision team (Inria Sophia-Antipolis Mediterranée), gathering together skills related with physiological recording in the retina, data analysis and theoretical tools to implement functional and biophysical models. This network aims to study the anticipatory response observed in the mammalian retina, characterizing its underlying mechanisms and the predictive coding capabilities present in this part of the nervous system.

8.4.2. Inria International Partners

8.4.2.1. Declared Inria International Partners

Institute of Neuroscience (ION, Newcastle, UK)

Institute for Adaptive and Neural Computation (ANC, School of Informatics University of Edinburgh, UK)

Universidad Tecnico Federico Santa María (Electronics Engineering Department, Valparaíso, Chile)

Centro Interdisciplinario de Neurociencia de Valparaíso (CINV, Valparaíso, Chile)

University of Genoa (DIBRIS, Genoa, Italy)

8.5. International Research Visitors

8.5.1. Visits of International Scientists

Prof. Sarah Barman (School of Computer Science and Mathematics, Kingston University)

Dr Matteo Di Volo (Unité de Neurosciences Information et Complexité, Gif sur Yvette, France)

Dr Cyril Eleftheriou (IIT, Genova)

Dr Maria-José Escobar (Universidad Tecnico Federico Santa María (Electronics Engineering Department, Valparaíso, Chile))

8.5.1.1. Internships

Téva Andréoletti (Apr–Aug 2018)

Adrianna Janik (Oct 2017–Mar 2018)

Paula Pawlowski (Apr–Sept 2018)

CAMIN Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

We have obtained a financial support from Occitanie Region for the CIFRE PhD thesis (Xynue Lu) with NEURORESP Company "PILE CIFRE" BREATHLOOP.

8.2. National Initiatives

- Inria ADT STIMBIO

  Participants : Christine Azevedo, Daniel Simon, Ronan Le Guillou, Benoît Sijobert.

  A 1-year engineer (R. LeGuillou) was funded by Inria ADT on the development of an architecture dedicated to FES-cycling platform.

- I-SITE MUSE COMPANIES AND CAMPUS grant

  Collaboration with academic local partners (CHU, IES) and NEURINNOV company on the spinal stimulation for bladder and bowel functions restoration. This is linked to an ongoing collaboration with Oslo University (Norway).

- LABEX NUMEV MEDITAPARK

  Collaboration with Montpellier Hospital (Neurology service) and the Montpellier Mindfulness Center to analyze the impact of meditation on upper limb tremor.

- EDF Foundation

  Collaboration with La Châtaigneraie Hospital on FES-assisted cycling. Financial support for a study on FES-cycling training method and performance otimization on individuals with complete spinal cord injury.

- I-SITE MUSE - EXPLORE

  Support for the visit of Henrique Resende (UFMG, Brazil) and Emersion Fachin (UNB, Brazil) as guest researchers from December to February 2019. Completed with a LIRMM laboratory financial aid.

8.3. European Initiatives

Program: EIT Health

Project acronym: Agilis

Project title: Restoration of Hand Functions in Tetraplegia through Selective Neural Electrical Stimulation

Duration: Jan. 2019 - June 2020

Coordinator: Camin Inria

Other partners: APHP, Univ. Heidelberg, CRF La Châtaigneraie, Neurinnov.

Abstract: Complete tetraplegia leads to inability to move, thus use, both hands. To date, there is no solution to restore this absolutely needed function for very common daily activities such as social interactions, washing, eating or self catheterizing. We aim at an innovative implanted stimulation of only two nerves associated with an intuitive interface. It will provide functional grasping without a third person and thus will drastically increase the autonomy of such people for the rest of their life.

8.4. International Initiatives

8.4.1. Inria Associate Teams Not Involved in an Inria International Labs

8.4.1.1. CACAO

Title: Lower limb electrical stimulation for function restoration

International Partner (Institution - Laboratory - Researcher):

UNB Brasilia (Brazil), Physiotherapy department, Emerson Fachin Martins.

Start year: 2016

See also: https://team.inria.fr/cacao/

Electrical stimulation (ES) can activate paralyzed muscles to support rehabilitation. ES applied to fully or partially paralyzed muscles artificially induces muscle contraction substituting or completing the normal volitional control. In CACAO team we join our efforts and specific expertise to develop approaches of lower limb function restoration in spinal cord injured individuals. Two main applications have been addressed: 1) Functional Electrical Stimulation (FES) to assist SCI individuals to perform pivot transfers and 2) FES-assisted cycling. We aim at proposing solutions that can have an effect on patients' quality of life, thus our choices intend to be realistic form a practical point of view.

8.4.1.2. Informal International Partners

CAMIN collaborates with Dr JL Boulland (Norwegian Center for Stem Cell Research at Oslo University Hospital in Norway) on FES-assisted bladder and bowel functions restoration.

8.5. International Research Visitors

Henrique Resende (UFMG, Brazil) and Emerson Fachin (UNB, Brazil) will spend 3 months in CAMIN team from December 2018 to February 2019 to work on FES-cycling project.

EPIONE Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

- N. Ayache and P. Robert are principal investigators of the project MNC3 (Médecine Numérique, Cerveau, Cognition, Comportement) funded by Idex Jedi UCA (2017-2021, 450k€). M. Lorenzi (Inria) actively participates to the supervision of this project with the help of V. Manera (ICP).
- Hervé Delingette is the principal investigator of the LungMark project funded by Idex Jedi UCA (2018-2021).
- Hervé Delingette is the principal investigator of the CIMPLE project, funded by Idex Jedi UCA (2018-2021), the region PACA and Oticon Medical. The region PACA and Oticon Medical are co-funding the Phd of Zihao Wang.
- Marco Lorenzi is principal investigator of the project Big Data for Brain Research, funded during 2017-20 by the Départment des Alpes Maritimes.
- Marco Lorenzi is principal investigator of the project MetaImaGen, funded by Idex Jedi UCA (2018-2020, 37k€).
- Maxime Sermesant is principal investigator of the project "The Digital Heart" and the innovation action "Digital Heart Phantom" with General Electrics, funded by Idex UCA Jedi. These projects gather the local cardiac research in academia, clinics and industry.

8.2. National Initiatives

8.2.1. Consulting for Industry

- Nicholas Ayache is a scientific consultant for the company Mauna Kea Technologies (Paris).
- Marco Lorenzi is a scientific consultant for the company MyDataModels (Sophia Antipolis).
- Xavier Pennec is a scientific consultant for the company Median Technologies (Sophia Antipolis)
- Maxime Sermesant is a scientific consultant for the company inHEART (Bordeaux)

8.2.2. Collaboration with national hospitals

The Epione-project team collaborates with the following 3 French IHU (University Hospital Institute): the IHU-Strasbourg (Pr J. Marescaux and L. Soler) on image-guided surgery, the IHU-Bordeaux (Pr M. Haïssaguere and Pr P. Jaïs) on cardiac imaging and modeling and the IHU-Pitié Salpétrière (Dr. O. Colliot and S. Durrleman) on neuroimaging.

We also have long term collaborations with the CHU Nice and Centre Antoine Lacassagne in Nice.

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

8.3.1.1. ERC ECSTATIC

Title: Electrostructural Tomography – Towards Multiparametric Imaging of Cardiac Electrical Disorders

Programm: H2020

Type: ERC

Duration: 2017 - 2022

Coordinator: U. Bordeaux

Inria contact: Maxime Sermesant

Cardiac electrical diseases are directly responsible for sudden cardiac death, heart failure and stroke. They result from a complex interplay between myocardial electrical activation and structural heterogeneity. Current diagnostic strategy based on separate electrocardiographic and imaging assessment is unable to grasp both these aspects. Improvements in personalized diagnostics are urgently needed as existing curative or preventive therapies (catheter ablation, multisite pacing, and implantable defibrillators) cannot be offered until patients are correctly recognized.

ECSTATIC aims at achieving a major advance in the way cardiac electrical diseases are characterized and thus diagnosed and treated, through the development of a novel non-invasive modality (Electrostructural Tomography), combining magnetic resonance imaging (MRI) and non-invasive cardiac mapping (NIM) technologies.

The approach will consist of: (1) hybridising NIM and MRI technologies to enable the joint acquisition of magnetic resonance images of the heart and torso and of a large array of body surface potentials within a single environment; (2) personalising the inverse problem of electrocardiography based on MRI characteristics within the heart and torso, to enable accurate reconstruction of cardiac electrophysiological maps from body surface potentials within the 3D cardiac tissue; and (3) developing a novel disease characterisation framework based on registered non-invasive imaging and electrophysiological data, and propose novel diagnostic and prognostic markers.

This project will dramatically impact the tailored management of cardiac electrical disorders, with applications for diagnosis, risk stratification/patient selection and guidance of pacing and catheter ablation therapies. It will bridge two medical fields (cardiac electrophysiology and imaging), thereby creating a new research area and a novel semiology with the potential to modify the existing classification of cardiac electrical diseases.

8.3.1.2. ERC G-statistics

Title: Biophysical Modeling and Analysis of Dynamic Medical Images

Programme: FP7

Type: ERC

Period: 2018-2023

Coordinator: Inria

Inria contact: Xavier Pennec

G-Statistics aims at exploring the foundations of statistics on non-linear spaces with applications in the Life Siences. Invariance under gauge transformation groups provides the natural structure explaining the laws of physics. In life sciences, new mathematical tools are needed to estimate approximate invariance and establish general but approximate laws. Rephrasing Poincaré: a geometry cannot be more true than another, it may just be more convenient, and statisticians must find the most convenient one for their data. At the crossing of geometry and statistics, G-Statistics aims at grounding the mathematical foundations of geometric statistics and to exemplify their impact on selected applications in the life sciences.

So far, mainly Riemannian manifolds and negatively curved metric spaces have been studied. Other geometric structures like quotient spaces, stratified spaces or affine connection spaces naturally arise in applications. G-Statistics will explore ways to unify statistical estimation theories, explaining how the statistical estimations diverges from the Euclidean case in the presence of curvature, singularities, stratification. Beyond classical manifolds, particular emphasis will be put on flags of subspaces in manifolds as they appear to be natural mathematical object to encode hierarchically embedded approximation spaces.

In order to establish geometric statistics as an effective discipline, G-Statistics will propose new mathematical structures and characterizations of their properties. It will also implement novel generic algorithms and illustrate the impact of some of their efficient specializations on selected

applications in life sciences. Surveying the manifolds of anatomical shapes and forecasting their evolution from databases of medical images is a key problem in computational anatomy requiring dimension reduction in non-linear spaces and Lie groups. By inventing radically new principled estimations methods, we aim at illustrating the power of the methodology and strengthening the "unreasonable effectiveness of mathematics" for life sciences.

8.3.2. Collaborations in European Programs, Except FP7 & H2020

Program: ERA CoSysMed
Project acronym: SysAFib
Project title: Systems medicine for diagnosis and stratification of atrial fibrillation
Duration: Mai 2016 - Mai 2019
Coordinator: Simula, Norway
Inria contact: Maxime Sermesant
Other partners: Inria, Helmholtz Zentrum München, Oslo University Hospital, Maastricht University, CardioCentro Ticino/CCMC
Abstract: Atrial fibrillation (AF) sharply increases the risk of stroke and is associated with a number of other severe complications, including heart failure. The SysAFib project aims to combine advanced data analysis and computer simulations with classical clinical approaches to create a decision support tool for treating AF. Diverse data sources, such as the individual patient's medical history, clinical measurements and genetic data will be combined into a single tool for optimizing and personalizing AF therapy. SysAFib's ultimate goal is to deliver the right treatment to the right patient at the right time, stopping AF in its tracks and ending the need for repeat invasive procedures.

8.4. International Initiatives

8.4.1. Inria International Labs

Inria@SiliconValley
Associate Team involved in the International Lab:

8.4.1.1. GeomStats

Title: Geometric Statistics in Computational Anatomy: Non-linear Subspace Learning Beyond the Riemannian Structure
International Partner (Institution - Laboratory - Researcher):
Stanford (United States) - Department of Statistics - Susan Holmes
Start year: 2018
See also: http://www-sop.inria.fr/asclepios/projects/GeomStats/
The scientific goal of the associated team led by X. Pennec is to develop the field of geometric statistics with key applications in computational anatomy. Computational anatomy is an emerging discipline at the interface of geometry, statistics, image analysis and medicine that aims at analysing and modelling the biological variability of the organs shapes at the population level. An important application in neuroimaging is the spatial normalization of subjects that is necessary to compare anatomies and functions through images in populations with different clinical conditions. Following the developments of the last 3 years of the associated team GeomStat, the new research directions have been broken into three axes. The first axis aims at continuing the progresses in theoretical and applied Geometric statistics, with a first theme studying the impact of curvature on the estimation with a finite sample, and a second axis extending the current work on Barycentric Subspace Analysis (BSA), notably with algorithms. The second axis aims at developing a hierarchical atlas of the brain anatomy based on the stratification of the space of image orbits under diffeomorphisms. The third axis explores three important applications of low-dimensional subspace learning in manifolds using BSA in neuroscience: the approximation of EEG signals for brain-computer interfaces (BCI); the acceleration and robustification of Tensor Distribution Functions (TDF) estimation in diffusion images; and the efficient inference in spaces of rank-deficient symmetric matrices for imaging-genetics from multi-centric databases.

8.4.2. Inria Associate Teams Not Involved in an Inria International Labs

8.4.2.1. PersoCardioLearn

Title: Personalization of Cardiac Models using Experimental Data and Machine Learning

International Partner (Institution - Laboratory - Researcher):

University of Toronto (Canada) - Sunnybrook Research Institute - Mihaela Pop

Start year: 2017

See also: https://team.inria.fr/asclepios/research/associated-team-persocardiolearn/

Multi-scale computer modelling is a powerful tool that could be used to simulate in silico cardiac electrical activity and biomechanical function of individual heart. Imaging and 3D heart models built from images can help us understand the basis of structurally-diseased hearts at organ level and to predict in silico the changes in electro-mechanical function as a consequence of muscle remodelling in pathologic state (e.g. chronic infarction, a major cause of death). We hypothesize that MRI-based predictive models can help us identify new opportunities to intervene or to predict the outcome of ablation therapy, which currently has low clinical success. However, these predictive models need to be validated and thoroughly tested in preclinical experiments prior to their integration into the clinical stage. Hence, the next logical step for our joint Inria-SB efforts is to expand our experimental-theoretical framework and to personalize fast 3D heart models from in vivo MR-EP data. This translational step involves numerous challenging tasks from the modelling perspective since the in vivo imaging and physiological signals are rather noisy and obtained at a poor spatial resolution, potentially leading to erroneous customization of mathematical model parameters. However, this collaboration employs a rare combination of experiments and modelling specialists. Moreover, the originality of the proposed approach is to build upon machine-learning techniques rather than on data assimilation methods that are more explored in the literature but have inherent limitations (robustness to noise, local minima...).

8.4.3. Inria International Partners

8.4.3.1. Informal International Partners

8.4.3.1.1. St Thomas' Hospital, King's College London, United Kingdom

Maxime Sermesant is a visiting lecturer in the Division of Imaging Sciences and Biomedical Engineering, St Thomas' Hospital, King's College London lead by Pr Reza Razavi. The XMR facility within this hospital is a unique opportunity to validate and exploit the cardiovascular modelling work.

8.4.3.1.2. Massachusetts General Hospital, Boston

A collaboration with Dr Jan Unklebach, Assistant Professor of Radiation Oncology and Dr Jayashree Kalpathy-Cramer, radiology instructor was initiated in 2013 around the topics of tumor growth modeling, radiotherapy planning and edema characterization from MRI.

8.4.3.1.3. University College London (UCL), London, UK

Marco Lorenzi is collaborator of the Translational Imaging Group of UCL, and with the UCL Institute od Ophtalmology. His collaboration is around the topic of spatio-temporal analysis of medical images, with special focus on brain imaging analysis and biomarker development. He is also collaborating with the "Progression Over Neurodegenerative Disorders" (POND) group (Prof. Daniel Alexander) for developing new computational models and techniques for learning characteristic patterns of disease progression using large longitudinal clinical data sets, with special focus on dementias.

8.4.3.1.4. Imaging Genetics Center (IGC), University of Southern California (USC), CA, USA

Marco Lorenzi is currently collaborator of IGC for the investigation of the complex relationship between brain atrophy and genetics in Alzheimer's disease, in particular for demonstrating the effectiveness of multivariate statistical models in providing a meaningful description of the relationship between genotype and brain phenotype.

8.4.3.1.5. Other International Hospitals

Collaborations with several other European hospitals have been established through the European projects VP2HF, MD PAEDIGREE and SysAFib.

8.5. International Research Visitors

8.5.1. Visits of International Scientists

8.5.1.1. Internships

- Svenja Hüning, PhD student with Johannes Wallner at Graz University in Austria visited the Epione team in November 2018 to work with Xavier Pennec on subdivision schemes on manifolds.
- Santiago Smith Silva Rincon, Master student at the National University of Bogota (CO), visited the Epione team from May to October 2018 to work with Marco Lorenzi on distributed learning methods in imaging-genetics.

GALEN-POST Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

Program: ANR PRC

Project acronym: CoMeDIC

Project title: Convergent Metrics for DIscrete Calculus

Duration: 2016-2021

Coordinator: J.-O. Lachaud (Univ. Rhones Alpes Savoie Mont-Blanc), Local: H. Talbot

Program: ANR PRCE

Project acronym: R-Vessel-X

Project title: Extraction et interprétation robustes des réseaux vasculaires dans les images biomédicales hépatiques

Duration: 2018-2022

Coordinator: A. Vacavant (Univ. Clermont Auvergne), local: H. Talbot

Program: ANR JCJC

Project acronym: LearnCost

Project title: Learning Model Constraints for Structured Prediction

Duration: 2014-2018

Coordinator: M. Blaschko

Program: ANR JCJC

Project acronym: MajIC

Project title: Majorization-Minimization Algorithms for Image Computing

Duration: 2017-2021

Coordinator: E. Chouzenoux

Program: ANR JCJC

Project acronym: AVENUE

Project title: A Visual memory network for scene understanding

Duration: 2018-2022

Coordinator: Dr. Karteek Alahari (Inria Grenoble - Rhône-Alpes). Local: F. Malliaros.

9.1.2. Others

Program: CNRS MASTODONS
Projet acronym: TABASCO
Project title: Traitement du bruit non Gaussien en spectroscopie
Duration: 2016-2018
Coordinator: E. Chouzenoux

Program: CNRS-CEFIPRA
Project acronym: NextGenBP
Project title: Looking Beyond Backpropagation in Deep Learning
Duration : 2017-2019
Coordinator: E. Chouzenoux

Program: CNRS MI
Projet acronym: SUPREMA
Project title: Super-résolution en microscopie biphotonique
Duration: 2018
Coordinator: E. Chouzenoux
Program: PHC - Campus France
Projet acronym: POLONIUM
Project title: When Poisson and Gauss meet in imaging
Duration: 2018-2020
Coordinator: E. Chouzenoux

9.2. European Initiatives

9.2.1. H2020 Projects

Program: H2020 ITN Marie Sklodowska-Curie
Project acronym: SUNDIAL
Project title: SUrvey Network for Deep Imaging Analysis and Learning
Duration: 2017-2021
Coordinator: R. Peletier (Univ. Groningen, NL), local: H. Talbot

9.3. International Initiatives

9.3.1. Informal International Partners

Sup'Com Tunis - Pr. Amel Benazza-Benhayia. Collaboration Topic: Multispectral imaging.
University of Patras, Greece - Dr. V. Megalooikonomou. Collaboration Topic: Biosignal analysis.
University of Pennsylvania - Prof. Aristeidis Sotiras. Collaboration Topic: Higher Order Graphs in biomedical image analysis.
University of Montréal, MILA - Dr. Eugene Belilovsky, Pr. Simon Lacoste-Julien. Collaboration Topic : Deep learning, scattering transform.
Berkeley University - Dr. Michael Eickenberg and Dr. Damien Scieur. Collaboration Topic : Deep learning.
KU Leuven - Pr. Matthew Blashcko. Collaboration Topic : Scattering transform.
University of Amsterdam - Dr. Jörn Jacobsen. Collaboration Topic : Deep learning.
Aristotle University of Thessaloniki, Greece - Prof. Apostolos N. Papadopoulos. Collaboration Topic: Graph mining and learning.
Indraprastha Information Institute Technology, Delhi, India - Dr. Angshul Majumdar. Collaboration Topic: Dictionary learning.
Universidad Técnica Federico Santa María, Valparaíso, Chile - Dr. Luis M. Briceño-Arias. Collaboration Topic: Stochastic optimization.
North Carolina State University - Prof. Patrick Louis Combettes. Collaboration Topic: Stochastic optimization.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

Dr. Luis M. Briceño-Arias, Universidad Técnica Federico Santa María, Valparaíso, Chile, 1 Jun. - 1 Jul. 2018, 21 Nov. - 21 Dec. 2018
Jyoti Maggu (PhD student), IIIT New Delhi, India, 05 Mar.-28 May 2018
Vanika Singhal (PhD student), IIIT New Delhi, India, 05 Mar.-20 Apr. 2018
Georgios Panagopoulos (PhD student), Ecole Polytechnique, 15 Jun. - 31 Jul. 2018

9.4.2. Visits to International Teams

9.4.2.1. Research Stays Abroad

M.C. Corbineau, Department of Physics, Informatics and Mathematics, Universita degli studi di Modena e Reggio Emilia, Modena, Italy, 20 Sep. - 20 Oct. 2018.

MATHNEURO Team

5. Partnerships and Cooperations

5.1. European Initiatives

5.1.1. FP7 Projects

5.1.1.1. HBP

Title: The Human Brain Project

Program: FP7

Duration: October 2013 - March 2016 (first part), then : April 2016 - March 2018 (second part) and then : April 2018 - March 2020 (third part)

Coordinator: EPFL

Partners:
see the webpage of the project.

Olivier Faugeras is leading the task T4.1.3 entitled “Meanfield and population models” of the Worpackage W4.1 “Bridging Scales”.

Inria contact: Olivier Faugeras (first part) and then : Romain Veltz (second and third part)

Understanding the human brain is one of the greatest challenges facing 21st century science. If we can rise to the challenge, we can gain profound insights into what makes us human, develop new treatments for brain diseases and build revolutionary new computing technologies. Today, for the first time, modern ICT has brought these goals within sight. The goal of the Human Brain Project, part of the FET Flagship Programme, is to translate this vision into reality, using ICT as a catalyst for a global collaborative effort to understand the human brain and its diseases and ultimately to emulate its computational capabilities. The Human Brain Project will last ten years and will consist of a ramp-up phase (from month 1 to month 36) and subsequent operational phases.
This Grant Agreement covers the ramp-up phase. During this phase the strategic goals of the project will be to design, develop and deploy the first versions of six ICT platforms dedicated to Neuroinformatics, Brain Simulation, High Performance Computing, Medical Informatics, Neuromorphic Computing and Neurorobotics, and create a user community of research groups from within and outside the HBP, set up a European Institute for Theoretical Neuroscience, complete a set of pilot projects providing a first demonstration of the scientific value of the platforms and the Institute, develop the scientific and technological capabilities required by future versions of the platforms, implement a policy of Responsible Innovation, and a programme of transdisciplinary education, and develop a framework for collaboration that links the partners under strong scientific leadership and professional project management, providing a coherent European approach and ensuring effective alignment of regional, national and European research and programmes. The project work plan is organized in the form of thirteen subprojects, each dedicated to a specific area of activity.
A significant part of the budget will be used for competitive calls to complement the collective skills of the Consortium with additional expertise.

5.2. International Research Visitors

5.2.1. Visits of International Scientists

Invitation of Andrey Shilnikov, Georgia State University (USA), January 2018

Invitation of Jean-Pierre Françoise, Sorbonne Université (Paris), April 2018

Invitation of Vivien Kirk, University of Auckland (New Zealand), May 2018

Invitation of Peter De Maesschalck, University of Hasselt (Belgium), June 2018

5.2.2. Visits to International Teams

Visit of Mathieu Desroches to Jean-Pierre Françoise (LJLL, Sorbonne Université, Paris) in October 2018

5.2.2.1. Research Stays Abroad

One-month research stay of Mathieu Desroches at BCAM (Bilbao, Spain) on an invited professor scholarship to work with Serafim Rodrigues, June 2018

MIMESIS Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

At the regional level, the MIMESIS team collaborates with

9.1.1. ICube Automatique Vision et Robotique (AVR)

We have been collaborating with the medical robotics team on percutaneous procedures, in particular robotized needle insertion (with Prof. Bernard Bayle), and needle tracking in medical images (with Elodie Breton). We are also collaborating with Jonathan Vappou on elastography.

9.1.2. ICube Informatique Géométrique et Graphique (IGG)

MIMESIS joined the IGG team and develops collaboration in the domain of dynamic topologies, mainly through the use of the CGoGN framework. CGoGN is a C++ library for the manipulation of meshes. It implements combinatorial maps and their multiresolution extensions and has been used in various high level application like the simulation of crowds of autonomous agents and the simulation of cuts, tears and fractures in the context of surgical simulations.

9.1.3. Institute of Image-Guided Surgery (IHU) Strasbourg

We have several active projects and collaborations with IHU Strasbourg in order to collect and use medical images (such as MRI, CT, Fluoroscopy and Ultrasound) before, during and after minimally-invasive surgical procedures (percutaneous, endovascular and laparoscopic). Such images represent an essential support for the development of numerical simulations for intra-operative assistance through augmented and virtual reality. Eventually, simulations will be used for the diagnostic, treatment as well as for training and teaching in medical domain. Yet, before being used in current clinical routine, such simulations must be validated on animal models. Through our collaboration with IHU, we use CT and MRI images to retrieve the anatomical model of internal structures, whereas fluoroscopic and ultrasound images can be used to retrieve 2D images of the physiology and the navigation of surgical instruments within the anatomy. In-vivo procedures can also be performed under ethical approval of MSER (reference to ethic protocol *APAFIS #15433-2018060815283960*). We also collaborate with IHU-Strasbourg fellow surgeons, such as Pr. Mario GIMENEZ and Dr. Alain GARCIA, that provide medical and technical support for medical aspects (see Fig. 11).

- *Authors:* Raffaella Trivisonne, Stéphane Cotin

9.2. National Initiatives

9.2.1. ADT (Action de Développement Technologique)

Team MIMESIS received a support for the development of the project **LOSAR: Liver Open Surgery with Augmented Reality** that aims at developing tools for a per-operative usage of research algorithms developed in the team. Although the current trend is to move towards minimally invasive surgery, open-liver surgery remains the standard treatment for most patients. For Augmented reality purpose, open surgery raises specific constraints compared to celioscopic surgery, such as larger deformations of the liver and unavoidable occlusions of the organ. During the year 2017, the Mimesis team has developed an augmented reality prototype for open liver surgery. This prototype was developed as part of research projects and a collaboration between the team Mimesis and the CHB Paul Brousse (first service of hepatobiliary surgery in France).

Figure 11. Environmental Set-Up for Image Acquisition. IHU-Strasbourg Platform.

Our goal is to be able to repeatedly test our method for one or more important publications in medical conferences. This type of publication requires to methodically repeat our solution on several patients. However, the steps are still insufficiently automated and the algorithm needs to be improved for greater reliability. These essential elements lie outside traditional research missions and require significant development and engineering effort. Indeed, an effort of automation and ergonomics will have to be made to make the use of the software sufficiently simple to be used in the operating room. Furthermore, the accuracy of the deformed model (anatomical distances modeled versus actual anatomical relationships) must also be verified and validated through experimentation.

9.2.2. ANR (Agence Nationale de la Recherche)

MIMESIS coordinates the ANR project entitled **SPERRY: SuPervisEd Robotic suRgerY - application to needle insertion**. Percutaneous medical procedures (using surgical needles) are among the least invasive approaches to accessing deep internal structures of organs without damaging surrounding tissues. Today, many surgical procedures rely on the use of needles allowing for complex interventions such as curie-therapies or thermoablations of tumors (cryoablation, radio frequencies). Unlike traditional open surgery, these approaches only affect a localized area around the needle reducing this way trauma and risks of complications. These treatments also offer new solutions for tumors or for metastases for which traditional methods may be contraindicated due to the age of the patient and the extent or location of the disease. Although they provide very good results, these interventions significantly increase the level of expertise required for practitioners.

In this project, we want to develop new solutions for the control of medical robots interacting with soft tissues. This work is motivated by recent advances in the field of medical simulation achieving a sufficient level of realism to help surgeons during the operation. These simulations are now used for training of surgeons, and even for visual assistance during the operation thanks to augmented reality. The maturity of these techniques now suggests the ability to use a simulation intraoperatively to control the motion of a robotic system for needle insertion. This is really a challenge, because in general, very few information can be extracted in real time from images during an intervention. We believe that even minimal knowledge of the mechanical behavior of structures, associated with the use of images can make it possible and allow a robot to reach a pre-identified target during a planning stage, without human intervention.

9.2.3. Inria Collaborations

MIMESIS is closely connected to the SOFA Consortium, created by Inria in November 2015 with the objective to support the SOFA community 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. MIMESIS actively participates at the development of SOFA and contributed to the evolution of the framework. Moreover, MIMESIS also participates in an initiative aiming at verification and validation of codes and algorithms of SOFA.

Further, MIMESIS actively collaborates with the following Inria teams:

MAGRIT: The team at Inria Grand Est focuses on research in computer vision and is also actively involved in computer-based solutions for the planning or the simulation of interventional radiology procedures, with a strong collaboration with the CHU in Nancy. We collaborate with MAGRIT in the area of interventional radiology and augmented reality. Currently, two PhD thesis are co-supervised by researcher from Magrit: the PhD thesis of Jaime Garcia Guevara and Raffaella Trivisonne.

DEFROST: The team conducts research in soft robotics. We continue mutual interaction with DEFROST mainly in the context of contact modeling.

9.2.4. National Collaborations

At the national level, the MIMESIS team collaborates with:

The TIMC laboratory*(Techniques de l'Ingénierie Médicale et de la Complexité)* in Grenoble: this large research group has a strong background in computer-aided surgery, medical imaging, registration, statistical and bio-mechanical modeling. We have regular interactions with various members of this group. We are collaborating with Yohan Payan (DR CNRS) on the modeling and simulation of the brain shift. A common PhD thesis started on that topic in late 2014. Other areas of interest are in the field of advanced soft tissue modeling and computer aided surgery.

The LML laboratory*(Laboratoire de Mécanique de Lille)*: a French research laboratory (UMR CNRS 8107) part of the Carnot institute ARTS. With more than two hundred researchers, LML focuses on the following research areas: mechanical reliability and Tribology, fluid mechanics, civil engineering and soil mechanics.

Hôpital Paul-Brousse a hospital in South Paris. We collaborate with *Centre Hépato-Biliaire* via the co-supervision of the Ph.D. thesis of Nicolas Golse, MD, who is a surgeon at the center.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

- **HiPerNav** (https://hipernav.eu) is an Innovative Training Network (ITN) funded through a Marie Skłodowska-Curie grant. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 722068. There is 14 fully funded and 2 partially funded PhD's working on the project. The project aims to improve soft tissue navigation through research and development, to improve several bottleneck areas:
  - Creating effective pre-operative model(s) and planning
  - Faster and more accurate intra-operative model updates
  - Faster and more accurate model-to-patient registration
  - More intuitive user-interaction and effective workflow
  - Usage of high performance computing (e.g. GPU)

  From these 14 PhD students, two of them are from the Mimesis team: **Jean-Nicolas Brunet** and **Sergei Nikolaev**.
- **Driven** ((https://driven.uni.lu/) The overall aim of the DRIVEN project is to boost the scientific excellence and innovation capacity in data-driven simulation of the University of Luxembourg (UL) and its high-quality Twinning partners: Institut National de Recherche en Informatique et en Automatique (Inria), University of Limerick (ULIM) and University of Texas at Austin (UT Austin). To achieve this aim, the 3 year project will build upon the existing strong research and innovation base of UL and its Twinning partners. The recently established Computational Sciences

interdisciplinary group is composed of members from different research units and disciplines as diverse as Earth Sciences, Life Sciences, Physics, Mathematics and Engineering, with the common goal to set up a network among application-driven scientists which can provide interdisciplinary expertise in the field and contribute to this platform of training and knowledge exchange. To boost their scientific excellence and technology transfer capacity in data-driven simulation, the partners will implement a research and innovation strategy focused on three sub-topics:

1. Mathematical foundations for data-driven simulations – UL with UT Austin,
2. Data-driven simulations for computer-assisted therapy – UL with Inria, and
3. Data-driven simulations for functional composite materials – UL with ULIM.

9.4. International Initiatives

9.4.1. Informal International Partners

- **CAMERA group, University of Bath, UK:** Collaboration on non-rigid registration using RGB-D sensors - Antoine Petit
- **PRISMA Lab, University of Naples, Italy:** Collaboration on soft object robotic manipulation, along with DEFROST team at Inria Lille, and collaboration on visual perception for robotic surgery - Antoine Petit.
- **University of Twente, Netherlands:** Thanks to our clinical partner IHU, we collaborate with Prof. Stefano Stramigioli, head of a group at Robotics and Mechatronics laboratory.
- **Faculty of Informatics, Masaryk University, Czech Republic:** We collaborate on simulation of living cells in fluorescent microscopy.
- **Team Legato, University of Luxembourg:** We have an active collaboration with Prof. Stéphane Bordas on error estimation in real-time simulations of deformable objects.
- **ARTORG Center for Biomedical Engineering Research, Bern, Switzerland:** Collaboration in the projects related to deep learning.

9.5. International Research Visitors

9.5.1. Internships

Domenico Idone (master student from Italy) did a six month internship in the team. The aim of the training period is to investigate a novel method to track catheter shape and location during vascular interventions. We have already experimented the use of a fiber optic, equipped with Fiber Bragg Grating sensors, embedded on a flexible plate, to determine its shape. This sensing system has allowed us to track the motion of the plate undergoing a two-dimensional deformation. The objective of this internship is to expand this work to the case of a three-dimensional deformation, which requires significant improvements over the previous approach.

Renée Geraats (Twente university) did a 2 months internship. She investigated different visualization solutions for augmented reality on fluoroscopic images of the liver and its vasculature, for the 2D3D Fusion project.

Daan Kuppens (Twente university) did a 2 months internship. He provided support on the acquisition of reliable porcine CT and X-ray fluoroscopic images fluoroscopic images, on CT segmentation of the liver and its vasculature and on clinical applications, for the 2D3D Fusion project.

Pim Hendricks (Twente university) did a 2 months internship. She provided support on the acquisition of reliable porcine CT and X-ray fluoroscopic images fluoroscopic images, and on clinical applications, for the 2D3D Fusion project.

MNEMOSYNE Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. PsyPhINe

Participant: Nicolas Rougier.

Project gathering researchers from: MSH Lorraine (USR3261), InterPsy (EA 4432), APEMAC, EPSaM (EA4360), Archives Henri-Poincaré (UMR7117), Loria (UMR7503) & Mnemosyne.

PsyPhiNe is a pluridisciplinary and exploratory project between philosophers, psychologists, neuroscientists and computer scientists. The goal of the project is to explore cognition and behavior from different perspectives. The project aims at exploring the idea of assignments of intelligence or intentionality, assuming that our intersubjectivity and our natural tendency to anthropomorphize play a central role: we project onto others parts of our own cognition. To test these hypotheses, we ran a series of experiments with human subject confronted to a motorized lamp that can or cannot interact with them while they're doing a specific task. We've organized our third national conference in Nancy gathering speakers from philosophy, robotics, art and psychology and closed a three years cycle. The group now aims at publishing a book gathering text from all the invited speakers.

9.2. National Initiatives

9.2.1. FUI Sumatra

Participants: Frédéric Alexandre, Thalita Firmo Drumond, Xavier Hinaut, Randa Kassab, Nicolas Rougier, Thierry Viéville.

This FUI project, supported by the Aerospace Valley Innovation Pole, gathers two industrial groups (Safran Helicopter and SPIE), three research labs and four SME. Its goal is to provide contextualized information to maintenance operators by the online analysis of the operating scene. We are concerned in this project with the analysis of visual scenes, in industrial contexts, and the extraction of visual primitives, categories and pertinent features, best decribing the scenes, with biologically inspired neuronal models.

Firstly, this is an opportunity for us to revisit the principles of deep network architectures by adapting principles that we will elaborate from the context of the hierarchical architecture of the temporal visual cortex. Secondly, we intend to exploit and adapt our model of hippocampus to extract more heterogenous features. This project is an excellent opportunity to associate and combine our models and also to evaluate the robustness of our models in real-world applications.

9.2.2. ANR SOMA (PRCI)

Participants: Nicolas Rougier, Remya Sankar.

This project is a convergence point between past research approaches toward new computational paradigms: adaptive reconfigurable architecture, cellular computing, computational neuroscience, and neuromorphic hardware:

1. SOMA is an adaptive reconfigurable architecture to the extent that it will dynamically re-organize both its computation and its communication by adapting itself to the data to process.
2. SOMA is based on cellular computing since it targets a massively parallel, distributed and decentralized neuromorphic architecture.
3. SOMA is based on computational neuroscience since its self-organization capabilities are inspired from neural mechanisms.
4. SOMA is a neuromorphic hardware system since its organization emerges from the interactions between neural maps transposed into hardware from brain observation.

This project represents a significant step toward the definition of a true fine-grained distributed, adaptive and decentralized neural computation framework. Using self-organized neural populations onto a cellular machine where local routing resources are not separated from computational resources, it will ensure natural scalability and adaptability as well as a better performance/power consumption tradeoff compared to other conventional embedded solutions.

9.2.3. ANR MACAQUE40

Participant: Nicolas Rougier.

Most of the theoretical models in economics proposed so far to describe money emergence are based on three intangible assumptions: the omniscience of economic agents, an infinite time and an extremely large number of agents (not bounded). The goal of this interdisciplinary study is to investigate the condition of apparition of a monetary economy in a more ecological framework provided with the assumption that the market is made up of a finite number of agents having a bounded rationality and facing a time constraint.

In this study, we propose a generic model and environment of monetary prospecting. Our first objective is to artificially identify structural (trading organisation, agents specialisation) and cognitive conditions (learning skills, memory and strategic anticipation abilities, tradeoff exploration/exploitation) that allowed money emergence. This will provide relevant environmental constraints that we will use during our manipulations in the laboratory. The agents that will be involved in these manipulations will be of two types: non-human primates (rhesus macaques) and humans.

9.2.4. Project Motus of the ANSES

Participant: André Garenne.

The MOTUS project (MOdulaTion dU Signal RF et effets sur le cerveau : approche in vivo et in vitro) is financed by the ANSES (the french national agency for health security). This 3 years project is studying the effects of GSM-RF on living matter and especially neuronal activity and development. Our main involvement concerns electrophysiological data and spike trains analysis as well as the development of pharmacological protocols to test GSM-RF effects hypotheses. Altogether, our experimental findings provide evidence for dose-dependent effects of RF signals on the bursting rate of neuronal cultures and suggest that part of the mechanism is nonthermal (publication in Journal of Neurophysiology). In an attempt to elucidate the depressing effect of GSM on in-vitro neuronal activity, pharmacological studies have also been realized on cortical cells.

9.3. International Initiatives

9.3.1. Participation in International Programs

9.3.1.1. Project LingoRob with Germany

LingoRob - Learning Language in Developmental Robots - is a project of the Programme Hubert Curien PHC Procope with Germany (University of Hamburg). The scientific objective of the collaboration is to better understand the mechanisms underlying language acquisition and enable more natural interaction between humans and robots in different languages, while modelling how the brain processes sentences and integrates semantic information of scenes. Models developed in both labs involve artificial neural networks, and in particular Echo State Networks (ESN), also known as pertaining to the Reservoir Computing framework. These neural models allow insights on high-level processes of the human brain, and at the same time are well suited as robot control platform, because they can be trained and executed online with low computational resources. The collaborators will also combine Deep Learning networks to the reservoir models already used in order to benefit from their very good feature extraction abilities.

NEUROSYS Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

Within the *Contrat de Projet État Région (CPER) IT2MP* 2015-2020 on *Technological innovations, modeling and Personalized Medicine*, we are contributing on platform SCIARAT (*cognitive stimulation, Ambient Intelligence, Robotic assistance" and Telemedicine*) observing electroencephalographic activity of humans during motor tasks.

8.2. National Initiatives

8.2.1. Inria project-Lab BCI-LIFT 2015-2018 (Brain-Computer Interfaces: Learning, Interaction, Feedback, Training)

Project leader: Maureen Clerc
Partners: 7 Inria project-teams (Aramis, Athena, Demar, Hybrid, Mjolnir, Neurosys, Potioc), univ. Rouen, Dycog team at Centre de Recherche en Neurosciences de Lyon.

BCI-LIFT is a research initiative to reach a next generation of non-invasive Brain-Computer Interfaces (BCI), more specifically BCI that are easier to appropriate, more efficient, and suit a larger number of people. With this concern of usability as our driving objective, we build non-invasive systems that benefit from advanced signal processing and machine learning methods, from smart interface design, and where the user immediately receives supportive feedback. What drives this project is the concern that a substantial proportion of human participants is currently categorized “BCI-illiterate” because of their apparent inability to communicate through BCI. Through this project we aim at making it easier for people to learn to use BCI, by implementing appropriate machine learning methods and developing user training scenarios.

8.2.2. Projet CNRS PEPS S2IH INS2I 2018 : MoveYouMind (Design and evaluation of a visual neurofeedback based on specific corticomotor areas using source localization for enhancing motor imagery)

Project leader: Laurent Bougrain
Partners: Neurosys, Cognitive and Systems Neurosciences (univ. Lorraine/CRAN), Perseus (univ. Lorraine)
This project aims at improving the functional recovery protocols of hemiplegic stroke patients by increasing the precision of the identification of the brain areas involved in a kinesthetic motor task of the upper limbs. The brain areas engaged during this rehabilitation task will be detected by specific source localization methods based on the signals obtained by an electroencephalographic acquisition system with variable geometry, which will inform and therefore guide the patient (and the nursing staff) during the functional rehabilitation by indicating to her/him if the activity which she/he produces is in the right motor area. The project aims to design and evaluate a visual neurofeedback based on active cortical areas within an existing brain-computer interface.

8.2.3. Projet CNRS PEPS S2IH INS2I 2018 : HDCHS (From Human-Human Handshaking to Human-Robot Handshaking)

Project leader: Patrick Hénaff
Partners: Neurosys, Perseus (univ. Lorraine), Cerco

This project interfaces robotics, neuroscience and experimental psychology. It is part of on-going research initiated at LORIA on the understanding of physical and cognitive phenomena that appear while two persons handshake, in order to reproduce them with a humanoid robot naturally interacting with a human. This act is studied because is a multimodal physical and social interaction, socially common but complex from a neuroscience and robotics point of view, because it involves physical, psychological and sensorimotor couplings which differ, depending on the social context. This project proposes novel handshaking experiments aiming at understanding the physical and psychological synchronization phenomena (coupling, locking, rhythmicity), best known as the « Human Dynamic Clamp » (HDC) paradigm, in order to propose models in adequation with the bio-inspired controllers developed at LORIA for the control of humanoid robots.

8.3. International Initiatives

8.3.1. Informal International Partners

- We hosted Takeshi Nishida (Kuytech, Japan) for five months and Sozo Inoue (Kuytech, Japan) for one week to prepare a collaboration on neurosciences and robotics. Laurent Bougrain visited Takeshi Nishida, Kiyohisa Natsume and Toshimasa Yamazaki in Kyutech. Asako Watanabe, a master student from Kuytech, will come for 3 weeks in the team in January 2019 to work on EEG markers of a motor task.
- We collaborate with Anton Popov (Kiev Polytechnic Institute, Ukraine) on feature extraction of brain signal and deep learning (L. Bougrain). Oleksii Avilov is a Ph.D student under a joint supervision arrangement between Kiev Polytechnic Institute and university of Lorraine.
- We also collaborate with Emel Demircan (Univ South California) to use EMG-informed Computed Muscle Control for dynamic simulations of movement available in OpenSim [0]. She stayed 3 weeks in Neurosys this year.
- We also collaborate with LieJune Shiau (university of Houston, Texas, USA) on more theoretical approaches concerning the role of intrinsic neuronal dynamics in network synchronization and brain oscillations (L. Buhry).

8.4. International Research Visitors

8.4.1. Visits of International Scientists

- Takeshi Nishida, Ass. Prof, Kuytech, Japan, 5 weeks (Jun.-Jul. 2018)
- Emel Demircan, Ass. Prof, Univ South California, USA, 3 weeks (Jun.-Jul. 2018)
- Sozo Inoue, Full Prof, Kuytech, Japan, 1 week (dec. 2018)

8.4.1.1. Internships

- Sooraj Sivakumar, Student, IIT Madras, India (Jan-Mar 2018)

[0] https://opensim.stanford.edu/

PARIETAL Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. Inserm-Inria project

This project is funded by the joint Inserm and Inria program 'médecine numérique' and is conducted in collaborations with our clinical partners from the Lariboisière hospital, Inserm uni U942 BioCANVAS (Biomarkers in Cardio-Neuro-VAScular diseases). It supports the PhD thesis of David Sabbagh.

Participants:

- Denis Engemann [coordinator, co-advisor]
- Alexandre Gramfort [thesis director, co-advisor]
- Etienne Gayat [clinical collaborator, co-advisor]
- Fabrice Vallée [clinical collaborator]
- David Sabbagh [PhD Student]

Post-operative delirium (POD) is a potential complication of anesthesia during surgery. It is often associated with adverse outcomes and is aggravated by aging. In elderly patients, post-operative complications have been estimated to incur tens of million US dollars of costs each year in the United States by prolonging hospitalization and potentially affecting health prognosis. Recent studies suggest that POD can already be prevented by improving electrophysiological monitoring of anesthesia depth and individual dosage of anesthetic agents. Doing so probably minimizes the time patients spend in a coma-like state that manifests itself in isoelectric burst suppression, an electroencephalogram (EEG) pattern characterized by alternation between quiescence and high-amplitude bursts, and causally linked to POD. However, such an enterprise, currently, depends on the trained clinical electrophysiologist and guidance by commercially provided EEG indices of states of consciousness. One such metric is the bispectral index (BIS), which, like other related metrics, does not explicitly take into account baseline changes related to normative aging and may therefore be biased when used naively.

While electrophysiological signatures of aging (e.g. drop in Alpha and Gamma band power), states of consciousness (e.g. drop in Theta band long-range connectivity) and drug response (e.g. anteriorization of alpha band power in propofol anesthesia) have been separately investigated in the past years, their common denominators are not known. It is therefore difficult to detect individual risk, choose the optimal dosage, and automate anesthesia monitoring readily for any patient in any hospital.

The goal of this research project is to build statistical models that enable prediction of burst suppression and subsequent POD by exploiting diverse EEG-signatures of states of consciousness in the context of aging. We approach this challenge by recasting it as a problem of learning brain-age from the point of view of electrophysiology of consciousness.

9.1.2. CoSmic project

Participants: Philippe Ciuciu [Correspondant], Carole Lazarus, Loubna El Gueddari.

This project is funded by CEA DRF-Impulsion.

This is a collaborative project with Jean-Luc Stark, (CEA) funded by the DRF-impulsion CEA program.

Compressed Sensing is a recent theory in maths that allows the perfect recovery of signals or images from compressive acquisition scenarios. This approach has been popularized in MRI over the last decade as well as in astrophysics (noticeably in radio-astronomy). So far, both of these fields have developed skills in CS separately. The aim of the COSMIC project is to foster collaborations between CEA experts in MRI (Parietal team within NeuroSpin) and in astrophysics (CosmoStat lab within the Astrophysics Department). These interactions will allow us to share different expertise in order to improve image quality, either in MRI or in radio-astronomy (thanks to the interferometry principle). In this field, given the data delivered by radio-telescopes, the goal consists in extracting high temporal resolution information in order to study fast transient events.

9.1.3. Metacog

Participants: Bertrand Thirion [Correspondant], Gaël Varoquaux, Jérome Dockès.

This project is funded by Digiteo.

This is a Digicosme project (2016-2019) and a collaboration with Fabian Suchanek (Telecom Paritech).

Understanding how cognition emerges from the billions of neurons that constitute the human brain is a major open problem in science that could bridge natural science –biology– to humanities –psychology. Psychology studies performed on humans with functional Magnetic Resonance Imaging (fMRI) can be used to probe the full repertoire of high-level cognitive functions. While analyzing the resulting image data for a given experiment is a relatively well-mastered process, the challenges in comparing data across multiple datasets poses serious limitation to the field. Indeed, such comparisons require to pool together brain images acquired under different settings and assess the effect of different *experimental conditions* that correspond to psychological effects studied by neuroscientists.

Such meta-analyses are now becoming possible thanks to the development of public data resources –OpenfMRI http://openfmri.org and NeuroVault http://neurovault.org. As many others, researchers of the Parietal team understand these data sources well and contribute to them. However, in such open-ended context, the description of experiments in terms of cognitive concepts is very difficult: there is no universal definition of cognitive terms that could be employed consistently by neuroscientists. Hence meta-analytic studies loose power and specificity. On the other hand, http://brainspell.org provide a set of curated annotation, albeit on much less data, that can serve as a seed or a ground truth to define a consensual ontology of cognitive concepts. Relating these terms to brain activity poses another challenge, of statistical nature, as brain patterns form high-dimensional data in perspective with the scarcity and the noise of the data.

The purpose of this project is to learn a semantic structure in cognitive terms from their occurrence in brain activation. This structure will simplify massive multi-label statistical-learning problems that arise in brain mapping by providing compact representations of cognitive concepts while capturing the imprecision on the definition these concepts.

9.1.4. HidimStat

Participants: Bertrand Thirion [Correspondant], Jerome-Alexis Chevalier, Joseph Salmon.

This project is funded by Digiteo.

This is a Digicosme project (2017-2020) and a collaboration with Joseph Salmon (Telecom Paritech).

The HiDimStat project aims at handling uncertainty in the challenging context of high dimensional regression problem. Though sparse models have been popularized in the last twenty years in contexts where many features can explain a phenomenon, it remains a burning issue to attribute confidence to the predictive models that they produce. Such a question is hard both from the statistical modeling point of view, and from a computation perspective. Indeed, in practical settings, the amount of features at stake (possibly up to several millions in high resolution brain imaging) limit the application of current methods and require new algorithms to achieve computational efficiency. We plan to leverage recent developments in sparse convex solvers as well as more efficient reformulations of testing and confidence interval estimates to provide several communities with practical software handling uncertainty quantification. Specific validation experiments will be performed in the field of brain imaging.

9.1.5. Template estimation for arbitrary alignments: application to brain imaging.

Participants: Bertrand Thirion [Correspondant], Thomas Bazeille.

This project is funded by Digiteo.

In the recent years, the nature of scientific inference has shifted quite substantially from model-based to predictive approaches, thanks to the generalization of powerful machine learning techniques. While this has certainly improved scientific standards, this has also obscured the objects and concepts on which inference is drawn. For instance, it is now possible –based on some initial data– to predict individual brain activity topographies, yet the very notion of a standard brain template has become increasingly elusive. Given the importance of establishing models for the progress of knowledge, we revisit the problem of model inference on data with high variance. Specifically, in a context where almost arbitrary transformation can successfully warp observations to each other with high accuracy, what is the common definition of a population model underlying all these observations? What is the working definition of a template ? We plan to leverage recent developments on optimal transport and multivariate analysis to build working definition of templates; we will use them in a brain imaging context to build a novel generation of brain templates.

9.1.6. AMPHI project

Participants: Bertrand Thirion [Correspondant], Joseph Salmon, Antonio Andre Monteiro Manoel.

This is a Digicosme project (2017-2020) and a collaboration with Joseph Salmon (Telecom Paritech) and Lenka Zdeborova (CEA, IPhT).

In many scientific fields, the data acquisition devices have benefited of hardware improvement to increase the resolution of the observed phenomena, leading to ever larger datasets. While the dimensionality has increased, the number of samples available is often limited, due to physical or financial limits. This is a problem when these data are processed with estimators that have a large sample complexity, such as multivariate statistical models. In that case it is very useful to rely on structured priors, so that the results reflect the state of knowledge on the phenomena of interest. The study of the human brain activity through neuroimaging belongs among these problems, with up to 10^6 features, yet a set of observations limited by cost and participant comfort. We are missing fast estimators for multivariate models with structured priors, that furthermore provide statistical control on the solution. Approximate message passing (AMP) methods are designed to work optimally with low- sample-complexity, they accommodate rather generic class of priors and come with an estimation of statistical significance. They are therefore well suited for our purposes. We want to join forces to design a new generation of inverse problem solvers that can take into account the complex structure of brain images and provide guarantees in the low-sample-complexity regime. To this end, we will first adapt AMP to the brain mapping setting, using first standard sparsity priors (e.g. Gauss-Bernoulli) on the model. We will then consider more complex structured priors that control the variation of the learned image patterns in space. Crucial gains are expected from the use of the EM algorithm for parameter setting, that comes naturally with AMP. We will also examine the estimators provided by AMP for statistical significance. AMPHI will design a reference inference toolbox released as a generic open source library. We expect a 3- to 10-fold improvement in CPU time, that will benefit to large-scale brain mapping investigations.

9.1.7. CDS2

Participants: Bertrand Thirion [Correspondant], Gaël Varoquaux, Guillaume Lemaitre, Joris Van Den Bossche.

CDS2 is an "Strategic research initiative" of the Paris Saclay University Idex http://datascience-paris-saclay.fr. Although it groups together many partners of the Paris Saclay ecosystem, Parietal has been deeply involved in the project. It currently funds a post-doc for Guillaume Lemaitre and an engineer positions for Joris van den Bossche. Alexandre Boucaud was funded till December as engineer.

9.2. National Initiatives

9.2.1. ANR

9.2.1.1. Neuroref: Mathematical Models of Anatomy / Neuroanatomy / Diffusion MRI

Participants: Demian Wassermann [Correspondant], Antonia Machlouzarides Shalit, Valentin Iovene.

While mild traumatic brain injury (mTBI) has become the focus of many neuroimaging studies, the understanding of mTBI, particularly in patients who evince no radiological evidence of injury and yet experience clinical and cognitive symptoms, has remained a complex challenge. Sophisticated imaging tools are needed to delineate the kind of subtle brain injury that is extant in these patients, as existing tools are often ill-suited for the diagnosis of mTBI. For example, conventional magnetic resonance imaging (MRI) studies have focused on seeking a spatially consistent pattern of abnormal signal using statistical analyses that compare average differences between groups, i.e., separating mTBI from healthy controls. While these methods are successful in many diseases, they are not as useful in mTBI, where brain injuries are spatially heterogeneous.

The goal of this proposal is to develop a robust framework to perform subject-specific neuroimaging analyses of Diffusion MRI (dMRI), as this modality has shown excellent sensitivity to brain injuries and can locate subtle brain abnormalities that are not detected using routine clinical neuroradiological readings. New algorithms will be developed to create Individualized Brain Abnormality (IBA) maps that will have a number of clinical and research applications. In this proposal, this technology will be used to analyze a previously acquired dataset from the INTRuST Clinical Consortium, a multi-center effort to study subjects with Post-Traumatic Stress Disorder (PTSD) and mTBI. Neuroimaging abnormality measures will be linked to clinical and neuropsychological assessments. This technique will allow us to tease apart neuroimaging differences between PTSD and mTBI and to establish baseline relationships between neuroimaging markers, and clinical and cognitive measures.

9.2.1.2. DirtyData: Data integration and cleaning for statistical analysis

Participants: Gaël Varoquaux [Correspondant], Patricio Cerda Reyes, Pierre Glaser.

Machine learning has inspired new markets and applications by extracting new insights from complex and noisy data. However, to perform such analyses, the most costly step is often to prepare the data. It entails correcting errors and inconsistencies as well as transforming the data into a single matrix-shaped table that comprises all interesting descriptors for all observations to study. Indeed, the data often results from merging multiple sources of informations with different conventions. Different data tables may come without names on the columns, with missing data, or with input errors such as typos. As a result, the data cannot be automatically shaped into a matrix for statistical analysis.

This proposal aims to drastically reduce the cost of data preparation by integrating it directly into the statistical analysis. Our key insight is that machine learning itself deals well with noise and errors. Hence, we aim to develop the methodology to do statistical analysis directly on the original dirty data. For this, the operations currently done to clean data before the analysis must be adapted to a statistical framework that captures errors and inconsistencies. Our research agenda is inspired from the data-integration state of the art in database research combined with statistical modeling and regularization from machine learning.

Data integrating and cleaning is traditionally performed in databases by finding fuzzy matches or overlaps and applying transformation rules and joins. To incorporate it in the statistical analysis, an thus propagate uncertainties, we want to revisit those logical and set operations with statistical-learning tools. A challenge is to turn the entities present in the data into representations well-suited for statistical learning that are robust to potential errors but do not wash out uncertainty.

Prior art developed in databases is mostly based on first-order logic and sets. Our project strives to capture errors in the input of the entries. Hence we formulate operations in terms of similarities. We address typing entries, deduplication -finding different forms of the same entity- building joins across dirty tables, and correcting errors and missing data.

Our goal is that these steps should be generic enough to digest directly dirty data without user-defined rules. Indeed, they never try to build a fully clean view of the data, which is something very hard, but rather include in the statistical analysis errors and ambiguities in the data.

The methods developed will be empirically evaluated on a variety of dataset, including the French public-data repository, data.gouv.fr. The consortium comprises a company specialized in data integration, Data Publica, that guides business strategies by cross-analyzing public data with market-specific data.

9.2.1.3. FastBig Project

Participants: Bertrand Thirion [Correspondant], Jerome-Alexis Chevalier, Tuan Binh Nguyen.

In many scientific applications, increasingly-large datasets are being acquired to describe more accurately biological or physical phenomena. While the dimensionality of the resulting measures has increased, the number of samples available is often limited, due to physical or financial limits. This results in impressive amounts of complex data observed in small batches of samples.

A question that arises is then : what features in the data are really informative about some outcome of interest ? This amounts to inferring the relationships between these variables and the outcome, conditionally to all other variables. Providing statistical guarantees on these associations is needed in many fields of data science, where competing models require rigorous statistical assessment. Yet reaching such guarantees is very hard.

FAST-BIG aims at developing theoretical results and practical estimation procedures that render statistical inference feasible in such hard cases. We will develop the corresponding software and assess novel inference schemes on two applications : genomics and brain imaging.

9.2.1.4. MultiFracs project

Participant: Philippe Ciuciu [Correspondant].

The scale-free concept formalizes the intuition that, in many systems, the analysis of temporal dynamics cannot be grounded on specific and characteristic time scales. The scale-free paradigm has permitted the relevant analysis of numerous applications, very different in nature, ranging from natural phenomena (hydrodynamic turbulence, geophysics, body rhythms, brain activity,...) to human activities (Internet traffic, population, finance, art,...).

Yet, most successes of scale-free analysis were obtained in contexts where data are univariate, homogeneous along time (a single stationary time series), and well-characterized by simple-shape local singularities. For such situations, scale-free dynamics translate into global or local power laws, which significantly eases practical analyses. Numerous recent real-world applications (macroscopic spontaneous brain dynamics, the central application in this project, being one paradigm example), however, naturally entail large multivariate data (many signals), whose properties vary along time (non-stationarity) and across components (non-homogeneity), with potentially complex temporal dynamics, thus intricate local singular behaviors.

These three issues call into question the intuitive and founding identification of scale-free to power laws, and thus make uneasy multivariate scale-free and multifractal analyses, precluding the use of univariate methodologies. This explains why the concept of scale-free dynamics is barely used and with limited successes in such settings and highlights the overriding need for a systematic methodological study of multivariate scale-free and multifractal dynamics. The Core Theme of MULTIFRACS consists in laying the theoretical foundations of a practical robust statistical signal processing framework for multivariate non homogeneous scale-free and multifractal analyses, suited to varied types of rich singularities, as well as in performing accurate analyses of scale-free dynamics in spontaneous and task-related macroscopic brain activity, to assess their natures, functional roles and relevance, and their relations to behavioral performance in a timing estimation task using multimodal functional imaging techniques.

This overarching objective is organized into 4 Challenges:

1. Multivariate scale-free and multifractal analysis,
2. Second generation of local singularity indices,
3. Scale-free dynamics, non-stationarity and non-homogeneity,
4. Multivariate scale-free temporal dynamics analysis in macroscopic brain activity.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. Neurolang

Title: Accelerating Neuroscience Research by Unifying Knowledge Representation and Analysis Through a Domain Specific Language

Programm: ERC Starting researcher

Duration: 01/03/2018 - 28/02/2023

Coordinator: Demian Wassermann

Inria contact: Demian Wassermann

Summary:

Neuroscience is at an inflection point. The 150-year old cortical specialization paradigm, in which cortical brain areas have a distinct set of functions, is experiencing an unprecedented momentum with over 1000 articles being published every year. However, this paradigm is reaching its limits. Recent studies show that current approaches to atlas brain areas, like relative location, cellular population type, or connectivity, are not enough on their own to characterize a cortical area and its function unequivocally. This hinders the reproducibility and advancement of neuroscience.

Neuroscience is thus in dire need of a universal standard to specify neuroanatomy and function: a novel formal language allowing neuroscientists to simultaneously specify tissue characteristics, relative location, known function and connectional topology for the unequivocal identification of a given brain region.

The vision of NeuroLang is that a unified formal language for neuroanatomy will boost our understanding of the brain. By defining brain regions, networks, and cognitive tasks through a set of formal criteria, researchers will be able to synthesize and integrate data within and across diverse studies. NeuroLang will accelerate the development of neuroscience by providing a way to evaluate anatomical specificity, test current theories, and develop new hypotheses.

NeuroLang will lead to a new generation of computational tools for neuroscience research. In doing so, we will be shedding a novel light onto neurological research and possibly disease treatment and palliative care. Our project complements current developments in large multimodal studies across different databases. This project will bring the power of Domain Specific Languages to neuroscience research, driving the field towards a new paradigm articulating classical neuroanatomy with current statistical and machine learning-based approaches.

9.3.1.2. SLAB (698)

Title: Signal processing and Learning Applied to Brain data

Programm: ERC Starting researcher

Duration: 01/04/2017 - 31/08/2021

Coordinator: Alexandre Gramfort

Partner: LTCI , Telecom ParisTech (France)

Inria contact: Alexandre Gramfort

Summary:

Understanding how the brain works in healthy and pathological conditions is considered as one of the challenges for the 21st century. After the first electroencephalography (EEG) measurements in 1929, the 90's was the birth of modern functional brain imaging with the first functional MRI and full head magnetoencephalography (MEG) system. In the last twenty years, imaging has revolutionized clinical and cognitive neuroscience.

After pioneering works in physics and engineering, the field of neuroscience has to face two major challenges. The size of the datasets keeps growing. The answers to neuroscience questions are limited by the complexity of the signals observed: non-stationarity, high noise levels, heterogeneity of sensors, lack of accurate models. SLAB will provide the next generation of models and algorithms for mining electrophysiology signals which offer unique ways to image the brain at a millisecond time scale.

SLAB will develop dedicated machine learning and signal processing methods and favor the emergence of new challenges for these fields. SLAB focuses on five objectives: 1) source localization with M/EEG for brain imaging at high temporal resolution 2) representation learning to boost statistical power and reduce acquisition costs 3) fusion of heterogeneous sensors 4) modeling of non-stationary spectral interactions to identify functional coupling between neural ensembles 5) development of fast algorithms easy to use by non-experts.

SLAB aims to strengthen mathematical and computational foundations of brain data analysis. The methods developed will have applications across fields (computational biology, astronomy, econometrics). Yet, the primary impact of SLAB will be on neuroscience. The tools and high quality open software produced in SLAB will facilitate the analysis of electrophysiology data, offering new perspectives to understand how the brain works at a mesoscale, and for clinical applications (epilepsy, autism, tremor, sleep disorders).

9.3.1.3. Neuroimaging power (262)

Title: Neuroimaging power

Programm: Marie Curie Fellowhip

Duration: 01/11/2016 - 31/10/2019

Coordinator: Inria

Partner: BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY (United States)

Inria contact: Bertrand Thirion

Summary:

There is an increasing concern about statistical power in neuroscience research. Critically, an underpowered study has poor predictive power. Findings from a low-power study are unlikely to be reproducible, and thus a power analysis is a critical component of any paper. This project aims to promote and facilitate the use of power analyses.

A key component of a power analysis is the specification of an effect size. However, in neuroimaging, there is no standardised way to communicate effect sizes, which makes the choice of an appropriate effect size a formidable task. The best way today to perform a power analysis is by collecting a pilot data set, a very expensive practice. To eliminate the need for pilot data, we will develop a standardised measure of effect size taking into account the spatial variance and the uncertainty of the measurements. Communicating effect sizes in new publications will facilitate the use of power analyses.

To further alleviate the need for pilot data, we will provide a library of effect sizes for different tasks and contrasts, using open data projects in neuroimaging. We will integrate our effect size estimator in open repositories NeuroVault and OpenfMRI. Consequently, these effect sizes can then serve as a proxy for a pilot study, and as such, a huge cost in the design of an experiment is eliminated.

A new experiment will not be identical to the open data and as such the hypothesised parameters might not be fully accurate. To address this issue, we present a flexible framework to analyse data mid-way without harming the control of the type I error rate. Such a procedure will allow re-evaluating halfway an experiment whether it is useful to continue a study, and how many more subjects are needed for statistically sound inferences. To make our methods maximally available, we will write a software suite including all these methods in different programming platforms and we will provide a GUI to further increase the use of power analyses.

9.3.1.4. HBP SGA1

Title: Human Brain Project Specific Grant Agreement 1

Programm: FET Flagship

Duration: 01/04/2016 - 31/02/2020

Coordinator: Katrin Amunts

Partners: 150 european labs, please see https://www.humanbrainproject.eu/en/open-ethical-engaged/contributors/partners

Inria contact: Bertrand Thirion

Summary

Understanding the human brain is one of the greatest scientific challenges of our time. Such an understanding can provide profound insights into our humanity, leading to fundamentally new computing technologies, and transforming the diagnosis and treatment of brain disorders. Modern ICT brings this prospect within reach. The HBP Flagship Initiative (HBP) thus proposes a unique strategy that uses ICT to integrate neuroscience data from around the world, to develop a unified multi-level understanding of the brain and diseases, and ultimately to emulate its computational capabilities. The goal is to catalyze a global collaborative effort. During the HBP's first Specific Grant Agreement (SGA1), the HBP Core Project will outline the basis for building and operating a tightly integrated Research Infrastructure, providing HBP researchers and the scientific Community with unique resources and capabilities. Partnering Projects will enable independent research groups to expand the capabilities of the HBP Platforms, in order to use them to address otherwise intractable problems in neuroscience, computing and medicine in the future. In addition, collaborations with other national, European and international initiatives will create synergies, maximizing returns on research investment. SGA1 covers the detailed steps that will be taken to move the HBP closer to achieving its ambitious Flagship Objectives.

9.3.1.5. HBP SGA2

Title: Interactive Computing E-Infrastructure for the Human Brain Project

Programm: FET Flagship

Duration: 01/04/2018 - 31/03/2020

Coordinator: Katrin Amunts

Partners: see https://www.humanbrainproject.eu/en/open-ethical-engaged/contributors/partners/

Inria contact: Bertrand Thirion

Summary:

The HBP Flagship was launched by the European Commission's Future and Emerging Technologies (FET) scheme in October 2013, and is scheduled to run for ten years. The Flagships, represent a new partnering model for visionary, long-term European cooperative research in the European Research Area, demonstrating the potential for common research efforts. The HBP has the following main objectives:

- Create and operate a European scientific Research Infrastructure for brain research, cognitive neuroscience, and other brain-inspired sciences
- Gather, organise and disseminate data describing the brain and its diseases
- Simulate the brain
- Build multi-scale scaffold theory and models for the brain
- Develop brain-inspired computing, data analytics and robotics
- Ensure that the HBP's work is undertaken responsibly and that it benefits society.

More information on the HBP's Flagship Objectives is available in the Framework Partnership Agreement.

The timeline of the Project is split into multiple phases, each of which will be covered by a separate funding agreement. The current phase is Specific Grant Agreement Two (SGA2), which spans the two-year period from April 2018–April 2020. The HBP is funded via several sources. Total funding is planned to be in the region of EUR 1 billion; around one half of which will be provided by the

European Union, and the other by Member States and private funding sources. The European Union contributed EUR 54 million to the Project in the Ramp-Up Phase (October 2013 to March 2016), EUR 89 million for the second phase (SGA1), and EUR 88 million for the current phase (SGA2). The FET Flagships Staff Working Document provides further information on how Flagships are funded.

9.4. International Initiatives

9.4.1. Inria International Labs

Inria@SiliconValley
Associate Team involved in the International Lab:

9.4.1.1. LargeBrainNets

Title: Characterizing Large-scale Brain Networks Using Novel Computational Methods for dMRI and fMRI-based Connectivity

International Partner (Institution - Laboratory - Researcher):

Stanford Cognitive & Systems Neuroscience Lab, Stanford Medical School, USA. Contact: Vinod Menon.

Start year: 2016

See also: http://www-sop.inria.fr/members/Demian.Wassermann/large-brain-nets.html

In the past two decades, brain imaging of neurotypical individuals and clinical populations has primarily focused on localization of function and structures in the brain, revealing activation in specific brain regions during performance of cognitive tasks through modalities such as functional MRI. In parallel, technologies to identify white matter structures have been developed using diffusion MRI. More recently, interest has shifted towards developing a deeper understanding of the brain's intrinsic architecture and its influence on cognitive and affective information processing. Using for this resting state fMRI and diffusion MRI to build the functional and structural networks of the human brain.

The human brain is a complex patchwork of interconnected regions, and graph-theoretical approaches have become increasingly useful for understanding how functionally connected systems engender, and constrain, cognitive functions. The functional nodes of the human brain and their structural inter-connectivity, collectively the "connectome", are, however, poorly understood. Critically, there is a dearth of computational methods for reliably identifying functional nodes of the brain and their structural inter-connectivity in vivo, despite an abundance of high-quality data from the Human Connectome Project (HCP). Devising and validating methods for investigating the human connectome has therefore taken added significance.

The first major goal of this project is to develop and validate appropriate sophisticated computational and mathematical tools for identifying functional nodes at the whole-brain level and measuring structural and functional connectivity between them, using state-of-the-art human brain imaging techniques and open-source HCP data. To this end, we will first develop and validate novel computational tools for (1) identifying stable functional nodes of the human brain using resting-state functional MRI and (2) measuring structural connectivity between functional nodes of the brain using multi-shell high-angular diffusion MRI. Due to the complementarity of the two imaging techniques fMRI and dMRI, our novel computational methods methods, the synergy between the two laboratories of this associate team will allow us to reveal in unprecedented detail the structural and functional connectivity of the human brain.

The second major goal of this project is to use our newly developed computational tools to characterize normal structural and functional brain networks in neurotypical adults.

Inria@SiliconValley

Associate Team involved in the International Lab:

9.4.1.2. Meta&Co

Title: Meta-Analysis of Neuro-Cognitive Associations

International Partner (Institution - Laboratory - Researcher):

Stanford (United States) - Psychology department. - Russel Poldrack

Start year: 2018

See also: http://team.inria.fr/parietal

Cognitive science and psychiatry describe mental operations: cognition, emotion, perception and their dysfunction. Cognitive neuroimaging bridge these mental concepts to their implementation in the brain, neural firing and wiring, by relying on functional brain imaging. Yet aggregating results from experiments probing brain activity into a consistent description faces the roadblock that cognitive concepts and brain pathologies are ill-defined. Separation between them is often blurry. In addition, these concepts and subdivisions may not correspond to actual brain structures or systems. To tackle this challenge, we propose to adapt data-mining techniques used to learn relationships in computational linguistics. Natural language processing uses distributional semantics to build semantic relationships and ontologies. New models are needed to learn relationships from heterogeneous signals: functional magnetic resonance images (fMRI), on the one hand, combined with related psychology and neuroimaging annotations or publications, on the other hand. Such a joint effort will rely on large publicly-available fMRI databases shared by Podrack Lab, as well as literature mining.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- June 2018: Prof. Lilianne Mujica-Parodi (Univ Stony-Brook, NY USA)
- April-June 2018: Dr Abderrahim Halimi (Edinburgh, UK)
- October 2018: Prof. Nikos Makris (Harvard Medical School)
- December 2018: Dr. Lang Chen (Stanford Medical University)

VISAGES Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. INCR: MUltiple Sclerosis Imaging Check-out (MUSIC)

Participants: Gilles Edan, Francesca Galassi, Olivier Commowick, Christian Barillot, Anne Kerbrat, Jean-Christophe Ferre.

The objective of this project is to investigate algorithms aimed at detecting, segmenting and following overtime the MS lesions, robustly enough to work on a multi-site clinical database. Methods are being evaluated on an amount of training and testing MS images with high quality segmentations from radiographers. The goal is to integrate the developed framework into a production workflow that will be employed by the clinical health network MUltiple Sclerosis Imaging Check-out (MUSIC), covering the western part of France.

9.1.2. ARED VARANASI

Participants: Christian Barillot, Camille Maumet, Xavier Rolland.

Thanks to the development of open science practices, more and more public datasets are available to the research community. In the field of brain imaging, these data, combined, bring a critical increase in sample size, necessary to build robust models of the typical and atypical brain. But, in order to build valid inferences on these data, we need to take into account their heterogeneity. Variability can arise due to multiple factors such as: differences in imaging instruments, in acquisitions protocols and even, in post-processing pipelines. In particular, the expansion of open source machine learning workflows creates a multitude of possible outputs out of the same dataset. The variations induced by this methodological plurality can be referred to as 'analytic variability' which will be the focus of the thesis funded in half by this ARED. The thesis will address two challenges: 1) How to combine neuroimaging data generated by different analysis pipelines? 2) How to publish neuroimages with an adequate level of metadata to enable their reuse? Methodological developments will combine machine learning techniques with methods from knowledge representation.

9.2. National Initiatives

9.2.1. Projet Fondation de France: PERINE

Participants: Élise Bannier, Isabelle Corouge, Julie Coloigner, Maia Proisy, Jean-Christophe Ferré, Christian Barillot.

This study evaluates the effect of prenatal exposure to neurotoxicants on the developing brain. Following previous studies in the PELAGIE cohort this MRI study involves ASL, Diffusion and working memory as well as motor inhibition BOLD fMRI together with neuropsychological tests in children. Inclusions have started in November 2014 and lasted for 2 years. The MRI acquisitions of the PERINE projects have all been performed with a total of 101 children participating to the project. A collaboration with an external PhD student started in January 2017 to process the functional MRI data of this project and Julie Coloigner was hired as a post-doc to work on the Diffusion and ASL data.

9.2.2. Projet Fondation de France: EPMR-MA

Participants: Pierre-Yves Jonin, Élise Bannier, Christian Barillot, Quentin Duché.

This project evaluates memory effects in healthy adults and in patients presenting cognitive impairments using BOLD fMRI and diffusion MRI. The inclusions of patients started in 2016 and all inclusions will be over by the end of 2017. Quentin Duché was hired to process the functional MRI and diffusion data end of 2016 and his contract was extended until May 2018.

9.2.3. Projet Fondation de France: Connectivity of the amygdala in depression

Participants: Christian Barillot, Jean-Marie Batail, Emmanuel Caruyer, Julie Coloigner, Gabriel Robert.

The onset of depression in teenagers and young adults increases the risk to develop a drug-resistant depression in the adulthood. This project aims at evaluating the role of early changes in the microstructure and connectivity of the amygdala. Using a cohort of drug-resistant patients (N=30), non drug-resistant patients (N=30) and controls (N=30), we will identify imaging biomarkers of the pathology. We will compute the same biomarkers in a group of young adults (N=180) and compare these with emotional and cognitive phenotypes in this population, searching for early differences in the development of the amygdala connectivity.

9.2.4. ANR "MAIA", 2015 generic projects program

Participants: Maia Proisy, Pierre Maurel, Antoine Legouhy, Olivier Commowick, Isabelle Corouge, Jean-Christophe Ferré, Christian Barillot.

Each year in France, 55 000 children are born prematurely, i.e., before the 37th week of gestation. Long-term studies of the outcome of prematurely born infants have clearly documented that the majority of such infants may have significant motor, cognitive, and behavioral deficits.

However, there is a limited understanding of the nature of the cerebral abnormality underlying these adverse neurologic outcomes. In this context, the emergence of new modalities of 3D functional MRI, e.g., Arterial Spin Labeling (ASL), or optical imaging technologies, e.g., Near InfraRed Spectroscopy (NIRS), brings new perspectives for extracting cognitive information, via metabolic activity measures. Other classical techniques devoted to cerebral signal measurement, such as ElectroEncephaloGraphy (EEG), provide cognitive information at the cortical level. Each of these various non-invasive imaging technologies brings substantial and specific information for the understanding of newborn brain development.

This project aims at developing innovative approaches for multi-image / multi-signal analysis, in order to improve neurodevelopment understanding methods. From a fundamental point of view, mathematics and computer science have to be considered in association with imaging physics and medicine, to deal with open issues of signal and image analysis from heterogeneous data (image, signal), considered in the multiphysics contexts related to data acquisition (magnetic, optic, electric signals) and biophysics modeling of the newborn brain. A sustained synergy between all these scientific domains is then necessary.

Finally, the sine qua non condition to reach a better understanding of the coupled morphological- cognitive development of premature newborns, is the development of effective software tools, and their distribution to the whole medical community. The very target of this project will be the design of such software tools for medical image / signal analysis, actually operational in clinical routine, and freely available. Academic researchers and industrial partners are working in close collaboration to reach that ambitious goal.

9.2.5. Fondation pour la recherche médicale (FRM) - Project "Hybrid EEG/IRM Neurofeedback for rehabilitation of brain pathologies

Participants: Élise Bannier, Jean-Marie Batail, Isabelle Bonan, Isabelle Corouge, Jean-Christophe Ferré, Jean-Yves Gauvrit, Pierre Maurel, Mathis Fleury, Giulia Lioi, Christian Barillot.

The goal of this project is to make full use of neurofeedback (NF) paradigm in the context of brain rehabilitation. The major breakthrough will come from the coupling associating functional and metabolic information from Magnetic Resonance Imaging (fMRI) to Electro-encephalography (EEG) to “optimize” the neurofeedback protocol. We propose to combine advanced instrumental devices (Hybrid EEG and MRI platforms), with new hybrid Brain computer interface (BCI) paradigms and new computational models to provide novel therapeutic and neuro-rehabilitation paradigms in some of the major mental and neurological disorders of the developmental and the aging brain (stroke, language disorders, Mood Depressive Disorder (MDD), ...). Though the concept of using neurofeedback paradigms for brain therapy has somehow been experimented recently (mostly through case studies), performing neurofeedback through simultaneous fMRI and EEG has almost never been done before so far (two teams in the world including us within the HEMISFER CominLabs project). This project will be conducted through a very complementary set of competences over

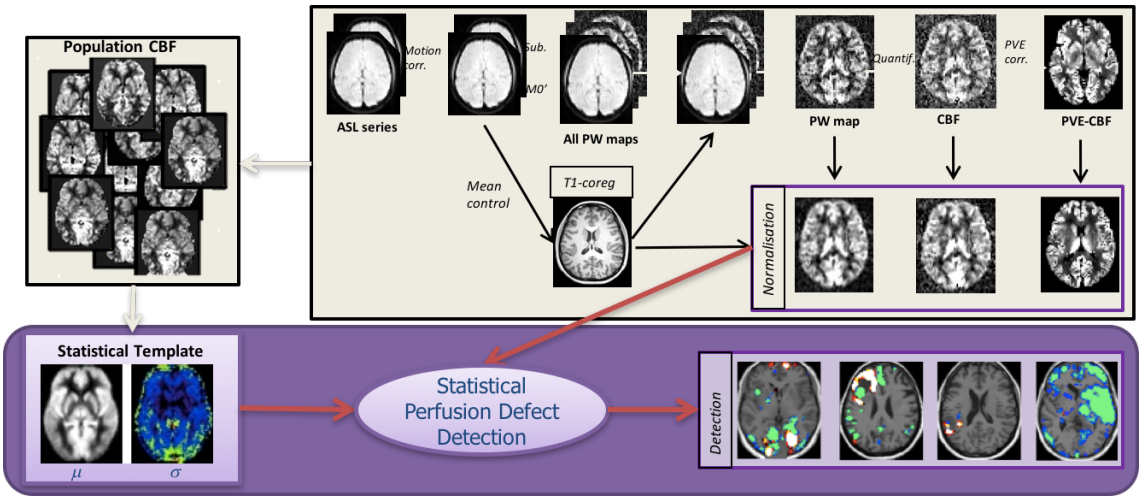

Figure 2. Processing workflow for quantification of Arterial Spin Labelling Cerebral Blood Flow with detection of abnormal perfusion

the different involved teams: VISAGES U1228, HYBRID and PANAMA Teams from Inria/Irisa Rennes and EA 4712 team from U. of Rennes I.

9.2.6. PHRC EMISEP: Evaluation of early spinal cord injury and late physical disability in Relapsing Remitting Multiple Sclerosis

Participants: Élise Bannier, Christian Barillot, Emmanuel Caruyer, Benoit Combès, Olivier Commowick, Gilles Edan, Jean-Christophe Ferré, Anne Kerbrat, Haykel Snoussi.

Multiple Sclerosis (MS) is the most frequent acquired neurological disease affecting young adults (1/1000 inhabitants in France) and leading to impairment. Early and well adapted treatment is essential in patients presenting aggressive forms of MS. This PHRC project focusses on physical impairment and especially on the ability to walk. Several studies, whether epidemiologic or based on brain MRI, have shown that several factors were likely to announce aggressive development of the disease, such as age, number of focal lesions on baseline MRI, clinical activity. However, these factors only partially explain physical impairment progression, preventing their use at the individual level. Spinal cord is often affected in MS, as demonstrated in postmortem or imaging studies. Yet, early radiological depiction of spinal cord lesions is not always correlated with clinical symptoms. Preliminary data, on reduced number of patients, and only investigating the cervical spinal cord have shown that diffuse spinal cord injury, observed via diffusion or magnetisation transfer imaging, would be correlated with physical impairment as evaluated by the EDSS score. Besides, the role of early spinal cord affection (first two years) in the evolution of physical impairment remains unknown.

In this project, we propose to address these different issues and perform a longitudinal study on Relapsing Remitting Multiple Sclerosis (RRMS) patients, recruited in the first year of the disease. Our goal is to show that diffuse and focal lesions detected spinal cord MRI in the first 2 years can be used to predict disease evolution and physical impairment at 5 years. Twelve centers are involved in the study to include 80 patients.

To date, all subjects have been included. H. Snoussi is working in the scope of his PhD thesis on diffusion imaging in the spinal cord starting with distortion correction.

B. Combès started as a post-doc in November 2016 to process the EMISEP imaging data, starting with morphological data processing (registration, segmentation) and magnetization transfer data processing.

9.2.7. Competitivity Clusters

9.2.7.1. The HEMISFER Project

Participants: Élise Bannier, Jean-Marie Batail, Isabelle Bonan, Isabelle Corouge, Claire Cury, Jean-Christophe Ferré, Jean-Yves Gauvrit, Pierre Maurel, Christian Barillot.

The HEMISFER project ("Hybrid Eeg-MrI and Simultaneous neuro-FEedback for brain Rehabilitation") will be conducted at Inria Rennes with the support of the Cluster of Excellence "CominLabs" [0]. The goal of HEMISFER is to make full use of the neurofeedback paradigm in the context of rehabilitation and psychiatric disorders. The major breakthrough will come from the use of a coupling model associating functional and metabolic information from Magnetic Resonance Imaging (fMRI) to Electro-encephalography (EEG) to "enhance" the neurofeedback protocol. We propose to combine advanced instrumental devices (Hybrid EEG and MRI platforms), with new man-machine interface paradigms (Brain computer interface and serious gaming) and new computational models (source separation, sparse representations and machine learning) to provide novel therapeutic and neuro-rehabilitation paradigms in some of the major neurological and psychiatric disorders of the developmental and the aging brain (stroke, attention-deficit disorder, language disorders, treatment-resistant mood disorders, etc.). This project will be conducted with the HYBRID and PANAMA Teams from Inria Rennes, the EA 4712 team from University of Rennes I and the ATHENA team from Inria Sophia-Antipolis. This work will benefit from the research 3T MRI and MRI-compatible EEG systems provided by the NeurInfo in-vivo neuroimaging platform on which these new research protocols will be set up. A budget of 500K€ provided by the CominLabs cluster to support this project (through experimental designs, PhDs, post-docs and expert engineers).

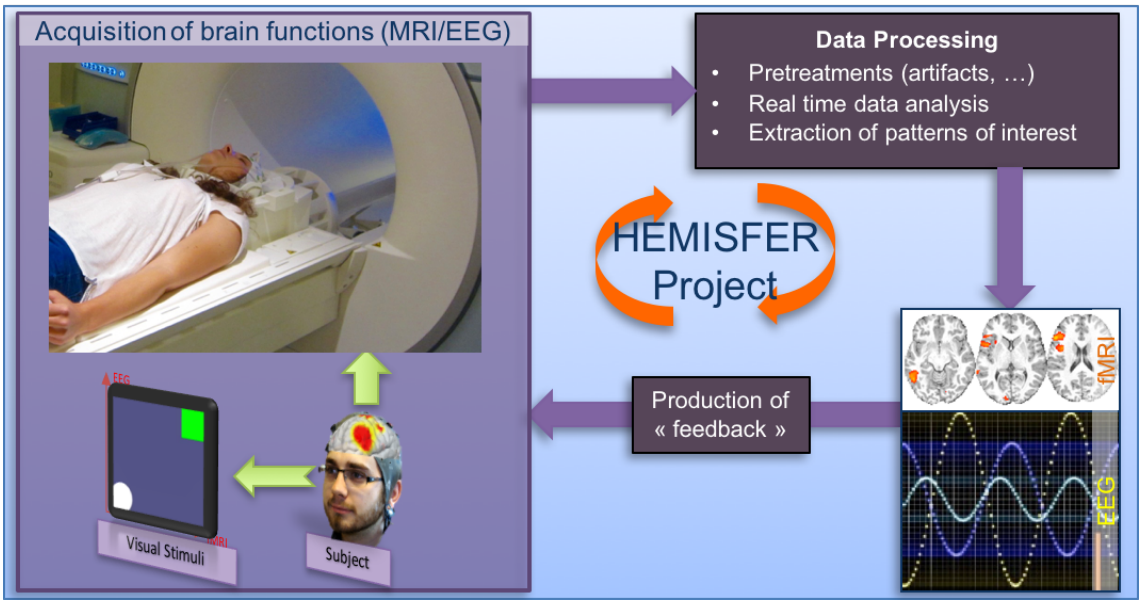

Figure 3. Principle of the Hemisfer project.

9.2.7.2. France Life Imaging (FLI)

Participants: Christian Barillot, Olivier Commowick, Michael Kain, Florent Leray, Julien Louis, Aneta Morawin, Mathieu Simon, Yao Chi.

[0] https://iww.inria.fr/cominlabs-newsletter/april-2013-four-projects-selected/#hemisfer

France Life Imaging (FLI) is a proposed large-scale research infrastructure project aimed at establishing a coordinated and harmonized network of biomedical imaging in France. This project was recently selected by the call "Investissements d'Avenir - Infrastructure en Biologie et Santé". One node of this project is the node Information Analysis and Management (IAM), a transversal node build by a consortium of teams that will contribute to the construction of a network for data storage and information processing. Instead of building yet other dedicated facilities, the IAM node will use already existing data storage and information processing facilities (LaTIM Brest; CREATIS Lyon; CIC-IT Nancy; VisAGeS U1228 Inria Rennes; CATI CEA Saclay; LSIIT/ICube Strasbourg) that will increase their capacities for the FLI infrastructure. Inter-connections and access to services will be achieved through a dedicated software platform that will be developed based on the expertise gained through successful existing developments. The IAM node has several goals. It aims first at building a versatile facility for data management that will inter-connect the data production sites and data processing for which state-of-the-art solutions, hardware and software, will be available to infrastructure users. Modular solutions are preferred to accommodate the large variety of modalities acquisitions, scientific problems, data size, and adapted for future challenges. Second, it aims at offering the latest development that will be made available to image processing research teams. The team VisAGeS fulfills multiple roles in this nation-wide project. Christian Barillot is the chair of the node IAM, Olivier Commowick is participating in the working group workflow and image processing and Michael Kain the technical manager. Apart from the team members, software solutions like MedInria and Shanoir will be part of the final software platform.

9.2.7.3. OFSEP

Participants: Élise Bannier, Christian Barillot, Olivier Commowick, Gilles Edan, Jean-Christophe Ferré, Michael Kain, Inès Fakhfakh.

The French Observatory of Multiple Sclerosis (OFSEP) is one of 10 projects selected in January 2011 in response to the call for proposal in the "Investissements d'Avenir - Cohorts 2010" program launched by the French Government. It allows support from the National Agency for Research (ANR) of approximately € 10 million for 10 years. It is coordinated by the Department of Neurology at the Neurological Hospital Pierre Wertheimer in Lyon (Professor Christian Confavreux), and it is supported by the EDMUS Foundation against multiple sclerosis, the University Claude Bernard Lyon 1 and the Hospices Civils de Lyon. OFSEP is based on a network of neurologists and radiologists distributed throughout the French territory and linked to 61 centers. OFSEP national cohort includes more than 50,000 people with Multiple Sclerosis, approximately half of the patients residing in France. The generalization of longitudinal monitoring and systematic association of clinical data and neuroimaging data is one of the objectives of OFSEP in order to improve the quality, efficiency and safety of care and promote clinical, basic and translational research in MS. For the concern of data management, the Shanoir platform of Inria has been retained to manage the imaging data of the National OFSEP cohort in multiple sclerosis.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. OpenAire-Connect

Participants: Christian Barillot, Michael Kain, Camille Maumet, Xavier Rolland.

Project title: **OpenAire-Connect**

Partners: PI: CNR, Italy; Athena Research And Innovation Center In Information Communication & Knowledge Technologies, Greece; Uniwersytet Warszawski, Poland; JISC LBG, UK; Universitaet Bremen, Germany; Universidade Do Minho, Portugal; CNRS (Visages, Creatis), France; Universita Di Firenze, Italy; Institut De Recherche Pour Le Developpement (IRD), France; European Organization For Nuclear Research (CERN), Switzerland; International Center For Research On The Environment And The Economy, Greece

Budget: 2M € (120k€ for CNRS)

Abstract: The OpenAire-Connect H2020 project will introduce and implement the concept of Open Science as a Service (OSaaS) on top of the existing OpenAIRE infrastructure, delivering out-of-the-box, on-demand deployable tools. OpenAIRE-Connect will adopt an end-user driven approach (via the involvement of 5 prominent research communities), and enrich the portfolio of OpenAIRE infrastructure production services with a Research Community Dashboard Service and a Catch-All Notification Broker Service. The first will offer publishing, interlinking, packaging functionalities to enable them to share and re-use their research artifacts (introducing methods, e.g., data, software, protocols). This effort, supported by the harvesting and mining "intelligence" of the OpenAIRE infrastructure, will provide communities with the content and tools they need to effectively evaluate and reproduce science. OpenAIRE-Connect will combine dissemination and training with OpenAIRE's powerful NOAD network engaging research communities and content providers in adopting such services. These combined actions will bring immediate and long-term benefits to scholarly communication stakeholders by affecting the way research results are disseminated, exchanged, evaluated, and re-used. In this project VisAGeS is acting, through CNRS, as the French coordinator to develop the link with the Neuroimaging research community. This will be performed in the context of the FLI-IAM national infrastructure.

9.3.1.2. EIT-Health

Participants: Christian Barillot, Michael Kain.

Abstract: EIT Health aims to promote entrepreneurship and develop innovations in healthy living and active ageing, providing Europe with new opportunities and resources. EIT Health will enable citizens to lead healthier and more productive lives by delivering products, services and concepts that will improve quality of life and contribute to the sustainability of healthcare across Europe. EIT Health is a strong, diverse and balanced partnership of best-in-class organisations in education, research, technology, business creation and corporate and social innovation. EIT Health intends to foster cooperation and unlock Europe's innovation and growth potential – developing and retaining the best talents, creating high-quality jobs and boosting the global competitiveness of European industry. VisAGeS is involved in this project through the Inserm and Inria institutions. Christian Barillot is representing Inria as one expert in the dedicated WG "Healthy Brain". VisAGeS is also concerned by the WG "big data"..

9.4. International Initiatives

9.4.1. Inria International Partners

9.4.1.1. BARBANT

Title: Boston and Rennes, a Brain image Analysis Team

International Partner (Institution - Laboratory - Researcher):

Harvard University (United States) - Medical School - Simon K. Warfield

See also: https://team.inria.fr/barbant/

Between 2012 and 2017, BARBANT was an Inria associate team shared between Inria VisAGeS research team and the Computational Radiology Laboratory at the Boston Children's hospital (Harvard Medical School). The collaboration continued in 2018 aiming at better understanding the behavior of normal and pathological Central Nervous System (CNS) organs and systems. Pathologies of particular interest to us are multiple sclerosis, psychiatric, and pediatric diseases such as pediatric multiple sclerosis or tuberous sclerosis. A major challenge is to characterize the future course of the pathological processes in each patient as early as possible in order to predict the progression of the disease and/or adverse neurological outcomes, and to develop better techniques for both monitoring response to therapy and for altering therapy (duration, dose and nature) in response to patient-specific changes in imaging characteristics. At term, the goal is to introduce objective figures to correlate qualitative and quantitative phenotypic markers coming from the clinic and image analysis, mostly at the early stage of the pathologies. This will allow for the selection or adaptation of the treatment for patients at an early stage of the disease. Sudhanya Chatterjee's PhD was performed in 2018 under this collaboration.

9.4.1.2. Informal International Partners

- Collaboration with Neuropoly, Polytechnique Montreal: Haykel Snoussi visited the group of Julien Cohen-Adad and received an Inria-MITACS fellowship for a 3 months period (Nov. 2017-Jan. 2018). He worked on the processing of diffusion-weighted images of multiple sclerosis patients' spinal cord in the context of the EMISEP project. We also collaborate with Neuropoly, Polytechnique Montreal through the EMISEP project: Spinal cord data from the EMISEP study was shared with the group in Montreal for manual lesion segmentation and topological analysis of the presence of lesions, in the brain and spinal cord. This work resulted in a common publication [12].
- Camille Maumet collaborates with Prof. Thomas Nichols and his group, NISOx at the Oxford Big Data Institute and with international members of the INCF on neuroimaging data sharing.
- In the context of a project at Neurinfo, Elise Bannier and Jean-Christophe Ferré collaborated with Tobias Kober from Lausanne, to evaluate a sequence named FLAWS, allowing Fluid and White Matter supression for anterior thalamic nucleus visualization.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- Jean-Baptiste Poline, Associate Professor at McGill University, Montreal, Canada will visit the team on Dec 18-19 and give a talk on reproducibility in neuroimaging.
- Alice Bates, Postdoctoral research fellow at Australian National University, Canberra, visited the team from Oct 8 to Oct 26. She gave a talk on signal sampling and processing for spherical data, and collaborated with the team on a project related to multidimensional diffusion MRI.

9.5.2. Visits to International Teams

9.5.2.1. Research Stays Abroad

- Haykel Snoussi visited NeuroPoly, Polytechnique Montréal, Canada, from Oct 30th 2017 to Jan 26 2018; he was awarded a MITACS-Inria Globalink research award.

AIRSEA Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

C. Prieur is co-leader of work-package 3 of the cross-disciplinary-project Trajectories from Idex Grenoble.

8.2. National Initiatives

8.2.1. ANR

A 4-year contract : ANR COCOA (COmprehensive Coupling approach for the Ocean and the Atmosphere). PI: E. Blayo. (Jan. 2017 - Dec. 2020). Other partners: Laboratoire des Sciences du Climat et de l'Environnement (UMR8212, Gif-sur-Yvette), Laboratoire de Météorologie Dynamique (UMR8539, Paris), Laboratoire d'Océanographie Physique et Spatiale (UMR6523, Brest), Centre National de Recherche Météorologique (UMR3589, Toulouse), Cerfacs (Toulouse). This project aims at revisiting the overall representation of air-sea interactions in coupled ocean-atmosphere models, and particularly in climate models, by coherently considering physical, mathematical, numerical and algorithmic aspects.

A 4-year contract : ANR HEAT (Highly Efficient ATmospheric modelling) http://www.agence-nationale-recherche.fr/?Project=ANR-14-CE23-0010.

A 4-year contract : ANR ADOM (Asynchronous Domain decomposition methods)

A 5-year contract with the French Navy (SHOM) on the improvment of the CROCO ocean model http://www.croco-ocean.org.

C. Prieur and E. Arnaud are involved as experts in project High-Tune http://www.agence-nationale-recherche.fr/Projet-ANR-16-CE01-0010 funded by ANR.

8.2.2. Other Initiatives

A. Vidard leads a group of projects gathering multiple partners in France and UK on the topic "Variational Data Assimilation for the NEMO/OPA9 Ocean Model", see 5.3 .

C. Prieur chaired GdR MASCOT NUM 2010-2017, in which are also involved M. Nodet, E. Blayo, C. Helbert, E. Arnaud, L. Viry, S. Nanty, L. Gilquin. She is still strong involved in thie group (co-chair) http://www.gdr-mascotnum.fr/doku.php.

LEFE/GMMC CASIS, Coupled Assimilation Strategies for the Initialisation of an ocean- atmospheric boundary layer System, A. Vidard en collaboration avec Mercator océan

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

H2020 project IMMERSE (Improving Models for Marine EnviRonment SErvices) is funded from 2018-12-01 to 2022-11-30 (Inria contact: Florian Lemarié, coordinator: J. Le Sommer, CNRS). The overarching goal of the project is to ensure that the Copernicus Marine Environment Monitoring Service (CMEMS) will have continuing access to world-class marine modelling tools for its next generation systems while leveraging advances in space and information technologies, therefore allowing it to address the ever-increasing and evolving demands for marine monitoring and prediction in the 2020s and beyond.

See also https://cordis.europa.eu/project/rcn/218810/factsheet/fr

8.3.2. Collaborations with Major European Organizations

Partner: European Center for Medium Range Weather Forecast. Reading (UK)

World leading Numerical Weather Center, that include an ocean analysis section in order to provide ocean initial condition for the coupled ocean atmosphere forecast. They play a significant role in the NEMOVAR project in which we are also partner.

Partner: Met Office (U.K) National British Numerical Weather and Oceanographic service. Exceter (UK).

We do have a strong collaboration with their ocean initialization team through both our NEMO, NEMO-ASSIM and NEMOVAR activities. They also are our partner in the NEMOVAR consortium.

8.4. International Initiatives

8.4.1. Inria Associate Teams Not Involved in an Inria International Labs

8.4.1.1. UNQUESTIONABLE

Title: UNcertainty QUantification is ESenTIal for OceaNic & Atmospheric flows proBLEms.

International Partner:

Massachusetts Institute of Technology (United States) - Aerospace Computational Design Laboratory - Youssef Marzouk

Start year: 2018

See also: https://team.inria.fr/unquestionable/

The ability to understand and predict the behavior of geophysical flows is of greatest importance, due to its strong societal impact. Numerical models are essential to describe the evolution of the system (ocean + atmosphere), and involve a large number of parameters, whose knowledge is sometimes really poor. The reliability of the numerical predictions thus requires a step of parameter identification. The Inria-AIRSEA team has a strong expertise in variational approaches for inverse problems. An alternative is the use of particle filters, whose main advantage is their ability to tackle non-gaussian frameworks. However, particle filters suffer from the curse of dimensionality. The main objective of the collaboration we propose between the Inria-AIRSEA team and the MIT UQ group is the understanding of potential low-dimensional structure underlying geophysical applications, then the exploitation of such structures to extend particle filter to high-dimensional applications.

F. Lemarié is involved in the Inria associate team NEMOLOCO with Santiago University (Chile)

8.4.2. Inria International Partners

8.4.2.1. Informal International Partners

C. Prieur collaborates with Jose R. Leon (Universdad de la república de Uruguay, Montevideo).

C. Prieur collaborates with K. Bertin (CIMFAV, Valparaíso).

F. Lemarié and L. Debreu collaborate with Hans Burchard and Knut Klingbeil from the Leibniz-Institut für Ostseeforschung in Warnemünde (Germany).

8.5. International Research Visitors

8.5.1. Visits of International Scientists

Tiangang Cui, associate professor at Monash University (Melbourne, Australia), has visited the AIRSEA team during two weeks in December 2018. The purpose of this visit is to continue the collaboration with O. Zahm on the question of the dimension reduction for Bayesian inverse problems. Tiangang Cui also gave a presentation in the "Bayes in Grenoble" seminar at Inria-Montbonnot (3rd Dec. 2018).

Nicholas Kevlahan, from McMaster University (Canada) is a visiting scientist of the AIRSEA team for 10 months starting September 2018.

8.5.2. Visits to International Teams

Olivier Zahm was invited by Prof. Fabio Nobile to spend one week at EPFL to discuss the possible future collaboration

Clémentine Prieur visited Durham (US) in the framework of the SAMSI program on Quasi-Monte Carlo and High-Dimensional Sampling Methods for Applied Mathematics (QMC). She was invited for a tutorial at the Opening Workshop : August 28 – September 1, 2018. I take part to several working groups of the program.

Clémentine Prieur visited the Isaac Newton Institute for Mathematical Sciences in Cambridge in June 2018. She was invited in the framework of a semester on Uncertainty quantification for complex systems : theory and methodologies.

F.-X. Le Dimet visited the Florida State University during 2 weeks in May 2018. He made one presentation

F.-X. Le Dimet visited the University of Wisconsin during one week in June 2018. He made 2 presentations.

F.-X. Le Dimet visited the Harbin Institute of Technology during two weeks. He gave a 16 hours cours on the Data Assimilation.

ANGE Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR MFG (2016-2021)

Participant: Julien Salomon.

Project acronym: MFG

Project title: Mean Field Games

Coordinator: Sébastien Boyaval (LHSV/ENPC)

Funding: 299 160 euros.

CMean field game theory (MFG) is a new and active field of mathematics, which analyses the dynamics of a very large number of agents. Introduced about ten years ago, MFG models have been used in different fields: economics, finance, social sciences, engineering,... MFG theory is at the intersection of mean field theory, mathematical game theory, optimal control, stochastic analysis, variation calculation, partial differential equations and scientific calculation. Drawing on an internationally recognized French team on the subject, the project seeks to obtain major contributions in 4 main directions: the "medium field" aspect (i.e., how to obtain macroscopic models from microscopic models); the analysis of new MFG systems; their numerical analysis; the development of new applications. In this period of rapid expansion of MFG models, the project seeks to foster French leadership in the field and attract new researchers from related fields.

9.1.2. ANR INFAMIE (2015-2019)

Participant: Boris Haspot.

Program: ANR Défi de tous les savoirs (DS10) 2015

Project acronym: INFAMIE

Project title: INhomogeneous Flows : Asymptotic Models and Interfaces Evolution

Coordinator: Raphaël Danchin (Univ. Paris-Est)

Funding: 232 960 euros.

Our project aims at a better mathematical understanding of several models for the evolution of inhomogeneous flows. Through three main lines of research (see below), we will pursue a twofold final objective. First, we want to develop the current theory of regular solutions for several equations for the evolution of fluids, proposing a new approach and developing tools that are likely to be efficient in various areas of PDEs. Second, for a few selected concrete systems that describe flows in the earth environment or in astrophysics, we wish to use this general approach to extract as much information as possible concerning the qualitative behavior of the solutions.

9.1.3. ANR SEDIFLO (2015-2019)

Participants: Emmanuel Audusse, Martin Parisot.

Program: ANR Défi 1 “Gestion sobre des ressources et adaptation au changement climatique” (JCJC)

Project acronym: SEDIFLO

Project title: Modelling and simulation of solid transport in rivers

Coordinator: Sébastien Boyaval (LHSV/ENPC)

Based on recent theoretical and experimental results, this project is aimed at modelling transport of sediments within rivers. It will rely on innovations from the point of view of rheology as well as advanced mathematical tools (asymptotic model reduction, PDE discretisation).

9.1.4. ANR Hyflo-Eflu (2016-2019)

Participants: Jérémy Ledoux, Martin Parisot, Jacques Sainte-Marie, Julien Salomon.

ANR project call: Energies marines renouvelables

Project acronym: Hyflo-Eflu

Project title: Hydroliennes flottantes et énergie fluviale

Coordinator: Julien Salomon

The project is a collaboration between the Inria-team ANGE, specialist of free surface flow and optimisation, and the industrial developers of the turbine, HYDROTUBE ENERGIE. The objective of the project HyFlo-EFlu is to deliver a numerical software able to simulate the dynamic of a floating water turbine in real context. For the academic partner, the main challenge is in the simulation of the floating structure at the scale of the river, and the modelling of the vertical and horisontal axis turbine. For the industrial partner, the objective is the validation of the stability of the structure and the performance in term of energy production.

9.1.5. ANR CHARMS (2016-2020)

Participant: Cindy Guichard.

ANR project call: Transformations et inter-conversions énergétiques

Project acronym: CHARMS

Project title: Modèles de réservoirs quantitatifs pour les systèmes hydrothermaux complexes

Coordinator: Simon Lopez (BRGM)

Funding: 73k euros for LJLL (in 767k euros for the whole project)

CHARMS ANR project is focused on the mathematical methods and software tools dedicated to the simulation of the physical models issued from geothermal engineering. The final objective is the achievement of a highly parallel code, validated on realistic cases.

9.1.6. CNRS Mocha (2017-2018)

Participant: Martin Parisot.

CNRS project call: LEFE

Project acronym: MOCHA

Project title: Multi-dimensiOnal Coupling in Hydraulics and data Assimilation

Coordinator: Martin Parisot

Funding: 14k euros

In collaboration with S. Barthélémy, N. Goutal, S. Ricci, M. Hoang Le.

Multi-dimensionnal coupling in river hydrodynamics offers a conveninent solution to properly model complex flow while limiting the computational cost and making the most of pre-exsiting models. The project aims to adapt the lateral interface coupling proposed in [35] to the implicit version and test it on real data for the Garonne River.

9.1.7. Inria Project Lab "Algae in Silico" (2015-2018)

Participants: Marie-Odile Bristeau, Yohan Penel, Jacques Sainte-Marie, Fabien Souillé.

In the aftermath of the ADT In@lgae (2013–2015), we developed a simulation tool for microalgae culture. An Inria Project Lab "Algae in Silico" has started in collaboration with Inria teams BIOCORE and DYLISS. It concerns microalgae culture for biofuel production and the aim is to provide an integrated platform for numerical simulation "from genes to industrial processes".

9.1.8. Inria Project Lab "CityLab" (2015-2018)

Participants: Vivien Mallet, Raphaël Ventura.

CityLab@Inria studies ICT solutions toward smart cities that promote both social and environmental sustainability.

9.1.9. GdR EGRIN (2017–2021)

Participants: Emmanuel Audusse, Bernard Di Martino, Nicole Goutal, Cindy Guichard, Anne Mangeney, Martin Parisot, Jacques Sainte-Marie.

EGRIN stands for Gravity-driven flows and natural hazards. J. Sainte-Marie is the head of the scientific committee of this CNRS research group and A. Mangeney is a member of the committee. Other members of the team involved in the project are local correspondents. The scientific goals of this project are the modelling, analysis and simulation of complex fluids by means of reduced-complexity models in the framework of geophysical flows.

9.1.10. ANR FireCaster (2017-2020)

Participants: Frédéric Allaire, Vivien Mallet.

ANR project call: DS0104

Project acronym: FireCaster

Project title: Plateforme de prévision incendie et de réponse d'urgence

Coordinator: Jean-Baptiste Filippi (Univ. Corse)

Funding: 442k euros

The goal of the FireCaster project is to prototype a fire decision support system at the national scale to estimate upcoming fire risk (H+24 to H+48) and in case of crisis, to predict fire front position and local pollution (H+1 to H+12).

9.1.11. ANR CENSE (2017-2020)

Participants: Antoine Lesieur, Vivien Mallet.

ANR project call: DS0601

Project acronym: CENSE

Project title: Caractérisation des environnements sonores urbains : vers une approche globale associant données libres, mesures et modélisations

Coordinator: Judicaël Picaut (IFSTTAR)

Funding: 856k euros

The CENSE project aims at proposing a new methodology for the production of more realistic noise maps, based on an assimilation of simulated and measured data through a dense network of low-cost sensors.

9.1.12. ANR RAVEX (2017-2020)

Participant: Anne Mangeney.

ANR project call: DS0106

Project acronym: RAVEX

Project title: Développement d'une approche intégrée pour la réduction des Risques Associés au Volcanisme EXplosif, de la recherche sur l'aléa aux outils de gestion de crise : le cas de la Martinique

Coordinator: Olivier Roche (IRD)

Funding: 619k euros

9.1.13. ANR CINE-PARA (2015-2019)

Participant: Julien Salomon.

ANR project call: DS0708
Project acronym: CINE-PARA
Project title: Méthodes de parallélisation pour cinétiques complexes
Coordinator: Yvon Maday (LJLL)

9.2. European Initiatives

9.2.1. FP7 & H2020 Projects

9.2.1.1. ERC Consolidator Grant (2013-2018)

Participants: Anne Mangeney, Hugo Martin.

The project SLIDEQUAKES is about detection and understanding of landslides by observing and modelling gravitational flows and generated earthquakes and is funded by the European Research Council (2 million euros). More precisely, it deals with the mathematical, numerical and experimental modelling of gravitational flows and generated seismic waves coupled with field measurements to better understand and predict these natural hazards and their link with volcanic, seismic and climatic activities.

9.2.1.2. EoCoE (2015-2018)

Participant: Vivien Mallet.

Title: Energy oriented Centre of Excellence for computer applications
Program: H2020
Duration: October 2015 - October 2018
Coordinator: Édouard Audit (CEA)
Partners: CEA (Commissariat à l'Énergie Atomique et aux Énergies Alternatives, France), Forschungszentrum Julich (Germany), Max Planck Gesellschaft (Germany), ENEA (Agenzia Nazionale Per le Nuove Tecnologie, l'energia E Lo Sviluppo Economico Sostenibile, Italy), CERFACS (European Centre for Research and Advanced Training in Scientific Computing, France), Instytut Chemii Bioorganicznej Polskiej Akademii Nauk (Poland), Universita Degli Studi di Trento (Italy), Fraunhofer Gesellschaft (Germany), University of Bath (United Kingdom), CYL (The Cyprus Institute, Cyprus), CNR (National Research Council of Italy), Université Libre de Bruxelles (Belgium), BSC (Centro Nacional de Supercomputacion, Spain)
Inria contact: Michel Kern (Serena team)
Abstract: The aim of the projevt is to establish an Energy Oriented Centre of Excellence for computing applications (EoCoE). EoCoE (pronounce "Echo") will use the prodigious potential offered by the ever-growing computing infrastructure to foster and accelerate the European transition to a reliable and low carbon energy supply. To achieve this goal, we believe that the present revolution in hardware technology calls for a similar paradigm change in the way application codes are designed. EoCoE will assist the energy transition via targeted support to four renewable energy pillars: Meteo, Materials, Water and Fusion, each with a heavy reliance on numerical modelling. These four pillars will be anchored within a strong transversal multidisciplinary basis providing high-end expertise in applied mathematics and HPC. EoCoE is structured around a central Franco-German hub coordinating a pan-European network, gathering a total of 8 countries and 23 teams. Its partners are strongly engaged in both the HPC and energy fields; a prerequisite for the long-term sustainability of EoCoE and also ensuring that it is deeply integrated in the overall European strategy for HPC. The primary goal of EoCoE is to create a new, long lasting and sustainable community around computational energy science. At the same time, EoCoE is committed to deliver high-impact results within the first three years. It will resolve current bottlenecks in application codes, leading to new modelling capabilities and scientific advances among the four user communities; it will develop cutting-edge mathematical and numerical methods, and tools to foster the usage of Exascale computing. Dedicated services for laboratories and industries will be established to leverage this expertise and to foster an ecosystem around HPC for energy. EoCoE will give birth to new collaborations and working methods and will encourage widely spread best practices.

9.2.2. Collaborations with Major European Organisations

9.2.2.1. CNRS PICS NHML (2017-2019)

Participants: Martin Parisot, Yohan Penel, Jacques Sainte-Marie.

Program: CNRS PICS (projet international de collaboration scientifique)

Project acronym: NHML

Project title: non-hydrostatic multilayer models

Duration: 01/17-12/19

Coordinator: Yohan Penel (Inria)

Other partners: IMUS (Sevilla, Spain)

Other Participants: Enrique Fernández-Nieto (Sevilla), Tomas Morales de Luna (Cordoba)

Funding: 12k euros

Abstract: This collaboration aims at designing a hierarchy of multilayer models with a non-hydrostatic pressure as a discretisation along the vertical axis of the Euler equations. The hierarchy relies on the degree of approximation of the variables discretised with a Discontinuous Galerkin method for the vertical direction. These innovative models will imply a theoretical study and the development of numerical tools in dimensions 1 and 2 before the modelling of other physical phenomena (viscosity effects, ...).

9.3. International Initiatives

9.3.1. Informal International Partners

Four collaborations with foreign colleagues are to be mentioned:

- **Spain** - A collaboration with Spanish researchers has been initiated in 2016 to derive accurate models and effecient algorithms for free surface flows including non-hydrostatic effects. ANGE applied in 2018 to the Inria Associate Team programme in order to strenghten the collaboration.
- **USA** A joint work with R. LeVeque (Univ. Seattle) and M. Berger (New York Univ.) consists in modelling the impact of asteroids on the generation of tsunamis.
- **Germany** A collaboration with researchers from the University of Constance has been initiated in 2018 about domain decomposition and identifaction algorithms (G. Ciaramella, S. Volkwein).
- **Hong-Kong** A collaboration with F. Kwok on time parallelization for assimilation algorithm has been initiated in 2018.

9.4. International Research Visitors

- Y. Penel spent twice two weeks (May, October)at the university of Sevilla (Spain) to collaborate with E. Fernández-Nieto.

9.4.1. Visits of International Scientists

- G. Ciaramella visited J. Salomon (28.05-01.06) to work on a reduction method for identification problem.

CASTOR Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. Inria Project Lab: FRATRES (Fusion Reactors Research and Simulation)

- Participants : Inria project-teams : CASTOR, IPSO, TONUS,
- Partners : IRFM-CEA, Max Planck Institute-IPP Garching, LJLL-Jussieu, IMT-Toulouse

Controlled nuclear fusion can be considered as an example of grand challenge in many fields of computational sciences from physical modelling, mathematical and numerical analysis to algorithmics and software development and several Inria teams and their partners are developing mathematical and numerical tools in these areas.
Since january 2015, H. Guillard is coordinating the Inria Project Lab FRATRES (https://team.inria.fr/ipl-fratres/) to organize these developments on a collaborative basis in order to overcome the current limitations of today numerical methodologies. The ambition is to prepare the next generation of numerical modelling methodologies able to use in an optimal way the processing capabilities of modern massively parallel architectures. This objective requires close collaboration between a) applied mathematicians and physicists that develop and study mathematical models of PDE; b) numerical analysts developing approximation schemes; c) specialists of algorithmic proposing solvers and libraries using the many levels of parallelism offered by the modern architecture and d) computer scientists. This Inria Project Lab will contribute in close connection with National and European initiatives devoted to nuclear Fusion to the improvement and design of numerical simulation technologies applied to plasma physics and in particular to the ITER project for magnetic confinement fusion.

Contact : Hervé Guillard

8.1.2. Defi : Infiniti : INterFaces Interdisciplinaires NumérIque et ThéorIque

- Participants: HervéGuillard, AnnaDegioanni[LAMPEA Aix-en-Provence], SilvanaCondemi[ADES, Marseille], ZhenyuXu

In the framework of the "Defi : Infiniti : INterFaces Interdisciplinaires NumérIque et ThéorIque" of the “Mission pour l’Interdisciplinarité” of CNRS, this work has associated Hervé Guillard to Anna Degioanni of the Laboratory LAMPEA - Laboratoire Méditerranéen de Préhistoire Europe-Afrique of Aix-en-Provence and Silvana Condemi of the ADES (Anthropologie bio-culturelle, droit, éthique et santé - UMR 7268) laboratory in Marseille. The purpose of this work was to propose a numerical model and to realize a software allowing paleo-anthropologist and pre-historians to study numerically the propagation and diffusion of Homo Sapiens in Europe between 50 000 and 30 000 years BP. A 6 month internship of Ms Zhenyu Xu, 3rd year student at the polytech’Nice school of engineers has been devoted to this project and the results have been presented at the "Journée de restitution 2018 du Défi Infiniti", (http://www.cnrs.fr/mi/spip.php?article1440&lang=fr)

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

8.2.1.1. EoCoE

Title: Energy oriented Centre of Excellence for computer applications

Programm: H2020

Duration: October 2015 - October 2018

Coordinator: CEA

Partners:

- Barcelona Supercomputing Center - Centro Nacional de Supercomputacion (Spain)
- Commissariat A L Energie Atomique et Aux Energies Alternatives (France)
- Centre Europeen de Recherche et de Formation Avancee en Calcul Scientifique (France)
- Consiglio Nazionale Delle Ricerche (Italy)
- The Cyprus Institute (Cyprus)
- Agenzia Nazionale Per le Nuove Tecnologie, l'energia E Lo Sviluppo Economico Sostenibile (Italy)
- Fraunhofer Gesellschaft Zur Forderung Der Angewandten Forschung Ev (Germany)
- Instytut Chemii Bioorganicznej Polskiej Akademii Nauk (Poland)
- Forschungszentrum Julich (Germany)
- Max Planck Gesellschaft Zur Foerderung Der Wissenschaften E.V. (Germany)
- University of Bath (United Kingdom)
- Universite Libre de Bruxelles (Belgium)
- Universita Degli Studi di Trento (Italy)

Inria contact: Michel Kern

The aim of the present proposal is to establish an Energy Oriented Centre of Excellence for computing applications, (EoCoE). EoCoE (pronounce "Echo") will use the prodigious potential offered by the ever-growing computing infrastructure to foster and accelerate the European transition to a reliable and low carbon energy supply. To achieve this goal, we believe that the present revolution in hardware technology calls for a similar paradigm change in the way application codes are designed. EoCoE will assist the energy transition via targeted support to four renewable energy pillars: Meteo, Materials, Water and Fusion, each with a heavy reliance on numerical modelling. These four pillars will be anchored within a strong transversal multidisciplinary basis providing high-end expertise in applied mathematics and HPC. EoCoE is structured around a central Franco-German hub coordinating a pan-European network, gathering a total of 8 countries and 23 teams. Its partners are strongly engaged in both the HPC and energy fields; a prerequisite for the long-term sustainability of EoCoE and also ensuring that it is deeply integrated in the overall European strategy for HPC. The primary goal of EoCoE is to create a new, long lasting and sustainable community around computational energy science. At the same time, EoCoE is committed to deliver high-impact results within the first three years. It will resolve current bottlenecks in application codes, leading to new modelling capabilities and scientific advances among the four user communities; it will develop cutting-edge mathematical and numerical methods, and tools to foster the usage of Exascale computing. Dedicated services for laboratories and industries will be established to leverage this expertise and to foster an ecosystem around HPC for energy. EoCoE will give birth to new collaborations and working methods and will encourage widely spread best practices.

8.2.2. Collaborations in European Programs, Except FP7 & H2020

EuroFusion Consortium

CASTOR participates to the following EuroFusion consortium projects :

Enabling research contract 2014-2018. (B. Nkonga, H. Guillard, A. Sangam) CfP-WP15-ENR-01/IPP-05, Grant agreement No 633053. «Global non-linear MHD modeling in toroidal X-point geometry of disruptions, edge localized modes, and techniques for their mitigation and suppression »

EUROfusion WPCD (Working Package Code Development):

- ACT1: Extended equilibrium and stability chain (participation)
- ACT2: Free boundary equilibrium and control (participation and coordination)

8.3. International Initiatives

8.3.1. Inria International Partners

8.3.1.1. Informal International Partners

- The team collaborates with TUC (Technical University of Crete, Prof. Argyris Delis) on extension of the shallow water model to turbulent flows. These common works overlap with the collaboration with Taiwan in the framework of the former AMOSS associate team.
- Collaboration with TIFR-Bangalore on MHD, one month invited at Bangalore (B. Nkonga and A. Bhole) C. Praveen will have 2months as invited professor at UCA in 2019.

8.3.2. Participation in Other International Programs

ITER Contracts (B. Nkonga):

- ITER IO/17/CT/4300001505: 2017-2019, "Non-linear MHD simulations for ITER QH-mode plasma with and without 3D magnetic field perturbations from in-vessel ELM control coils". (150KE)

COFFEE Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

The team is involved in the IDEX project UCA-JEDI.

- PhD of Laurence Beaude (october 2015 - december 2018) co-funded by BRGM and Region PACA and dealing with the simulation of geothermal systems, supervised by Roland Masson, Konstantin Brenner from LJAD-Inria and by Simon Lopez, Farid Smai from BRGM.

9.2. National Initiatives

9.2.1. ANR

- ANR CHARMS (Quantitative Reservoir Models for Complex Hydrothermal Systems), Roland Masson and Konstantin Brenner: december 2016 - december 2020, partners BRGM (leader), LJAD-Inria, Storengy, MdS, LJLL.
- ANR JCJC PRECIS (Effect of a shock wave on a structure with contact using mesh refinement and parallelism), Laurent Monasse: april 2018 - april 2021, partners Inria (leader), Ecole des Ponts, CEA, Université Paris-Est.

9.2.2. National and European networks

- GdR MANU.

  The research group MANU has activities centered around scientific computing, design of new numerical schemes and mathematical modelling (upscaling, homogenization, sensitivity studies, inverse problems,...). Its goal is to coordinate research in this area, as well as to promote the emergence of focused groups around specific projects
- S. Junca is involved in GdR 3437 DYNOLIN “Dynamique non linéaire” and GdR MecaWave.
- LJAD-Inria and BRGM are the French partners of the Norvergian, German French project InSPiRE "International Open Source Simulation Software Partnership in Research and Education” which has just been accepted by the Research Council of Norway with the code ComPASS as one of the softwares of this project together with Dune, Dumux and OPM.

9.3. International Research Visitors

9.3.1. Visits of International Scientists

- Martin Gander (Genève), UCA invited professor 18/06 – 18/07, collaboration on reduced fracture models and DDM for coupling liquid gas Darcy and free gas flows. Co-organisation with Martin Gander, Stella Krell, Victorita Dolean, Roland Masson of the summer school on DDM: 19,20,21/06 https://math.unice.fr/~krell/ColloqueDD/index.php
- Felix Kwok (Hong Kong): 11/06 – 25/06 on nonlinear domain decomposition for the Richards equation.

FLUMINANCE Project-Team

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. Comins'lab: SEACS : Stochastic modEl-dAta-Coupled representationS for the analysis, simulation and reconstruction of upper ocean dynamics

Participant: Etienne Mémin.

duration 48 months. The SEACS project whose acronym stands for: "Stochastic modEl-dAta-Coupled representationS for the analysis, simulation and reconstruction of upper ocean dynamics" is a Joint Research Initiative between the three Britanny clusters of excellence of the "Laboratoires d'Excellence" program: Cominlabs, Lebesgue and LabexMer centered on numerical sciences, mathematics and oceanography respectively. Within this project we aim at studying the potential of large-scale oceanic dynamics modeling under uncertainty for ensemble forecasting and satellite image data assimilation.

8.1.2. ANR BECOSE : Beyond Compressive Sensing: Sparse approximation algorithms for ill-conditioned inverse problems.

Participant: Dominique Heitz.

duration 48 months. The BECOSE project aims to extend the scope of sparsity techniques much beyond the academic setting of random and well-conditioned dictionaries. In particular, one goal of the project is to step back from the popular L1-convexification of the sparse representation problem and consider more involved nonconvex formulations, both from a methodological and theoretical point of view. The algorithms will be assessed in the context of tomographic Particle Image Velocimetry (PIV), a rapidly growing imaging technique in fluid mechanics that will have strong impact in several industrial sectors including environment, automotive and aeronautical industries. The consortium gathers the Fluminance and Panama Inria research teams, the Research Center for Automatic Control of Nancy (CRAN), The Research Institute of Communication and Cybernetics of Nantes (IRCCyN), and ONERA, the French Aerospace Lab.

8.1.3. ANDRA project

Participants: Jocelyne Erhel, Tangi Migot.

Contract with ANDRA (National Agency for Nuclear Waste) Duration: three years from November 2015. Title: reactive transport in fractured porous media Coordination: Jocelyne Erhel. Partners: Geosciences Rennes. Abstract: Even in small numbers, fractures must be carefully considered for the geological disposal of radioactive waste. They critically enhance diffusivity, speed up solute transport, extend mixing fronts and, in turn, modify the physicochemical conditions of reactivity around possible storage sites. This year, we studied geochemistry models, which could be coupled with flow and transport models.

8.1.4. IFPEN project

Participants: Jocelyne Erhel, Bastien Hamlat.

Contract with IFPEN (Institut Français du Pétrole et Energies Nouvelles) Duration: three years from October 2016. Title: Fully implicit Formulations for the Simulation of Multiphase Flow and Reactive Transport Coordination: Jocelyne Erhel. Abstract: Modeling multiphase flow in porous media coupled with fluid-rock chemical reactions is essential in order to understand the origin of sub-surface natural resources and optimize their extraction. This project aims to determine optimal strategies to solve the coupled transport and chemical reaction equations describing the physical processes at work in reactive multiphase flow in porous media. Three different formulations show great potential to accurately solve these equations. Two are fully implicit ("Reactive Coats" and "Semi-smooth Newton") and one is an operator splitting approach. These formulations are still incomplete at the moment. The work will focus on extending the existing formulations to more complex physical phenomena, study their stability, convergence and theoretical equivalence. Another objective is to provide practical solutions to efficiently solve the resulting non-linear systems.

8.1.5. ANR-MN: H2MNO4 project

Participants: Yvan Crenner, Benjamin Delfino, Jean-Raynald de Dreuzy, Jocelyne Erhel, Lionel Lenôtre.

Contract with ANR, program Modèles Numériques
Duration: four years from November 2012 until April 2017.
Title: Original Optimized Object Oriented Numerical Model for Heterogeneous Hydrogeology.
Coordination: Jocelyne Erhel and Géraldine Pichot, with Fabienne Cuyollaa.
Partners: Geosciences Rennes, University of Poitiers, University of Lyon 1, Andra, Itasca.
International collaborations: University of San Diego (USA), UPC, Barcelona (Spain)
Web page: http://h2mno4.inria.fr/
Abstract: The project H2MNO4 develops numerical models for reactive transport in heterogeneous media. It defines six mathematical and computational challenges and three applications for environmental problems with societal impact.

8.1.6. GDR MANU

Participants: Yvan Crenner, Jocelyne Erhel, Bastien Hamlat.

Title: Mathematics for Nuclear industry
Duration: From 2016 to 2019
Coordination: C. Cancès
Webpage: http://gdr-manu.math.cnrs.fr/
Abstract: The working group MANU is a follow-up to the group MOMAS. It covers many subjects related to mathematical modeling and numerical simulations for problems arising from nuclear industry and nuclear waste disposal. The team organizes a workshop on reactive transport, Paris, February 2018.

8.1.7. LEFE MANU: MSOM

Participants: Etienne Mémin, Long Li.

Title: Multiple Scale Ocean Model
Duration: From 2018 to 2021
Coordination: Bruno Deremble (CNRS LMD/ENS Paris)
Abstract: The objective of this project is to propose a numerical framework of a multiscale ocean model and to demonstrate its utility in the understanding of the interaction between the mean current and eddies.

8.2. International Initiatives

8.2.1. Inria Associate Teams Not Involved in an Inria International Labs

8.2.1.1. LFD-FLU

Title: Large-scale Fluid Dynamics analysis from FLow Uncertainty

International Partner (Institution - Laboratory - Researcher):

Universidad de Buenos Aires (Argentina) - Faculty of Engineering - Guillermo Artana

Start year: 2016

See also: http://www.irisa.fr/prive/memin/LFD-FLU/

The first objective of this associate team is primarily concerned with the establishment of efficient fluid flow image data analysis procedures. This concerns for instance data assimilation issues to reconstruct meaningful numerical representation of experimental fluid flows for analysis purpose. The second objective focuses on the incorporation of uncertainties in the flow dynamical evolution models.

8.2.1.2. Informal International Partners

Imperial College, London (UK), Collaboration with Dan Crişan and Darryl Holm on Stochastic transport for the upper ocean dynamics

Chico California State University (USA), We have pursued our collaboration with the group of Shane Mayor on the GPU implementation of wavelet based motion estimator for Lidar data. This code is developped in coproperty between Inria and Chico.

8.2.2. Participation in Other International Programs

Royal Society funding, collaboration between Dominique Heitz, Etienne Mémin and Sylvain Laizet (Imperial College) on Stochastic large-eddies simulation and data assimilation for the reconstruction of 3D turbulent flows.

8.2.3. Participation in Other International Programs

8.2.3.1. International Initiatives

MATH-GEO

Title: MATHematical methods for GEOphysical flows

International Partners (Institution - Laboratory - Researcher):

Universidad de Buenos Aires (Argentina) - CIMA (Centro de investigaciones del mar y de la Atmósfera) - Juan Ruiz

Universidad de la Republica Uruguay (Uruguay) - IMFIA: Instituto de Mecánica de los Fluidos e Ingeniería Ambiental, INCO: Instituto de Computación, Facultad de Ingeniería - Mónica Fossati

CMM (Chile) - Center for Mathematical Modeling - Axel Osses

Universidad San Ignacio de Loyola (USIL) (Peru) - Faculty of Engineering Alejandro Paredes

Duration: 2018 - 2019

Start year: 2018 http://mathgeo.cima.fcen.uba.ar

Nonlinear processes, such as advection and turbulent mixing, play a central role in geophysical sciences. The theory of nonlinear dynamical systems provides a systematic way to study these phenomena. Its stochastic extension also forms the basis of modern data analysis techniques, predictability studies and data assimilation methods. Contributions in the field of Topology and Dynamics of Chaos include methods conceived to unveil the structure organizing flows in phase space, building the gap between data and low-dimensional modeling. Low-order models in climate dynamics are highly desirable, since they can provide solutions in cases where high-resolution numerical simulations cannot be implemented, as in short-term wind forecasting. At the same time, the procedure provides a tool-kit for model validation, emulation or inter-model comparison, with interesting prospects in all fields of oceanographic and atmospheric sciences, including climate detection and attribution. The strategy constitutes an unprecedented and promising perspective, offering an original approach to the subject, with mathematical concepts that are not necessarily widespread in the geophysics scientific community. This proposal gathers specialists with a know-how in the most challenging aspects of the focused research field: coherent structure detection in fluid flows for the exploration and interactive visualization of scientific data (LIMSI France), data assimilation and fluid motion analysis from image sequences (Inria Rennes), numerical models and data assimilation (CMM-Chile) stochastic models for climate dynamics with application to El Niño Ocean models (USIL-Peru), mathematical methods for weather and climate (CIMA-UBA & IMIT / IFAECI, Argentina), geophysical flows and dynamical systems (LMD France), mixing structures and Lagrangian analysis of multisatellite data (LOCEAN France), marine and estuarine hydrodynamic and water properties numerical models (INCO & IMFIA-Uruguay), in situ measurements of oceanographic conditions (CEBC France, in program with CNES France and CONAE Argentina), global modelling technique and topological characterization of flows (CORIA with CESBIO, France).

8.3. International Research Visitors

8.3.1. Visits of International Scientists

- 1 week visit of Souhila Sabit (Researcher University of Tiaret, Algeria) to work with Jocelyne Erhel.
- 3 weeks visit of Alejandro Gronskis (Researcher Conicet Argentina) to work with Dominique Heitz, Etienne Mémin and Pranav Chandramouli within the associate team LFD
- 3 weeks visit of Guillermo Artana (Professor U. of Buenos Aires) to work with Dominique Heitz, Christophe Collewet and Johan Carlier within the associate team LFD
- 10 days visit of Georg Gottwald (Professor U. of Sydney) to work with Etienne Mémin.

LEMON Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

Cart'Eaux project (European Regional Development Fund (ERDF)): in partnership with colleagues of LIRMM and HSM (Montpellier) and with Berger-Levrault company, Carole Delenne and Benjamin COMMANDRE are developing a methodology that will collect and merge multi-sources data in the aim of mapping urban drainage networks for hydraulic modeling purpose. This chain of treatment includes: i) detection of manhole covers from remote sensing data (aerial images, numerical elevation models...), 2) development of an algorithm to retrieve the network from the detected points and other information such as roads or topography, 3) data manning to extract useful characteristics for the hydraulic model, from various databases available or from documents automatically gathered from the web. A confidence index will be given to each characteristic assessed and a sensitivity analysis will enable the software to propose a hydraulic model together with an associated uncertainty.

The GeRIMU project (Gestion du Risque d'Inondation en Milieu Urbain) will be based on the SW2D computational code. The purpose is to optimize and implement the commercial version of the code into a complete software chain for the forecasting and scenario appraisal for rainfall-generated urban floods on the scale of the urban area. The test and application site is the entire urban area of Montpellier.

9.2. National Initiatives

Antoine Rousseau is member of the ANR project ANSWER (PI Céline Casenave), 2016-2019

Gwladys Toulemonde is head of a project (2016-2018) funded by INSU via the action MANU (MAthematical and NUmerical methods) of the LEFE program. This project, called Cerise, aims to propose methods for simulating scenarii integrating spatio-temporal extremes fields with eventual asymptotic independence for impact studies in environmental sciences. Fatima PALACIOS-RODRIGUEZ is also a member of this project.

9.3. International Initiatives

9.3.1. Inria International Labs

Antoine Rousseau collaborates with Inria Chile through the partnership with MERIC in Chile. Two visits every year.

9.3.1.1. Associated team NEMOLOCO

Title: NEw MOdeLing tOols for Coastal Oceanography

International Partner (Institution - Laboratory - Researcher):

Pontificia Universidad Católica de Chile (Chile) - CIGIDEN - Rodrigo Cienfuegos

Start year: 2017

See also: https://team.inria.fr/LEMON/en/

The NEMOLOCO project targets the improvement of models in the coastal zone. Expected contributions concern: - design and implementation of domain decomposition and coupling techniques for coastal modeling - high resolution ocean simulation (including nesting) thanks to the software ROMS-CROCO, applied to biological tracers tracking.

9.3.2. Inria International Partners

9.3.2.1. Declared Inria International Partners

In 2015, the *Marine Energies Research International Center* (MERIC) was launched in Chile by CORFO. Antoine Rousseau is the scientific coordinator for Inria, and several members of LEMON, CARDAMOM and TOSCA research teams will be involved in this 8 years project driven by DCNS. Antoine Rousseau is involved in the research line *advanced modeling for marine energy*.

9.3.2.2. Informal International Partners

Vincent Guinot collaborates with B.F. Sanders (University of California Irvine, USA)

Carole Delenne and Vincent Guinot collaborate with S. Soares-Frazao (Unité de Génie Civil, Université catholique de Louvain, Belgium)

Gwladys Toulemonde collaborates with C. Gaetan (Università Ca' Foscari - Venezia)

9.3.3. Participation in Other International Programs

Antoine Rousseauwas member of a successfull application to the REDES (Conicyt, Chile) program with H. Ramirez (CMM, Santiago) and P. Gajardo (UTFSM, Valparaiso).

9.4. International Research Visitors

Rodrigo Cienfuegos (PUC Santiago, Chile) visited Paris for two weeks in June (collaboration around TsunamiLab).

MAGIQUE-3D Project-Team

8. Partnerships and Cooperations

8.1. Regional Initiatives

8.1.1. Partnership with I2M in Bordeaux supported by Conseil Régional d'Aquitaine

title: Imaging complex materials.
Coordinator: Hélène Barucq
Other partners: I2M CNRS Université Bordeaux I

The detection, localization and monitoring of the defect evolution in composite materials, concrete and more generally heterogeneous materials is a challenging problem for Aeronautics and energy production. It is already possible to localize defects in homogeneous materials by using methods based on ultrasonic inspection and sometimes, they are usable in particular heterogeneous materials, most of the time in 2D. Classical methods rely on the correspondence between the distance and the propagation time of the wave traveling between the defect and the receivers. In complex media, such a correspondence may be lapsed, for instance when the velocity depends on the frequency (dispersion) or of the propagation direction (anisotropy). The defect signature can also be embedded in the acoustic field sent by the structure (multiple reflections). The complexity of the propagation in heterogeneous materials makes then difficult the accurate localization of the defect, in particular in 3D.

Topological imaging techniques can be applied to heterogeneous media. They can find the positions of defects from two simulations performed in a safe experimental medium. They have been developed at I2M laboratory to carry on 2D single/multi mode inspection in isotropic and anisotropic waveguides. They have also been applied to a highly reflecting medium observed with a single sensor. The objective of this work is to extend the technique to 3D problems. In particular, we are going to handle detection in composite plates and in highly heterogeneous media including a collection of small scatterers.

This project is supported by the Conseil Régional d'Aquitaine, for a duration of 2 years.

8.2. National Initiatives

8.2.1. Depth Imaging Partnership

Magique-3D maintains active collaborations with Total. In the context of Depth Imaging, Magique-3D coordinates research activities dealing with the development of high-performance numerical methods for solving wave equations in complex media. This project has involved 2 other Inria Team-Projects (Hiepacs and Nachos) which have complementary skills in mathematics, computing and in geophysics. DIP is fully funded by Total by the way of an outline agreement with Inria.

In 2014, the second phase of DIP has begun. Lionel Boillot has been hired as engineer to work on the DIP platform. Six PhD students have defended their PhD since 2014 and they are now post-doctoral researchers or engineers in Europe. DIP is currently employing 2 PhD students and one post-doctoral researcher.

8.2.2. PRE Concert

Magique 3D is hosting an Inria "exploratory research project" (PRE) about modeling and designing wind musical instruments. This project is funding the post-doctoral position of Robin Tournemenne since July 2017.

8.2.3. ANR Num4Sun

The ANR has launched a specific program for supporting and promoting applications to European or more generally International projects. Magique-3D has been selected in 2016 after proposing a project to be applied as a FET project on the occasion of a call that will open in 2017 April. This project will gather researchers of the MPS (https://www.mps.mpg.de/en), of the BSC (https://www.bsc.es/), of the BCAM (http://www.bcamath.org/en/), of Heriot-Watt University (https://www.hw.ac.uk/) and Inria teams.

A kick-off meeting has been held in November 2016 in Strasbourg and a second one in Paris in July 2017. Thanks to this support, we have submitted a ETPHPC proposal in September 2017 The project is funded for 18 months starting from August 2016. The funding amounts 30000€.

8.2.4. ANR NonLocalDD

Magique 3-D is a partner of the ANR project entitled "Non Local Domain Decomposition Methods in Electromagnetics" that begins in october 2015. The aim of this project is to develop domain decomposition methods for the efficient solution of acoustics and Maxwell's equation either with boundary integral equations or finite element volume method. To obtain an exponential convergence of the iterative solution, non-local operators are studied and optimized to achieve a faster convergence. A post-doctoral student Marcella Bonazzoli has been hired by Magique 3-D in 2017 to study multi-domain integral equations for wave propagation. This student is supervised by Xavier Claeys, a partner of the NonLocalDD ANR project.

8.2.5. Grant from Fondation Blaise Pascal

The project Louis 14.0 has been selected by the Fondation Blaise Pascal as one of their supported projects for 2019. See more about the project at https://project.inria.fr/louis14point0/, in french.

8.3. European Initiatives

8.3.1. H2020 Projects

8.3.1.1. Mathrocks

Title: Multiscale Inversion of Porous Rock Physics using High-Performance Simulators: Bridging the Gap between Mathematics and Geophysics

Program: H2020

Duration: April 2018 - March 2022

Coordinator: Universidad Del Pais Vasco (EHU UPV)

Partners:

- Bcam - Basque Center for Applied Mathematics Asociacion (Spain)
- Barcelona Supercomputing Center - Centro Nacional de Supercomputacion (Spain)
- Universidad Del Pais Vasco Ehu Upv (Spain)
- Universitat Politecnica de Catalunya (Spain)
- REPSOL SA (Spain)
- Pontificia Universidad Catolica de Valparaiso (Chile)
- Curtin University of Technology (Australia)
- The University of Texas System (USA)
- University Nacional de Columbia (Colombia)
- Pontificia Universidad Catolica de Chile (Chile)
- Universidad Central de Venezuela (Venezuela)
- University de Buenos Aires (Argentina)
- Macquarie University (Australia)

Inria contact: Hélène BARUCQ

We will develop and exchange knowledge on applied mathematics, high-performance computing (HPC), and geophysics to better characterize the Earth´s subsurface. We aim to better understand porous rocks physics in the context of elasto-acoustic wave propagation phenomena. We will develop parallel high-continuity isogeometric analysis (IGA) simulators for geophysics. We will design and implement fast and robust parallel solvers for linear equations to model multi-physics electromagnetic and elasto-acoustic phenomena. We seek to develop a parallel joint inversion workflow for electromagnetic and seismic geophysical measurements. To verify and validate these tools and methods, we will apply the results to: characterise hydrocarbon reservoirs, determine optimal locations for geothermal energy production, analyze earthquake propagation, and jointly invert deep-azimuthal resistivity and elasto-acoustic borehole measurements. Our target computer architectures for the simulation and inversion software infrastructure consists of distributed-memory parallel machines that incorporate the latest Intel Xeon Phi processors. Thus, we will build a hybrid OpenMP and MPI software framework. We will widely disseminate our collaborative research results through publications, workshops, postgraduate courses to train new researchers, a dedicated webpage with regular updates, and visits to companies working in the area. Therefore, we will perform a significant role in technology transfer between the most advanced numerical methods and mathematics, the latest super-computer architectures, and the area of applied geophysics.

8.4. International Initiatives

8.4.1. Inria International Partners

8.4.1.1. Declared Inria International Partners

8.4.1.1.1. MAGIC2

Title: Advance Modeling in Geophysics

International Partner (Institution - Laboratory - Researcher):

California State University at Northridge (United States) - Department of Mathematics - Djellouli Rabia

The Associated Team MAGIC was created in January 2006 and renewed in January 2009. At the end of the program in December 2011, the two partners, MAGIQUE-3D and the California State University at Northridge (CSUN) decided to continue their collaboration and obtained the “Inria International Partner” label in 2013.

See also: https://project.inria.fr/magic/

The ultimate objective of this research collaboration is to develop efficient solution methodologies for solving inverse problems arising in various applications such as geophysical exploration, underwater acoustics, and electromagnetics. To this end, the research program will be based upon the following three pillars that are the key ingredients for successfully solving inverse obstacle problems. 1) The design of efficient methods for solving high-frequency wave problems. 2) The sensitivity analysis of the scattered field to the shape and parameters of heterogeneities/scatterers. 3) The construction of higher-order Absorbing Boundary Conditions.

In the framework of Magic2, Rabia Djellouli (CSUN) visited Magique 3D in February 2018

8.5. International Research Visitors

8.5.1. Visits of International Scientists

- José M. Carcione (Istituto Nazionale di Oceanografia e di Geofisica Sperimentale, OGS) visited Magique 3D in December 2018.
- Guy Chavent (Inria Rocquencourt, Emeritus professor) visited Magique 3D in December 2018.
- Barbara Romanowicz (Berkeley Seismological Laboratory, Collège de France) visited Magique 3D in November 2018

- Mounir Tlemcani (Université d'Oran, Algeria) visited Magique 3D in March 2018.
- Rabia Djellouli (CSUN) visited Magique 3D in February 2018.

8.5.2. Visits to International Teams

8.5.2.1. Research Stays Abroad

- Justine Labat visited Benjamin Stamm, RTWH Aachen University, Germany, in December 2018.
- In the framework of DIP, Pierre Jacquet visited Total Research Center at Houston, USA, in December 2018.

SERENA Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

MILC (DMI RFSI, 2018–2019): "Mesure et Intégrale de Lebesgue en Coq", with LIPN (Université de Paris 13), and TOCCATA (Inria Saclay - Île-de-France). SERENA representants are François Clément and Vincent Martin (UTC).

GiS: scientific collaboration network between ten public institutions from the Paris (Ile-de-France) region, focused on natural resources and environment. The project-team SERENA is a member.

9.2. National Initiatives

9.2.1. ANR

ANR HHOMM: "Hybrid high-order methods on polyhedral meshes", Theoretical foundations and applications (up to software development) for the recently-devised Hybrid high-order methods. Coordinated by D. Di Pietro, University of Montpellier. SERENA representant is A. Ern, period 2015–2019.

ANR DEDALES: "Algebraic and geometric domain decomposition for subsurface flow". The project aims at developing high performance software for the simulation of two phase flow in porous media. It specifically targets parallel computers where each node is itself composed of a large number of processing cores, such as are found in new generation many-core architectures.

The partners are HIEPACS, Laboratoire Analyse, Géométrie et Application, University Paris 13, Maison de la Simulation, and ANDRA. SERENA representants are M. Kern (grant leader) and M. Vohralík, period 2014–2018. The project ended in October 2018.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

- EoCoE: "Energy Oriented Center of Excellence" This project is coordinated by Maison de la Simulation and gathers 23 partners from 13 countries to use the tremendous potential offered by the ever-growing computing infrastructure to foster and accelerate the European transition to a reliable low carbon energy supply using HPC (High Performance Computing). SERENA representant M. Kern, period 2015–2018.
- ERC GATIPOR: "Guaranteed fully adaptive algorithms with tailored inexact solvers for complex porous media flows". The subject of this consolidator grant are new approaches to porous media multiphase flows: inexact Newton-multigrid solvers, local stopping criteria, adaptivity, and a posteriori error control. The goal is to guarantee the overall simulation error and to speed-up importantly the present-day simulations. SERENA representant is M. Vohralík (grant leader), period 2015–2020.
- PRACE: "Partnership for Advanced Computing in Europe" The mission of PRACE is to enable high-impact scientific discovery and engineering research and development across all disciplines to enhance European competitiveness for the benefit of society. PRACE has an extensive education and training effort for effective use of the Research Infrastructure. M. Kern is the French representative for training, and is in charge of the French node of the Prace training network, organizing 10-12 courses each year (period 2017-2019).

9.3.2. Collaborations in European Programs, Except FP7 & H2020

OPENCPS

Program: ITEA 3

Project acronym: OPENCPS

Project title: Open cyber-physical system model-driven certified development

Duration: Dec 2015–Dec 2018

Coordinator: Magnus Eek

Other partners: AB SKF, CEA, ELTE-Soft Kft., ESI Group, EDF, Wqua Simulation AB, Ericsson, IncQuery Labs Kft., KTH, Linköping University, RTE, SICS, SIREHNA, Saab AB, Sherpa Engineering, Siemens Industrial Torbumachinery AB, VTT Technical Research Center of Finland Ltd.

Abstract: Cyber-physical systems put increasing demands on reliability, usability, and flexibility while, at the same time, lead time and cost efficiency are essential for industry competitiveness. Tools and environments for model-based development of cyber-physical systems are becoming increasingly complex and critical for the industry: tool interoperability, vendor lock-ins, and tool life-cycle support are some of the challenges. The project focuses on interoperability between the standards Modelica/UML/FMI, improved execution speed of (co-)simulation, and certified code generation.

SERENA representants are Sébastien Furic and Pierre Weis.

9.4. International Initiatives

9.4.1. Inria International Partners

9.4.1.1. Informal International Partners

Erik Burman, Professor at University College London, UK, unfitted methods.

Jean-Luc Guermond, Professor at Texas A&M University, USA, finite element methods.

Ulrich Rüde, Professor at Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, multigrid methods.

Mary Wheeler, professor, University of Texas at Austin, USA, porous media applications.

Barbara Wohlmuth, Professor at Technical University of München, Germany, mixed finite element methods.

9.4.2. Participation in Other International Programs

Alexandre Ern participated for two weeks in Jul 2018 as an invited scientist in the ESI Program on Numerical Analysis on Complex PDE in the Sciences, Vienna, Austria (https://www.esi.ac.at/activities/events/2018/numerical-analysis-of-complex-pde-models-in-the-sciences).

9.5. International Research Visitors

9.5.1. Visits of International Scientists

Iain Smears, lecturer at University College London, March 26–30.

Thirupathi Gudi, Professor at Indian Institute of Science, Bangalore, India, January 15–February 28.

Jean-Luc Guermond, Professor at Texas A&M University, College Station, Texas, May 1–June 15.

Iain Smears, lecturer at University College London, June 18–27, and Christian Kreuzer, Professor at University Dortmund, June 18–29.

Carsten Carstensen, Professor at Humboldt University, Berlin, August 20–September 20.

Roland Becker, Professor at University of Pau, September 17–20.

Hend Ben Ameur, Professor at IPEST and member of ENIT-Lamsin, Tunis, Tunisia, November 19–30.

Théophile Chaumont-Frelet, junior researcher at Inria Sophia Antipolis, November 22–23.

9.5.1.1. Internships

Intissar Addali, 2nd year internship at ENSTA ParisTech, from May to Aug 2018, supervised by Karol Cascavita and Alexandre Ern.

9.5.2. Visits to International Teams

9.5.2.1. Research Stays Abroad

Alexandre Ern visited the research group of Prof. Victor Calo, Curtin University, Perth, Australia, in November 2018.

Martin Vohralík was invited for two weeks stay to Charles University, Prague for collaboration with J. Málek, April 2018.

STEEP Project-Team

7. Partnerships and Cooperations

7.1. Regional Initiatives

7.1.1. QAMECS / MOBIL'AIR : ATMOSPHERIC POLLUTION: Characterization of novel exposure markers, of biological, health, economic and societal impacts and evaluation of public policies

Project funded by ADEME, Grenoble metropolis, IDEX Université Grenoble Alpes
Duration: 2016 – 2022
Project coordinator : Remy Slama (INSERM) and Sandrine Mathy (GAEL, CNRS). Inria Coordinator: Emmanuel Prados
Other partners: Air Rhône-Alpes, CNRS, Sciences Po Grenoble, Inserm, IAB, Université Grenoble-Alpes
Abstract: Urban atmospheric pollution is one of the main threats to human health that can be to some extent controlled by public action. In Europe, many cities have implemented various types of low emission zones (LEZ, focused on traffic and heating emissions), France being a notable exception. Although fine particulate matter (PM2.5) is usually assessed through its mass concentration, other metrics, such as PM chemical speciation as well as the so far little considered oxidative potential (OP) of PM, are worth considering, both in terms of associations with human health and in the context of monitoring of the efficiency of LEZ. QAMECS covers all dimensions from atmospheric emissions, impact of meteorological conditions on air pollution human behaviours related to transportation, environmental levels, health, associated economic costs and societal awareness. The project relies on environmental measurements, modelling, repeated observational (representative) population studies, an existing mother-child cohort, a controlled human experiment, health impact and related economic assessment. It is conducted by a consortium of specialists of chemistry and physics of air pollution, economics, sociology, epidemiology, geography, in relation with local authorities. It will bring results important for urban planning, public health, and more fundamental research on the measurement of PM and assessment of their biological and health impact.

7.2. National Initiatives

7.2.1. AF Filières : Analyse des Flux des Filières biomasse pour des stratégies régionales de bioéconomie

Project funded by ADEME
Duration: 2017-2019
Coordinator: Jean-Yves COURTONNE (Equipe STEEP, Inria) [Emmanuel Prados (STEEP/Inria) for Inria partner]
Other partners: Equipe STEEP, Inria, Grenoble Rhônalpénergie-Environnement (RAEE), Lyon Laboratoire d'Economie Forestière (LEF), INRA / AgroParisTech Nancy.
Keywords: Environmental assessment, Ecological accounting, Material Flow Analysis, Sustainable supply chains, Multicriteria analysis.
Abstract: Flow analyses of biomass supply chains for regional bioeconomy policies. The goals of the project are the following:

- Improve knowledge on the material flows of the forest-wood and agri-food supply chains in France at national and regional levels,
- Provide a holistic vision of the situation by associating environmental and socio-economic indicators to material flows,
- Provide a more precise assessments (quantitatively and qualitatively) in the case of the Auvergne-Rhône-Alpes region.

TONUS Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

The thesis of Pierre Gerhard devoted to numerical simulation of room acoustics is supported by the Alsace region. It is a joint project with CEREMA (Centre d'études et d'expertise sur les risques, l'environnement, la mobilité et l'aménagement) in Strasbourg.

9.2. National Initiatives

9.2.1. Contracts with Industry

We are involved in a common project with the company AxesSim in Strasbourg. The objective is to help to the development of a commercial software for the numerical simulation of electromagnetic phenomena. The applications are directed towards antenna design and electromagnetic compatibility. This project was partly supported by DGA through "RAPID" funds. A CIFRE PhD has started in AxesSim on the same kinds of subjects in March 2015 (Bruno Weber). The new project is devoted to the use of runtime system in order to optimize DG solvers applied to electromagnetism [28]. The resulting software will be applied to the numerical simulation of connected devices for clothes or medicine. The project is supported by the "Banque Publique d'Investissement" (BPI) and coordinated by the Thales company.

9.2.2. National projects

- PEPS "initiative Jeunes" CNRS . E. Franck, F. Drui, C. Courtès, "Design and analysis of implicit kinetic schemes".

9.2.3. IPL FRATRES

The TONUS project belongs to the IPL FRATRES (models and numerical methods for Tokamak).
We detail the activity founded by the IPL FRATRES:

- Guillaume Morel was a post-doctoral fellow until October 2018, under the joint supervision of Nicolas Crouseilles (team IPSO, Inria Rennes) and Michel Mehrenmerger.
- Work session in Saint Etienne de Tinée with Inria CASTOR TEAM in July 2018.
- IPL Workshop in Alsace with Inria TEAM CASTOR AND MINGUS + exterior in November 2018.

9.2.4. HPC resources

- GENCI projet *Simulations 3D de plasmas deux espèces avec des méthodes particulaires et semi-lagrangiennes*: 400 000 scalar computing hours accepted in October 2017 on supercomputer OCCIGEN. Coordinator: Sever Hirstoaga
  Participants: Yann Barsamian, Sever Hirstoaga, Michel Mehrenberger.
- PRACE project *SME HPC Adoption Programme in Europe: full simulation of an electromagnetic wave inside and outside a fully modelled human body*: 40 000 GPU computing hours accepted in October 2017 on supercomputer Piz Daint. Coordinator: Bruno Weber
  Participants: Philippe Helluy, Bruno Weber.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. Eurofusion 2028

- Eurofusion Enabling Research Project ER15-IPP05 Extension (1/2018-12/2018): "Global non-linear MHD modelling in toroidal geometry of disruptions, edge localized modes, and techniques for their mitigation and suppression" (Principal Investigator: Matthias Hoelzl, Max-Planck Institute for Plasma Physics, Garching).
  Participant: Emmanuel Franck.
- EoCoE-II (2019-2022): the European center of excellence EoCoE-II brings together 20 partners from 7 European countries around exascale computing for energy-oriented numerical models. Eurofusion project MAGYK, Mathematics and Algorithms for GYrokinetic and Kinetic models (2019-2021), led by E. Sonnendrucker.
  Participant: Michel Mehrenberger.

9.4. International Initiatives

9.4.1. Participation in International Programs

- **Participants**: David Coulette, Emmanuel Franck, Philippe Helluy [local coordinator].
  ANR/SPPEXA "EXAMAG" is a joint French-German-Japanese project. Its goal is to develop efficient parallel MHD solvers for future exascale architectures. With our partners, we plan to apply highly parallelized and hybrid solvers for plasma physics. One of our objectives is to develop Lattice-Boltzmann MHD solvers based on high-order implicit Discontinous Galerkin methods, using SCHNAPS and runtime systems such as StarPU.

9.5. International Research Visitors

9.5.1. Visits of International Teams

9.5.1.1. Research Stays Abroad

- Lukas Tannhaüser from Würzburg University was invited in February 2018.

9.5.2. Visits to International Teams

9.5.2.1. Research Stays Abroad

- Philippe Helluy, Emmanuel Franck and Florence Drui visited Christian Klingenberg at Würzburg University.
- Philippe has been invited to a scientific stay at the University of Tokyo in February 2018. Collaboration about Vlasov-Poisson modeling with Naoki Yoshida.
- Emmanuel Franck visited Eric Sonnendruecker at IPP Gaching twice.

BIOCORE Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. National programmes

- **ANR-Phycover:** The overall objective of the PHYCOVER project (2014-2018) is to identify a modular wastewater treatment process for the production of biogas. The method combines three modules. First, a high-rate algal pond is dedicated to the treatment of municipal wastewater. Then, an anaerobic digester capable of co-digesting biomass products (and others organic matter resources) to significantly reduce biological and chemical contaminants while producing a sustainable energy as biogas is analysed. A final module transforms the residual carbon, nitrogen and phosphorus into high-value microalgae dedicated to aquaculture and green chemistry.
- **ITE-OPALE:** The goal of the Institut de la Transition Énergétique - OPALE project (2016-2019) is to increase the lipid content of microalgae by specific selection pressure. The project relies on the strain already selected during the Facteur 4 project, whose productivity was 4 times higher than the wild type. We expect to still increase strain performances up to 10 times the productivity of the wild type.
- **ANR-FunFit:** The objective of this project (2013-2018) is to develop a trait-based approach linking individual fitness of fungal plant pathogens to ecological strategies. The idea is to derive eco-epidemiological strategies from fitness optimization in colonized environments and during colonization, as well as understanding the coexistence of sibling species. This project is co-coordinated by F. Grognard.
- **ANR-TripTic:** The objective of this project (2014-2018) is to document the biological diversity in the genus of the minute wasps *Trichogramma*, and to study the behavioral and populational traits relevant to their use in biological control programs.
- **ANR-ICycle:** This project (2016-2020) aims at understanding the communication pathways between the cell division cycle and the circadian clock, using mathematical modeling and control theory to construct and implement two coupled synthetic biological oscillators. Project coordinated by M. Chaves.
- **ANR - Maximic:** The goal of the project (2017-2021) is to design and implement control strategies in a bacterium from producing at maximal rate a high value product. It is coordinated by H. de Jong (IBIS Grenoble), and involves members of Biocore and McTao.
- **Plan Cancer - Imodrez:** The objective of this project (2018-2021) is to understand cancer drug response heterogeneity using tumor single-cell dynamics and developing mathematical models and computational approaches. A project coordinated by J. Roux (IRCAN) and funded by Inserm - Plan Cancer.
- **SIGNALIFE:** Biocore is part of this Labex (scientific cluster of excellence) whose objective is to build a network for innovation on Signal Transduction Pathways in life Sciences, and is hosted by the University of Nice Sophia Antipolis.
- **UMT FIORIMED:** FioriMed is a Mixed Technology Unit created in January 2015 to strengthen the production and dissemination of innovation to the benefit of ornamental horticulture. Horticultural greenhouses are seen as a "laboratory" for the actual implementation of agroecology concepts with the possibility of generic outcomes being transfered to other production systems. The main partners of UMT FioriMed are ASTREDHOR (National Institute of Horticulture) and the ISA Joint Research Unit of INRA-CNRS-Univ. Nice.

- **ADEME Phytorecolt:** The goal of this project (2017-2019) is to develop an automated and optimized procedure for microalgae harvesting. A project coordinated by H. Bonnefond.

9.1.2. Inria funding

- **Inria Project Lab, Algae** ***in silico*****:** (2014-2018) The Algae in silico Inria Project Lab, funded by Inria and coordinated by O. Bernard, focuses on the expertise and knowledge of biologists, applied mathematicians and computer scientists to propose an innovative numerical model of microalgal culturing devices. The latest developments in metabolic modeling, hydrodynamic modeling and process control are joined to propose a new generation of advanced simulators in a realistic outdoor environment. The project gathers 5 Inria project teams and 3 external teams.
- **Inria Project Lab, Cosy:** (2017-...) This proposal aims at exploiting the potential of state-of-art biological modeling, control techniques, synthetic biology and experimental equipment to achieve a paradigm shift in control of microbial communities. We will investigate, design, build and apply an automated computer-driven feedback system for control of synthetic microbial communities, not just accounting for but rather leveraging population heterogeneity in the optimal accomplishment of a population-level task. The development of methodologies of general applicability will be driven by and applied to two different applications closely connected with real-world problems in the biomedical and biotechnological industry. The consortium is composed of the four Inria project-teams IBIS, BIOCORE, COMMANDS, NON-A, the Inria Action Exploratoire INBIO, as well as the external partners BIOP (Université Grenoble Alpes, including members of IBIS), MaIAge (INRA), and YoukLAB (TU Delft).

9.1.3. INRA funding

- **MoGeR:** “From knowledge to modeling: towards a user-friendly simulation tool to test crop resistance management scenarios in the Phoma-oilseed rape case study”, INRA Metaprogramme SMaCH, 2017–2019. This is a follow-up of the K-Masstec project, which focused on sustainable strategies for the deployment of genetic resistance in the field, based on molecular knowledge on avirulence genes.
- **ABCD:** INRA SPE is funding the project ABCD "Augmentative Biological Control; optimizing natural ennemies Deployment" (2017-2019) in which Biocore is a partner with INRA Sophia Antipolis.

9.1.4. Networks

- **GDR Invasions Biologiques:** The objectives of this GDR are to encourage multidisciplinary research approaches on invasion biology. It has five different thematic axes: 1) invasion biology scenarios, 2) biological invasions and ecosystem functioning, 3) environmental impact of invasive species, 4) modeling biological invasions, 5) socio-economics of invasion biology. L. Mailleret is a member of the scientific comittee of the GDR .
- **ModStatSAP:** The objective of this INRA network is to federate researchers in applied mathematics and statistics and to promote mathematical and statistical modeling studies in crop and animal health. S. Touzeau is a member of the scientific committee.
- **Seminar:** BIOCORE organizes a regular seminar “Modeling and control of ecosystems” at the station zoologique of Villefranche-sur-Mer, at INRA-ISA or at Inria.

9.2. European Initiatives

9.2.1. Collaborations in European Programs, Except FP7 & H2020

Program: **PHC-Pessoa** Partenariat Hubert Curien with Portugal, managed by Campus France

Project acronym: **LTSB**

Project title: Logic Tools for Systems Biology

Duration: 01/2018 - 12/2018

Coordinator: M. Chaves

Other partners: M.A. Martins, University of Aveiro

Abstract: This project aims at developing Boolean, piecewise linear and other hybrid tools for analysis of biological networks.

9.2.2. Collaborations with Major European Organizations

Imperial college, Department of Chemical engineering (UK),

Modeling and optimization of microalgal based processes.

University of Padova, Italy.

Modeling and control of microalgal production at industrial scale.

9.3. International Initiatives

9.3.1. Inria International Labs

Associate Team involved in the International Lab: **Inria Chile**

9.3.1.1. GREENCORE

Title: Modeling and control for energy producing bioprocesses

International Partners (Institution - Laboratory - Researcher):

PUCV (Chile) - Escuela de Ingenieria Bioquimica (EIB) - David Jeison

UTFSM (Chile) - Departamento de Matematica - Pedro Gajardo

Univ. Chile (Chile) - Centro de modelacion matematica - Hector Ramirez

Inria coordinator: O. Bernard

Start year: 2014

See also: https://team.inria.fr/eagreencore/

The worldwide increasing energy needs together with the ongoing demand for CO2 neutral fuels represent a renewed strong driving force for the production of energy derived from biological resources. In this scenario, the culture of oleaginous microalgae for biofuel and the anaerobic digestion to turn wastes into methane may offer an appealing solution. The main objective of our proposal is to join our expertise and tools, regarding these bioprocesses, in order to implement models and control strategies aiming to manage and finally optimize these key bioprocesses of industrial importance. By joining our expertise and experimental set-up, we want to demonstrate that closed loop control laws can significantly increase the productivity, ensure the bioprocess stability and decrease the environmental footprint of these systems. This project gathers experts in control theory and optimization (BIOCORE, UTFSM) together with experts in bioprocesses (PUCV and CMM) and software development.

Associate Team involved in the International Lab: **LIRIMA**, International Laboratory for Research in Computer Science and Applied Mathematics

9.3.1.2. EPITAG

Title: Epidemiological Modeling and Control for Tropical Agriculture

International Partner (Institution - Laboratory - Researcher):

Université de Douala (Cameroon) - Department of Mathematics and Computer Science - Samuel Bowong

Inria coordinator: S. Touzeau

Start year: 2017

See also: https://team.inria.fr/epitag/

EPITAG gathers French and Cameroonian researchers, with a background in dynamical systems and control and with an interest in crop diseases. Crop pests and pathogens are responsible for considerable yield losses. Their control is hence a major issue, especially in Cameroon, where agriculture is an important sector in terms of revenues and employment. To help design efficient strategies for integrated pest management, mathematical models are particularly relevant. Our main objective is to study the epidemiology and management of tropical crop diseases, with a focus on Cameroon and Sub-Saharan Africa. Our approach consists in developing and analysing dynamical models describing plant-parasite interactions, in order to better understand, predict and control the evolution of damages in crops. To ensure the relevance of our models, "end users" are closely associated. We focus on various pathosystems, such as cocoa plant mirids, coffee berry borers, coffee leaf rust and plantain plant-parasitic nematodes.

9.3.2. Inria International Partners

- NTNU (Norwegian University of Science and Technology), Trondheim, Norway. The project involves turning wastes into bioenergy with anaerobic digestion.
- University Ben Gurion : Microalgal Biotechnology Lab (Israel), Member of the ESSEM COST Action ES1408 European network for algal-bioproducts (EUALGAE). Modeling of photosynthesis.
- University of Manitoba: Department of Mathematics (Canada). Julien Arino hosted Nicolas Bajeux for 5 months. Invasion in metapopulations.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

Luca Scardovi, University of Toronto, Canada, from Feb 2018 until June 2018. Long-term visit, to establish a new collaboration on the coupling and synchronization of biological oscillators.

Daniel Figueiredo, University of Aveiro, Portugal, 17-25 Oct 2018. Visit in the context of PHC-Pessoa project to work on the development of logical tools for systems biology.

Israël Tankam Chedjou, University of Yaoundé 1, Cameroon, April-August 2018. 5-month stay in the context of the EPITAG associate team.

Yves Fotso Fotso, University of Dschang, Cameroon, April-September 2018. 5-month stay in the context of the EPITAG associate team.

Clotilde Djuikem, University of Douala, Cameroon, May-July 2018. 3-month stay in the context of the EPITAG associate team.

9.4.2. Visits to International Teams

9.4.2.1. Sabbatical programme

O. Bernard is currently spending a one year sabbatical at NTNU (Norwegian University of Science and Technology), Trondheim, Norway. He works on a project to turn wastes into bioenergy with anaerobic digestion. Many challenges must be solved, from the theoretical stage up to the implementation.

9.5. Other Visits

Hussein Kanso, PhD student at INRA Avignon, a 2-week visit in the context of the work on modeling of sugar metabolism in peach fruit (collaboration with V. Baldazzi).

9.6. Project-team seminar

BIOCORE organized a 3-day seminar in September in Bauduen (Var). On this occasion, every member of the project-team presented his/her recent results and brainstorming sessions were organized.

CARMEN Project-Team

7. Partnerships and Cooperations

7.1. Regional Initiatives

7.1.1. PhD thesis O. Bouhamama

L. Weynans and L. Bear (Liryc) obtained funding for a PhD thesis from the Université de Bordeaux, for a project titled "Méthodes numériques pour la résolution du problème inverse en électrocardiographie dans le cas d'anomalies structurelles du tissu cardiaque." Candidate O. Bouhamama started in October 2018.

7.1.2. CALM

The project "Cardiac Arrhythmia Localization Methods," granted by the Région Nouvelle-Aquitaine, with matching from funds held by our clinical collaboraters H. Cochet and P. Jaïs, has started. The purpose of this project is to develop a tool that can predict the exit site of an arrhythmia with moderate accuracy (1 cm) in an absolute sense, with respect to the anatomy of the heart in situ, and with a resolution of about 2 mm in a relative sense, with respect to a nearby pacing site. This tool must fulfill the following criteria:

- it uses only data that are already recorded in the cathlab by other systems: ECG data and electroanatomical mapping data;
- it must work in nearly real-time; catheter displacement advice must be available within 5 seconds after a paced beat;
- it must work automatically, requiring the operator only to indicate which ECG data correspond to the target arrhythmia; and
- it must be safe and easy to operate.

We will in the first place test a number of proposed methods using synthetic data, produced with our realistic models of cardiac electrophysiology and accurate geometric models of different patients. This in-silico testing phase will answer a number of important practical questions. Subsequently we will use offline clinical data, and within 2 years we aim to build a clinical prototype that can be tested (without interfering in the procedure) in the cathlab. In order to work real-time we will initially use very simple methods. However, the clinical prototype and the collectoin of synthetic data that we created will later serve also as a platform to test also more sophisticated inverse methods.

7.2. National Initiatives

7.2.1. ANR EXACARD

We started a collaboration with the STORM team at Inria Bordeaux Sud-Ouest to work on further scaling of the Propag code, to push the limit from about 10^4 to 10^6 parallel processors. A proposal for this project was funded this year by ANR. It allows a postdoc to be employed for 2 years.

7.2.2. ANR MITOCARD

The MITOCARD project (Electrophysiology of Cardiac Mitochondria), coordinated by S. Arbault (Université de Bordeaux, ISM), was granted by the ANR in July 2017. The objective of MITOCARD is to improve understanding of cardiac physiology by integrating the mitochondrial properties of cell signaling in the comprehensive view of cardiac energetics and rhythm pathologies. It was recently demonstrated that in the heart, in striking contrast with skeletal muscle, a parallel activation by calcium of mitochondria and myofibrils occurs during contraction, which indicates that mitochondria actively participate in Ca2+ signaling in the cardiomyocyte. We hypothesize that the mitochondrial permeability transition pore (mPTP), by rhythmically depolarizing inner mitochondrial membrane, plays a crucial role in mitochondrial Ca2+ regulation and, as

a result, of cardiomyocyte Ca2+ homeostasis. Moreover, mitochondrial reactive oxygen species (ROS) may play a key role in the regulation of the mPTP by sensing mitochondrial energetics balance. Consequently, a deeper understanding of mitochondrial electrophysiology is mandatory to decipher their exact role in the heart's excitation-contraction coupling processes. However, this is currently prevented by the absence of adequate methodological tools (lack of sensitivity or selectivity, time resolution, averaged responses of numerous biological entities). The MITOCARD project will solve that issue by developing analytical tools and biophysical approaches to monitor kinetically and quantitatively the Ca2+ handling by isolated mitochondria in the cardiomyocyte.

MITOCARD is a multi-disciplinary project involving 4 partners of different scientific fields: the CARMEN team as well as

- **ISM**, the largest chemistry laboratory of the Université de Bordeaux, where the necessary measurement methods will be developed;
- **Liryc**, where mitochondria are studied at all levels of integration from the isolated mitochondrion to the intact heart; and
- **LAAS**, the MiCrosystèmes d'Analyse (MICA) group at the Laboratory of Analysis and Architecture of Systems, which develops the biological microsensors for this project.

The project will

- develop chips integrating 4 different electrochemical microsensors to monitor in real-time key mitochondrial signaling parameters: Ca2+, membrane potential, quinone reduction status, O2 consumption, and ROS production;
- develop microwell arrays integrating ring nanoelectrodes to trap single mitochondria within micrometric chambers and measure locally by combined fluorescence microscopy and electrochemical techniques intra- (by fluorescence) and extra-mitochondrial (electrochemistry) metabolites; and
- develop a mathematical model of mitochondrial Ca2+ and ROS handling built on existing knowledge, new hypotheses, and the measured data.

The model may serve both to assess biological assumptions on the role of mitochondria in Ca2+ signaling and to integrate pathological data and provide clues for their global understanding.

7.2.3. GENCI

GENCI (*grand équipement national de calcul intensif*) is the agency that grants access to all national high-performance resources for scientific purposes in France. GENCI projects have to be renewed yearly. Our project renewal *Interaction between tissue structure and ion-channel function in cardiac arrhythmia*, submitted in September 2018, has been granted 8 million core-hours on the three major systems Irene, Occigen, and Turing. This compute time is primarily destined for our research into the interaction between ionic and structural heart disease in atrial fibrillation, Brugada syndrome, and early repolarisation syndrome [7] [65], and for new HPC developments [27].

7.3. European Initiatives

7.3.1. Collaborations with Major European Organizations

BCAM (Basque Center for Applied Mathematics), Bilbao, Spain: L. Gerardo-Giorda.

We develop surrogate models of Radiofrequency Catheter Ablation for machine learning purposes, with the ambition to provide real-time estimations of lesion depths to clinicians (M. Leguèbe, Y. Coudière).

7.4. International Initiatives

7.4.1. Inria International Labs

International Laboratory for Research in Computer Science and Applied Mathematics

Associate Team involved in the International Lab:

7.4.1.1. EPICARD

Title: inversE Problems In CARDiac electrophysiology

International Partner (Institution - Laboratory - Researcher):

ENIT (Tunisia) - Department of Intelligence Science and Technology - Nabil Gmati

Start year: 2018

See also: https://team.inria.fr/carmen/epicard/

Model personalization is a very challenging question in the numerical modeling community, especially for medical applications like cardiac electrophysiology. Our main idea is to adapt the input data like model parameters and boundary conditions of the electrophysiological measurements. There are two mathematical problems raising from this challenge. The first issue is the identifiability of the parameters and the sensitivity of the identification problem to the measured data. The question is: For given measurements, could we prove that there exist a set of parameters that allows to fit these measurements? The second issue is, how can we estimate parameters, when they are identifiable,? Our idea is to provide a theoretical analysis for the identification of each of the parameters and to construct suitable numerical methods to estimate them.

7.4.2. Inria International Partners

7.4.2.1. Informal International Partners

Y. Coudière works with the group of Prof. Y. Bourgault from the Department of Mathematics and Statistics of the University of Ottawa (Canada). Some results on the numerical analysis of time-stepping methods from C. Douanla's PhD were carried out together, as well as some theoretical results on parameter identification in the PhD of A. Gérard.

M. Potse works with the group of Prof. U. Schotten at Maastricht University (The Netherlands) and the Center for Computational Medicine in Cardiology at the *Università della Svizzera italiana* (Lugano, Switzerland) on simulation studies of atrial fibrillation [56]. The Maastricht group was partially funded by the FP7 project EUTRAF and our simulations were supported by GENCI (section 7.2.3).

N. Zemzemi works with Cesare Corrado at King's College London on the development of new eikonal models allowing conduction velocity adaptation [16].

DRACULA Project-Team

6. Partnerships and Cooperations

6.1. National Initiatives

6.1.1. ANR

- ANR SinCity "Single cell transcriptomics on genealogically identified differentiating cells", 2017-2020.
  Participant: Olivier Gandrillon [Coordinator].
- Olivier Gandrillon participates in the ANR MEMOIRE (head Jacqueline Marvel) dedicated to "MultiscalE MOdeling of CD8 T cell Immune REsponses". 2018-2021.
- Fabien Crauste participates in the ANR MEMOIRE (head Jacqueline Marvel) dedicated to "MultiscalE MOdeling of CD8 T cell Immune REsponses". 2018-2021.
- Thomas Lepoutre is a member of the ANR KIBORD (head L. Desvillettes) dedicated to “kinetic and related models in biology". 2014-2018: https://www.ljll.math.upmc.fr/kibord/.

6.1.2. Other projects

- Association France Alzheimer Sciences Médicales: PAMELA “Prion et Alzheimer : Modélisation et Expérimentation d’une Liaison Agressive”, 2014-2017 (https://www.youtube.com/watch?v=X0mLf8IJhV4).
  Participants: Mostafa Adimy, Samuel Bernard, Thomas Lepoutre, Laurent Pujo Menjouet [Coordinator], Léon Tine.
- Thomas Lepoutre is a member of the ERC MESOPROBIO (head V. Calvez) dedicated to "Mesoscopic models for propagation in biology". 2015-2020: .

6.2. European Initiatives

6.2.1. FP7 & H2020 Projects

Fabien Crauste and Olivier Gandrillon participates in the EU RTN network COSMIC (head Antpoine. van Kampen) dedicated to "Combatting disorders of adaptive immunity with systems medicine"). 2018-2021. https://cosmic-h2020.eu

6.3. International Initiatives

6.3.1. MODELLING_LEUKEMIA

Title: Modeling quiescence and drug resistance in Chronic Myeloid Leukemia

International Partner (Institution - Laboratory - Researcher):

University of Maryland (United States) - Center for Scientific Computation and Mathematical Modeling (CSCAMM) - Levy Doron

Start year: 2016

See also: http://dracula.univ-lyon1.fr/modelling_leukemia.php

This project is dedicated to the mathematical modelling of chronic myeloid leukemia and treatment effects. We focus especially on the interplay between the immune response and treatment. This has a potential impact on the study of treatment cessation. This work is conducted in close collaboration with a clinician.

6.3.2. Participation in Other International Programs

6.3.2.1. Indo-French Center of Applied Mathematics

Mathematical modeling of hematopoiesis process in application to chronic and acute myelogenous leukemia

Title: Mathematical modeling of hematopoiesis process in application to chronic and acute myelogenous leukemia

International Partner (Institution - Laboratory - Researcher):

(India)- Subhas Khajanchi

Duration: 2018 - 2021

Start year: 2018

6.4. International Research Visitors

6.4.1. Visits of International Scientists

Antone dos Santos Benedito, PHD student on Adding temperature and anthropogenic actions in the study of spatial-temporal behavior of insectplague Chrysodeixis Includens. Institute of Biosciences, São Paulo State University (UNESP), Botucatu, Brazil not a team member but visiting for 6 months (from September 1st 2018 to February 28, 2019)

6.4.2. Visits to International Teams

Paul Lemarre is visiting University of Merced in 2018-2019.

M3DISIM Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. Other funding

IPM-MS project (for Imagerie Polarimétrique de Mueller pour la réalisation d'un système original de caractérisation des propriétés mécaniques des Matériaux Structurés). 50k€ funded by the LABEX Lasips. This project, which involves the LPICM laboratory (Ecole Polytechnique, CNRS), the LMS (Ecole Polytechnique, CNRS, Mines ParisTech) and the Centre des Matériaux (Mines ParisTech), aims at developing an optical tool to study the link between the mechanical properties of a material and its hierarchical organization. Despite the development of new methods to observe the microstructure, one of the limitations is the number of observations that can be obtained on a given sample in a realistic experimental time. To overcome this difficulty, we are planning to use the Mueller polarimetry to obtain at a fast rate (a few frames per second, compared to a few frames per half-hour) relevant information on the local anisotropy of biological (heart, skin) and composite (short fibers composite) samples.

G. Bureau, software engineer in the team, was funded by an Inria Reo industrial contract with Kephalios, a startup working on innovative artificial valves devices.

9.2. European Initiatives

9.2.1. Collaborations with Major European Organizations

Partner 1: Division of Biomedical Engineering & Imaging Sciences (BMEIS), St Thomas' Hospital, King's College London, UK

clinical-modeling topics mostly encompassing congenital heart diseases (BMEIS acts as "Other participant" in the Inria Associate team ToFMOD, and R. Chabiniok additionally performs clinical MRI exams at St Thomas' hospital 0.5 days / week.

Partner 2: Department of Mathematics, Faculty of Nuclear Sciences and Physical Engineering, Czech Technical University in Prague, Czech Republic

model-constrained image registrations, trans-valvular flow in pathological valves.

Partner 3: Institute for Clinical and Experimental Medicine in Prague

Cardiovascular MRI

9.3. International Initiatives

9.3.1. Inria Associate Teams Not Involved in an Inria International Labs

9.3.1.1. ToFMod

Title: Cardiac Biomechanical Modeling of Chronic Right Ventricular Loading

International Partner (Institution - Laboratory - Researcher):

UT Southwestern Medical Center, Dallas,Texas (United States), Mohammad Tarique Hussain

Start year: 2018

See also: https://m3disim.saclay.inria.fr/associated-team/

This collaboration aims at addressing a crucial issue in cardiology of congenital heart diseases, namely, the optimal timing of pulmonary valve replacement (PVR) in patients with surgically repaired tetralogy of Fallot (ToF) prone to chronic pulmonary regurgitation or right ventricular outflow tract stenosis. Our strategy consists in exploiting the predictive power of biomechanical modeling to shed light in the decision process. We will start by a detailed proof-of-concept study, based on datasets that will be acquired in patients indicated for percutaneous PVR, prior to the procedure, and in the follow-up at 3- and 12-months post-PVR. These datasets will be first used to calibrate the Inria M3DISIM patient-specific heart model simulating a cardiac cycle (at each follow-up time point) to access the myocardial properties – namely, the active contractility and passive stiffness. The instantaneous tissue properties will be statistically analyzed and compared with the level of reverse remodeling – i.e. the positive outcome of PVR. Secondly, the data at each time point will be used to calibrate and further develop the models of long-term tissue remodeling created by the M3DISIM researchers. It is only by combining such invaluable longitudinal data with biomechanical modeling expertise that progress can be achieved in the above objective, indeed.

9.4. International Research Visitors

9.4.1. Invited researchers

- T. Hussain, A. Tandon (Senior researchers at UTSW Medical Center Dallas): joint work in the scope of the Inria Associate team ToFMOD
- F. Regazzoni (3rd year PhD student from MOX, Milan, Italy): From Sept 2018, joint work on model learning and data assimilation coupling.

9.4.2. Internships

- K. Solovska (Czech Technical University and IKEM Prague): 1-30 August 2018, collaborative work with M. Genet and R. Chabiniok in the scope of the Inria Associate team ToFMOD

MAMBA Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

9.1.1.1. ANR Blanc 2014-2018 "Kibord"

This project gathers several members of the MAMBA team together with the ENS Cachan and Université Paris-Dauphine on the mathematical study of PDE models with application to biology.

9.1.1.2. ANR iLITE 2016 - 2020

Jean-Charles Duclos-Vallée, Paul Brousse Hospital, Villejuif. Partners are several departments in Paul Brousse Hospital, ENS Cachan, University of Compiègne and several companies all over France, and REO team, Inria Paris. The pursued objective is the bioengineering design of an artificial liver intended for liver replacement.

9.1.1.3. ANR InTelo 2017-2020

Telomere dynamics, headed by Teresa Teixeira (IBPC, Paris).

9.1.1.4. INCa/DGOS; PRT-K 2018-2021

Khê HOANG-XUAN, Hôpital Universitaire La Pitié Salpêtrière, Paris. Mathematical modeling at micro and macroscopic level of primary central nervous system lymphomas (PCNSL).

9.1.2. ITMO Cancer 2016 - 2020, HTE call (heterogeneity of tumours in their ecosystems)

9.1.2.1. ITMO Cancer EcoAML

Early leukaemogenesis in Acute Myelogenous Leukaemia (AML), 8 teams headed by François Delhommeau (CDR St Antoine, Paris).

9.1.2.2. ITMO Cancer MoGlImaging

Treatment-induced treatment resistance and heterogeneity in glioblastoma, 8 teams headed by Elizabeth Moyal (INSERM, Toulouse).

9.2. European Initiatives

9.2.1. Collaborations in European Programs, Except FP7 & H2020

Program: Celtic+

Project acronym: Sendate

Project title:Secure Networking for a Data Center Cloud in Europe

April 2016/May 2019

Coordinator: Nokia

Other partners: Siemens, IMT, ...

9.3. International Initiatives

9.3.1. Inria Associate Teams Not Involved in an Inria International Labs

9.3.1.1. MaMoCeMa

Title: Mathematical modeling of cell motility and of autophagy

International Partner (Institution - Laboratory - Researcher):

University of Vienna (Austria) - Wolfgang Pauli Institute - Christian Schmeiser

Start year: 2018

Numerous fruitful collaborations have been developed these last years between the WPI and the Inria team MAMBA. Diane Peurichard – newly recruited permanent member of the team MAMBA – worked two years (2016-2017) with Christian Schmeiser – member of the present project – through a post-doctoral contract at the university of Vienna. In collaboration with the biologists of IST, they developed mathematical tools to understand how cells move through adhesion-based and adhesion-free motion with applications in cancer development, prevalent theme of the team MAMBA. Collaborations WPI-MAMBA are presently maintained and ensured by the sabbatical of Marie Doumic – MAMBA team leader –, working at the university of Vienna with Christian Schmeiser and the PhD student Julia Delacour. They have initiated a collaboration on the mathematical modeling of autophagy, which requires both C. Schmeiser's expertise in biomechanics and M. Doumic's knowledge on aggregation processes. This team will also benefit of the strong links that C. Schmeiser has developed with the two biologists teams of S. Martens (on autophagy) and M. Sixt (on cell movement).

Of note, C. Schmeiser has been a laureate for the "Chaire d'excellence" program of the FSMP. As such, he is for six months in Paris, and delivered a course at IHP on entropy methods. Many of his students and collaborators visited him (D. Oelz, G. Jankowiak, L. Kanzler, G. Favre, L. Neumann...), and participated to a joint Mamba-MaMoCeMa meeting on December 6th, still strengthening our links.

9.3.2. Participation in Other International Programs

9.3.2.1. International Initiatives

ECOS Nord C17M01

Title: News methods for controle of dengue and arobivroses epidemics

International Partner (Institution - Laboratory - Researcher):

Universidad del Valle (Colombia) - Department of Mathematics - Olga Vasilieva

Duration: 2017 - 2019

Start year: 2017

The overall goal of the project is the development of mathematical models and theory-based control methods, contributing to the improvement of epidemiological surveillance and the control of dengue and other serious diseases transmitted by mosquitoes Aedes aegypti (chikungunya, yellow fever, zika fever). More specifically, it :

- Develops modeling framework for the biological control of mosquito populations (through the use of natural predators, Wolbachia bacteria etc.).
- Proposes and evaluates control strategies based on the use of biological agents and on their possible combinations with traditional control measures (such as removal of reproduction, spraying insecticides and / or larvicides, use of mosquito nets, repellents, etc.).
- Compares the results of biological control strategies (and their combinations) with those of traditional control using a cost / efficiency approach.
- Includes in the developments the spatial aspects of the questions above.

BMBF (Germany) / LiSym; 2016-2020 LiSym addresses liver diseases and regeneration, namely, steatosis, fibrosis and cirrhosis, and acute on chronic liver failure. Dirk Drasdo is co-coordinator of one sub-project, participant in one of the other ones, and member of the leadership board

BMBF (Germany) / MSDILI; 2016-2019 MS-DILI addresses multiscale modeling of drug-induced liver disease focusing on the role of APAP. Dirk Drasdo participates in this project.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

- Prof. Olga Vasilieva (Universidade del Valle, Cali, Colombia) was invited during three weeks, together with Edwin Bairros, PhD student.
- Prof. Yukihiko Nakata (Shimane University, Matsue, Japan) was hosted during one week in the framework of the French program Exploration France.
- Prof. C. Schmeiser (university of Vienna, Austria) was visiting during four month, from september 2018, and should stay until february 2019.
- Prof. D. Oelz (university of Queensland, Australia) visited from Dec. 5th to Dec. 21st.
- Jieling Zhao, Postdoc from IfADo
- Paul van Liedekerke, Research engineer from IfADo

9.4.1.1. Internships

Ismael Gonzalez Valverde (University of Zaragoza) visited our team for 3 months working on implementation of the meshing of liver micro-structures in modeling of liver regeneration within TiSim.

9.4.2. Visits to International Teams

9.4.2.1. Sabbatical programme

Marie Doumic was in Vienna for a sabbatical stay until July 2018.

MONC Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. Plan Cancer

9.1.1.1. NUMEP

Plan Cancer NUMEP: 2016–2019. Numerics for Clinical Electroporation Funding: 460 kE Partners: Inria Team MONC, Institut de Pharmacologie de Toulouse, CHU J. Verdier de Bondy Duration: Octobre 2016—Septembre 2019 Project leader: C. Poignard Co-PI: M-P. Rols (IPBS), O. Séror (CHU J. Verdier)

9.1.1.2. Dynamo

Plan Cancer DYNAMO: 2015–2018. Dynamical Models for Tissue Electroporation Funding: 370 kE Partners: Laboratoire Ampère, Lab. Vectorology and Anticancerous Therapies (IGR), Inria Team MONC Duration: Octobre 2015—Septembre 2018 Project leader: R. Scorretti (Laboratoire Ampère) Co-PI: L.M. Mir (IGR), C. Poignard (Inria Team MONC)

9.1.1.3. Moglimaging

- Project acronym - Moglimaging: Modeling of Glioblastoma treatment-induced resistance and heterogeneity by multi-modal imaging.
- Partners -
- Duration - from Nov. 2016 to Nov 2019.
- Coordinator - E. Cohen-Jonathan Moyal, Institut Universitaire du Cancer Toulouse / Local coordinator - O. Saut.
- Team participants - S. Benzekry, A. Collin, C. Poignard, O. Saut.

9.1.1.4. Systems Biology of Renal Carcinoma

- Title: Plan Cancer Systems Biology of Renal Carcinoma using a Mouse RCC model
- Partners : LAMC, INSERM-Univ. Bordeaux.
- Duration - June 2018 to June 2021
- Team participants: O. Saut, S. Benzekry (co-PI)
- 116.64k€

9.1.2. Transnation call: INCA/ARC

- Title: Minimally and non-invasive methods for early detection and/or progression of cancer
- Acronym: TRANSCAN
- Team participants: A. Collin, C. Poignard, O. Saut (local PI)
- Total funds: 1M150, Monc's share 275k€.

9.1.3. Competitivity Clusters

- Labex TRAIL (http://trail.labex.u-bordeaux.fr): MOD Project Consolidation. 1 2-years post-doc position (100k€), led by A. Collin, 1 PhD funding (100k€) led by O. Saut.

9.2. European Initiatives

MONC is partner of the European Lab EBAM devoted to electroporation. C.Poignard is member of the steering committee.

9.3. International Initiatives

9.3.1. Inria International Labs

Inria@SiliconValley

Associate Team involved in the International Lab:

9.3.1.1. Num4SEP

Title: Numerics for Spherical Electroporation

International Partner (Institution - Laboratory - Researcher):

University of California, Santa Barbara (United States) - Department of Mechanical Engineering - Frederic Gibou

Start year: 2017

See also: http://num4sep.bordeaux.inria.fr/

Electroporation-based therapies (EPTs) consist in applying high voltage short pulses to cells in order to create defects in the plasma membrane. They provide interesting alternatives to standard ablative techniques, for instance for deep seated badly located tumors. However their use is still limited due to a lack of knowledge of tissue electroporation. The goal of the associate team is to focus on the multiscale numerical modeling of spheroid electroporation, in order to provide new insights in electroporation at the mesoscopic scales (spheroids provide interesting tumor-like biological models). Benefiting from the expertise of F. Gibou's team in HPC for multiphysics, and the expertise of the team MONC in tumor growth and cell electroporation modeling, the goal of the associate team Num4SEP is to obtain accurate and efficient numerical tools for the quantitative evaluation of the EPTs at the mesoscopic scale.

9.3.2. Inria Associate Teams Not Involved in an Inria International Labs

9.3.2.1. METAMATS

Title: Modeling ExperimenTAl MetAsTasiS

International Partner (Institution - Laboratory - Researcher):

Roswell Park Cancer Institute (United States) - Department of Cancer Genetics Department of Medicine Department of Pharmacology and Therapeutics (Graduate Program) - John Ebos

Start year: 2017

See also: http://metamats.bordeaux.inria.fr/

The aim of the METAMATS associate team is to bring together a cancer biology experimental laboratory led by John ML Ebos (Roswell Park Cancer Institute) and the inria MONC team composed of applied mathematicians. The Ebos laboratory is specialized in the study of anti-cancer therapeutics (in particular, novel biologically targeted therapeutics such as anti-angiogenics and immunotherapies) on the development of metastases and produces unique, hard-to-obtain data sets on this process' dynamics. The MONC team is specialized in mathematical models in oncology, with a dedicated axis about modeling support and methodological development for analysis of data from preclinical studies. In particular, the work of S. Benzekry puts emphasis on proposing, studying and validating mathematical models of metastatic development under the action of various therapeutic modalities. Indeed, metastatic expansion remains the main challenge in the treatment of cancer and integrative studies combining experiments, mathematical models and clinical data have the potential to yield predictive computational tools of help to assist both the design of clinical trials and clinical oncologists in therapeutic decisions such as the control of the toxicity/efficacy balance or the optimal combination of treatment modalities.

9.3.3. Other international initiatives

MONC is partner of the European Lab EBAM devoted to electroporation. C.Poignard is member of the steering committee.

9.3.4. Informal International Partners

- Collaboration with Jonathan Mochel at the Department of Biomedical Sciences of Iowa State University (Ames, Iowa, USA). Development of mechanistic pharmacokinetics/pharmacodynamics models for comparative oncology (i.e. translational oncology across species integrating veterinary medicine). Sebastien Benzekry is Affiliate Assistant Professor at Iowa State University.
- Collaboration between Sebastien Benzekry and the laboratory of Yuval Shaked at the Rappaport Faculty of Medicine of the Technion (Israel Institute of Technology, Haifa, Israel). Our joint work deals with validating mathematical models of host-mediated resistance mechanisms to anti-cancer therapies.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

June 2018: Visit of John Ebos (Roswell Park Cancer Institute, Buffalo, USA) in the context of the METAMATS Inria Associate team.

NUMED Project-Team

5. Partnerships and Cooperations

5.1. National Initiatives

5.1.1. ANR

CNRS InFIniti, 2017-2018 (P. Vigneaux): 12ke in 2018

REO Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

9.1.1.1. ANR Project "IFSMACS"

Participants: Muriel Boulakia, Céline Grandmont [local coordinator].

Period: 2015-2019.
The objective of this project, coordinated by Takéo Takahashi (Inria Nancy Grand-Est), is the mathematical analysis of systems involving structures immersed in a fluid. This includes the asymptotic analysis, the study of the controllability and stabilization of fluid-structure interaction systems, the understanding of the motion of self-propelled structures and the analysis and development of numerical methods to simulate fluid-structure systems.

9.1.1.2. Participation to other ANR projects

- Laurent Boudin is a member of the ANR Blanc project Kibord on kinetic models in biology and related domains
- Laurent Boudin is a member of the ANR TecSan Oxhelease
- Céline Grandmont is a member of the ANR TecSan Oxhelease
- Irene Vignon Clementel is a member of the project iLite (09/16-), RHU-santé grant, a large French hospital-medical research consortium that aims at developing innovations for liver and tissue engineering (Inria PI: Dirk Drasdo).

9.2. European Initiatives

9.2.1. Collaborations in European Programs, Except FP7 & H2020

9.2.1.1. SimInhale COST

Participant: Irene Vignon Clementel.

Action MP1404, a pan-European network of experts in the field of inhaled medicine.

9.3. International Research Visitors

9.3.1. Visits of International Scientists

9.3.1.1. Internships

- Charu Mittal, Visiting PhD student, Indian Institute of Technology Bombay, March 2018–August 2018

SISTM Project-Team

9. Partnerships and Cooperations

9.1. Regional Initiatives

The team have strong links with :

- Research teams of the research center INSERM U1219 : "Injury Epidemiology, Transport, Occupation" (IETO), "Biostatistics", "Pharmacoepidemiology and population impact of drugs", "Multimorbidity and public health in patients with HIV or Hepatitis" (MORPH3Eus), "Computer research applied to health" (ERIAS) emerging research team.
- Bordeaux and Limoges CHU ("Centre Hospitalier Universitaire").
- Institut Bergonié, Univ Bordeaux through the Euclid platform
- Inria Project-team MONC, M3DISIM and CQFD

The project team members are involved in:

- EUCLID/F-CRIN clinical trials platform (Laura Richert)
- The research project “Self-management of injury risk and decision support systems based on predictive computer modelling. Development, implementation and evaluation in the MAVIE cohort study” funded by the Nouvelle-Aquitaine regional council (Marta Avalos).
- Phenotyping from Electronic Health Records pilot project in cooperation with with the ERIAS Inserm emerging team in Bordeaux and the Rheumatology service from the Bordeaux Hospital (Boris Hejblum)
- A cancer research project in collaboration with Inria MONC team on glioblastoma

9.2. National Initiatives

- Labex Vaccine Research Institute (VRI) There are strong collaborations with immunologists involved in the Labex Vaccine Research Institute (VRI) as Rodolphe Thiébaut is leading the Data science division (previously Biostatistics/Bioinformatics) http://vaccine-research-institute.fr.
- Collaboration with Inserm PRC (pôle Recherche clinique).
- Collaboration with Inserm Reacting (REsearch and ACTion targeting emerging infectious diseases) network

9.2.1. Expert Appraisals

- Rodolphe Thiébaut is a member of the CNU 46.04 (Biostatistiques, informatique médicale et technologies de communication).
- Rodolphe Thiébaut is a member of the Scientific Council of INSERM.
- Mélanie Prague is an expert for ANRS (France Recherche Nord&Sud Sida-HIV Hépatites) in the CSS 3 (Recherches cliniques et physiopathologiques dans l’infection à VIH) and AC 47 (Dynamique et contrôle des épidémies VIH et hépatites).
- Laura Richert is an expert for the PHRC (Programme hospitalier de recherche Clinique).
- Marta Avalos is an expert for the ANSM (Agence nationale de sécurité du médicament et des produits de santé)

9.2.2. Various Partnership

The project team members are involved in:

- DRUGS-SAFE platform funded by ANSM (Marta Avalos). Initiated in 2015-2018. Renewed for 2019.
- F-CRIN (French clinical research infrastructure network) was initiated in 2012 by ANR under two sources of founding "INBS/Infrastructures nationales en biologie et en santé" and "Programme des Investissements d'avenir". (Laura Richert)
- I-REIVAC is the French vaccine research network. This network is part of the "Consortium de Recherche en Vaccinologie (CoReVac)" created by the "Institut de Microbiologie et des Maladies Infectieuses (IMMI)". (Laura Richert)
- INCA (Institut National du Cancer) funded the project « Evaluation de l'efficacité d'un traitement sur l'évolution de la taille tumorale et autres critères de survie : développement de modèles conjoints. » (Principal PI Virginie Rondeau Inserm U1219, Mélanie Prague is responsible of Work package 4 mechanistic modeling of cancer: 5800 euros).
- Contrat Initiation ANRS MoDeL-CI: Modeling the HIV epidemic in Ivory Coast (Principal PI Eric Ouattara Inserm U1219 in collaboration with University College London, Mélanie Prague is listed as a collaborator).

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

The member of SISTM Team are involved in EHVA (European HIV Vaccine Alliance):

Program: Most information about this program can be found at http://www.ehv-a.eu.

Coordinator: Rodolphe Thiébaut is Work Package leader of the WP10 "Data Integration".

Other partners: The EHVA encompasses 39 partners, each with the expertise to promote a comprehensive approach to the development of an effective HIV vaccine. The international alliance, which includes academic and industrial research partners from all over Europe, as well as sub-Saharan Africa and North America, will work to discover and progress novel vaccine candidates through the clinic.

Abstract: With 37 million people living with HIV worldwide, and over 2 million new infections diagnosed each year, an effective vaccine is regarded as the most potent public health strategy for addressing the pandemic. Despite the many advances in the understanding, treatment and prevention of HIV made over the past 30 years, the development of broadly-effective HIV vaccine has remained unachievable. EHVA plans to develop and implement:

Discovery Platform with the goal of generating novel vaccine candidates inducing potent neutralizing and non-neutralizing antibody responses and T-cell responses

Immune Profiling Platform with the goal of ranking novel and existing (benchmark) vaccine candidates on the basis of the immune profile

Data Management/Integration/Down-Selection Platform, with the goal of providing statistical tools for the analysis and interpretation of complex data and algorithms for the efficient selection of vaccines

Clinical Trials Platform with the goal of accelerating the clinical development of novel vaccines and the early prediction of vaccine failure.

9.3.2. Collaborations in European Programs, Except FP7 & H2020

Program: The EBOVAC2 project is one of 8 projects funded under IMI Ebola+ programme that was launched in response to the Ebola virus disease outbreak. The project aims to assess the safety and efficacy of a novel prime boost preventive vaccine regimen against Ebola Virus Disease (EVD). Project acronym: EBOVAC2 Project title: EBOVAC2 Coordinator: Rodolphe Thiébaut Other partners: Inserm (France), Labex VRI (France), Janssen Pharmaceutical Companies of Johnson

& Johnson, London School of Hygiene & Tropical Medicine (United Kingdom), The Chancellor, Masters and Scholars of the University of Oxford (United Kingdom), Le Centre Muraz (Burknia Faso), Inserm Transfert (France) Given the urgent need for an preventive Ebola vaccine strategy in the context of the current epidemic, the clinical development plan follows an expedited scheme, aiming at starting a Phase 2B large scale safety and immunogenicity study as soon as possible while assuring the safety of the trial participants.

Phase 1 trials to assess the safety and immunogenicity data of the candidate prime-boost regimen in healthy volunteers are ongoing in the UK, the US and Kenya and Uganda. A further study site has been approved to start in Tanzania. Both prime-boost combinations (Ad26.ZEBOV prime + MVA-BN-Filo boost; and MVA-BN-Filo prime + Ad26.ZEBOV boost) administered at different intervals are being tested in these trials.

Phase 2 trials (this project) are planned to start as soon as the post-prime safety and immunogenicity data from the UK Phase I are available. Phase 2 trials will be conducted in healthy volunteers in Europe (France and UK) and non-epidemic African countries (to be determined). HIV positive adults will also be vaccinated in African countries. The rationale for inclusion of European volunteers in Phase 2, in addition to the trials in Africa, is to allow for higher sensitivity in safety signal detection in populations with low incidence of febrile illnesses, to generate negative control specimens for assay development, to allow for inclusion of health care workers or military personnel that may be deployed to Ebola-endemic regions.

EBOVAC3 As a follow-up project, the IMI-2 funded EBOVAC3 project, has started in 2018. In this project, the vaccine strategy will be further evaluated in specific populations in Africa (infants in Guinea and Sierra Leone; and front line workers in RDC). The project includes a work package on modelling, which is led by Rodolphe Thiebaut.

9.3.3. Collaborations with Major European Organizations

University of Oxford;

London School of Hygiene and Tropical Medicine;

University Hospital Hamburg;

Heinrich Pette Institute for Experimental Virology, Hambourg;

MRC, University College London;

MRC Biostatistics Unit, University of Cambridge.

9.4. International Initiatives

- Prevac-Up: this EDCTP-funded research program will collect and analyze important information on the effectiveness and maintainability of Ebola vaccination in sub-Saharan Africa.
- NIPAH program: a Franco-Chinese collaboration of 1 million euros per country over 5 years to develop a program to better understand Nipah Virus infection, its physiopathology and to develop new tools for diagnosis, treatment and prevention.

9.4.1. Inria International Labs

Inria@SiliconValley
Associate Team involved in the International Lab:

9.4.1.1. SWAGR

Title: Statistical Workforce for Advanced Genomics using RNAseq

International Partner (Institution - Laboratory - Researcher):

RAND Corporation (United States) - Statistics group - Denis Agniel

Start year: 2018

See also: https://team.inria.fr/swagr/

The SWAGR Associate Team aims at bringing together a statistical workforce for advanced genomics using RNAseq. SWAGR combines the biostatistics experience of the SISTM team from Inria BSO with the mathematical expertise of the statistics group at the RAND Corporation in an effort to improve RNAseq data analysis methods by developing a flexible, robust, and mathematically principled framework for detecting differential gene expression. Gene expression, measured through the RNAseq technology, has the potential of revealing deep and complex biological mechanisms underlying human health. However, there is currently a critical limitation in widely adopted approaches for the analysis of such data, as edgeR, DESeq2 and limma-voom can all be shown to fail to control the type-I error, leading to an inflation of false positives in analysis results. False positives are an important issue in all of science. In particular in biomedical research when costly studies are failing to reproduce earlier results, this is a pressing issue. SWAGR propose to develop a rigorous statistical framework modeling complex transcriptomic studies using RNAseq by leveraging the synergies between the works of B. Hejblum and D. Agniel. The new method will be implemented in open-source software as a Bioconductor R package, and a user friendly web-application will be made available to help dissemination. The new method will be applied to clinical studies to yield significant biological results, in particular in vaccine trials through existing SISTM partnerships. The developed method is anticipated to become a new standard for the analysis of RNAseq data, which are rapidly becoming common in biomedical studies, and has therefore the potential for a large impact.

9.4.2. Inria International Partners

Fred Hutchinson Cancer center, Seattle;

Baylor Institute for Immunology (Dallas);

Duke University -Duke Global Health Institute, Elizabeth Turner.

Harvard University - Department of Population Medicine - Rui Wang. M. Prague is a co-PI in an amfAR project for co-supervizion of a PhD student.

university of San Diego UCSD / Harvard School of public health - NIH program project grant "Revealing Reservoirs During Rebound", Harvard School of Public Health (HSPH) and the University of California, San Diego (P01AI131385, total budget $1.5M/yr for 5 years starting Oct 2017, both university manage the funding. Mélanie Prague is part of modelling unit of the "Quantitative Methods" research project (budget $220,000/yr). The principal investigator for this core is Victor de Grutolla (HSPH) The overall goal of this grant is to characterize viral rebound following antiretroviral therapy cessation in cohorts of patients who have started therapy early in infection, as well as in a cohort of terminally-ill patients who will interrupt therapy before death and subsequently donate their bodies to research.

Harvard University - program for evolutionary dynamics - Alison hill and Martin Nowak. Project submitted by M Prague for the Inria associated team with this laboratory.

Collaborations through clinical trials: NIH and University of Minnesota for the Prevac trial, NGO Alima for the Prevac trial, Several African clinical sites for Ebovac2 and Prevac trials;

Tianxi Cai from Harvard University on developing methods for the linkage and analysis of Electronic Health Records data (Boris Hejblum).

Katherine Liao from Harvard University on the analysis of Electronic Health Records data in the context of Rheumatoid Arthritis (Boris Hejblum).

Sylvia Richardson from MRC Biostatistics Unit Cambridge University on the scaling up of nonparametrics Bayesian appraches to Big data (Boris Hejblum).

Machine learning team Data61 at CSIRO, Australia (Marta Avalos)

9.5. International Research Visitors

9.5.1. Visits to International Teams

Marta Avalos visited Marcela Henríquez Henríquez 1 week in December 2018, Medical School, Pontifical Catholic University of Chile (Chile). Travel grant from the French Embassy in Chile and the French Institute of Chile

Boris Hejblum visited the RAND Corporation for a week in July 2018 for a research collaboration with Denis Agniel (Santa-Monica, USA).

Boris Hejblum visited the MRC BSU for 10 days in October 2018 for a research collaboration with Sylvia Richardson & Paul Kirk.

Chloé Pasin visited Harvard School of Public Health on May 9-11 2018 and Columbia University, Departement of Pathology and Cell Biology on May 14-17 2018.

Mélanie Prague got invited in University of Montreal (Canada) for a 3-days research trip in the pharmacy department on December 19-22 2018 to be member of the jury comittee of the PhD defense of Steven Sanche (Effet des antire´troviraux sur la pathoge´ne`se du VIH), as well as giving an invited talk.

Mélanie Prague spent 3 weeks in Boston as an invited researcher in Harvard School of Public Health & Department of evolutionary dynamics, Biostatistics department in January and february 2018.

9.5.1.1. Research Stays Abroad

- Laura Richert spent 6 months (March-August 2018) as a visting researcher at the Heinrich Pette Institut for Experimental Virology, Research Department Virus Immunology, Hamburg, Germany (head: Marcus Altfeld).

XPOP Project-Team

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

Mixed-Effects Models of Intracellular Processes: Methods, Tools and Applications (MEMIP)

Coordinator: Gregory Batt (InBio Inria team)

Other partners: InBio and IBIS Inria teams, Laboratoire Matière et Systèmes Complexes (UMR 7057; CNRS and Paris Diderot Univ.)

9.1.2. Institut National du Cancer (INCa)

Targeting Rac-dependent actin polymerization in cutaneous melanoma - Institut National du Cancer

Coordinator: Alexis Gautreau (Ecole Polytechnique)

Other partners: Laboratoire de Biochimie (Polytechnique), Institut Curie, INSERM.

9.2. International Initiatives

9.2.1. International Initiatives

SaSMoTiDep

Title: Statistical and Stochastic modeling for time-dependent data

International Partners (Institution - Laboratory - Researcher):

Universidad de Valparaiso (Chile) - Centro de Investigación y Modelamiento de Fenómenos Aleatorios Valparaíso (CIMFAV) - Cristian Meza Becerra

Universidad Nacional de Colombia (Colombia) - Department of Statistics - Viswanathan Arunachalam

Duration: 01/01/2018 - 31/12/2019

Start year: 2018

See also: https://sasmotidep.uv.cl

In many applications, multiple measurements are made on one or several experimental units over a period of time. Such data could be called time-dependent data. From a statistical point of view, if we consider only one experimental unit, we can use a time series analysis. In the other hand, if we consider experimental designs (or observational studies) for several experimental units (or subjects) where each subject is measured at several points in time, we can use the term longitudinal data. In this project, we propose to study several statistical and stochastic models for repeated measures using parametric and non-parametric approaches. In particular, we will study the inference in complex mixed effects models, we will propose novel segmentation models for multiple series, non-parametric methods in dependent models and stochastic models. We will apply these methods to real data from several fields as biometrics, reliability, population dynamics and finance.

9.3. International Research Visitors

9.3.1. Visits of International Scientists

Ricardo Rios, Universidad Central de Venezuela, Caracas: September 2018.