ENS Lyon RESEARCH 2007-2009

RESEARCH AT ENS LYON

2007-2009

École normale supérieure de Lyon
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UNIVERSITÉ DE LYON

ENS LYON

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RESEARCH AT ENS LYON

2007-2009

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►EXPLORE, DISCOVER AND INNOVATE...◄

► To explore, discover and innovate are the main aims of the ENS de Lyon, strongly associated with transferring knowledge to and training talented young students.

The ENS de Lyon is then continuously developing a core of research laboratories and facilites where researchers, faculty and students work constantly side by side.

Interdisciplinarity is a key strategic focus of our institution. All combinations are allowed, making it the leading force of innovation and thereby constructing the Science of tomorrow.

In keeping with our outward engagement, all our academic programs are developed in close partnership with many other research and university institutions within the consortium of Université de Lyon.

This endeavour is clearly successful in that many of our talented students become privileged actors in higher education and research both in public and semi-public institutions and in the industrial and economic sectors.

Wherever you come from, if you are driven by the advancement of knowledge, then come join us in our pursuit of excellence.

Pr. Jacques Samarut
Director

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- **Didier Roux,** Director R&D, Saint-Gobain
- **Jacques Vincent** (President of the board), Vice-Chairman and Chief Operating Officer, Groupe Danone

►WOMEN AND MEN, DRIVEN BY A PASSION◄

► At the ENS de Lyon, cutting edge research *(see page 106 awards and distinctions)* is achieved through innovation *(see page 105 – contracts)*, transdisciplinary initiatives and a strong international engagement. 75 teams of researchers work together across 14 laboratories under shared supervision with the best-known international names in research organisations, such as CNRS, INRA, Inserm, INRIA, and others.

Our 360 researchers and 100 post-doctoral students, supported by 245 administrative and technical staff are not just French, American, German, English, Romanian, or Chinese – they are first and foremost women and men who are driven by a common passion for research, collaboration and a crossdisciplinary approach, working in laboratories equipped with the best research and technical facilities *(see page 103)*. At the ENS de Lyon our research teams strive to give the best of themselves for the benefit of Science, but also to achieve standards of excellence at the institution itself.

The ENS de Lyon is located at the heart of a dynamic business hub in Lyon where biotechnology, fundamental and applied research, higher education and entrepreneurs rub shoulders and interact with each other. Our research themes are a reflection of this reality.

This document retraces some aspects of the research conducted at the ENS de Lyon over the last three years.

Pr Chantal Rabourdin-Combe
Director of Research

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►ASTROPHYSICS RESEARCH CENTER - CRAL◄

► **Director** ► **Bruno Guiderdoni,** *senior researcher - bguider@obs.univ-lyon1.fr* ◄
► **Total personnel** ► *65 staff and 15 students* ◄
► **Partners** ◄ *CNRS, UCB Lyon 1* ◄
► **Web** ◄ *http://www-obs.univ-lyon1.fr* ◄

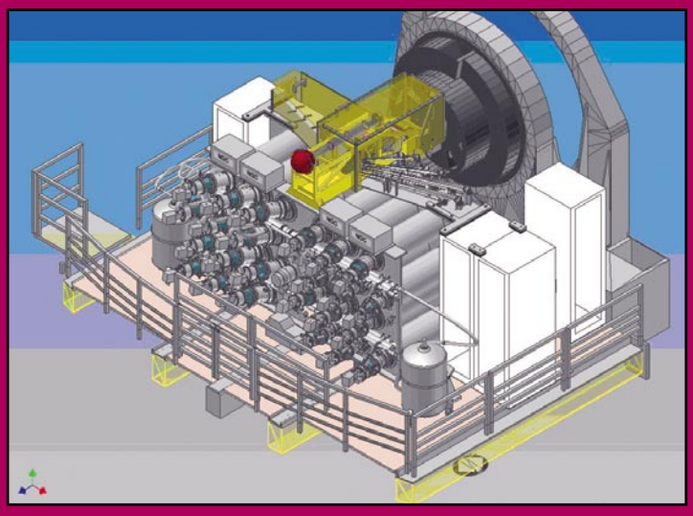
► The Lyon Center for Astrophysics Research (CRAL) works out of two locations, one at the ENS Lyon and the other at the Observatory of Lyon located in Saint Genis Laval. This laboratory is internationally renowned for its contributions to the physics of stars and exoplanets, the study of the dynamical evolution of galaxies, the theory of structure formation, the theory and characterization of dark energy, and the development of experimental physics and algorithms for high-resolution observations. The CRAL is currently involved in the construction of MUSE, a 2nd generation integral field unit spectrograph to be delivered to the ESO's Very Large Telescope in Chile in 2011. The center is also contributing to the NIRSpec spectrograph for the forthcoming James Webb Space Telescope (to be launched in 2013), to concept studies for the ESO European Extremely Large Telescope, and to the development of numerical simulations of structure formation for the Horizon numerical project. CRAL researchers actively participate in the teaching of physics and astrophysics at the ENS Lyon and at the Université Claude Bernard Lyon 1. The CRAL also pilots a regional network of institutions that support public outreach in astrophysics.

CURRENT RESEARCH TOPICS
Plasma physics applied to stars and exoplanets, the formation and evolution of galaxies, stars and planets, large-scale structures and cosmology, new concepts and technologies for instrumentation and observation

AREAS OF APPLICATION
Theory and observation

INDUSTRIAL PARTNERS
ESO, ESA, EADS-Astrium

EQUIPMENT
Optical benches, mechanical devices, metrology



▲
The CRAL leads a consortium of European laboratories that are building MUSE, an 8-ton instrument with cutting-edge technology that will permit scientists to observe 90,000 spectra in a single observation, to be delivered to the Very Large Telescope of the European Southern Observatory in Chile in 2011. MUSE will probe the formation of galaxies at a distance corresponding to an epoch when the universe was only 1 billion year old.

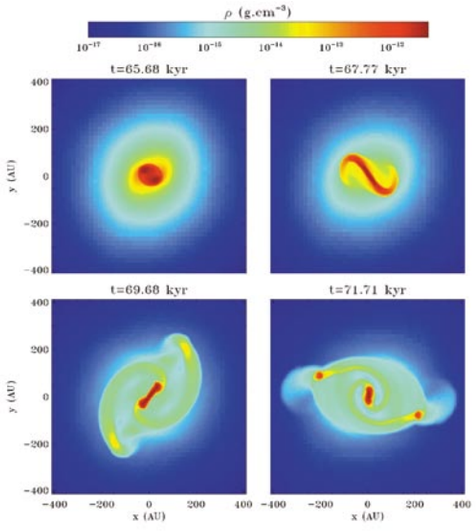
►ASTROPHYSICS RESEARCH CENTER - CRAL◄

►CRAL-ENS◄

► **Team leader** ► ***Gilles Chabrier,*** *research director first class - gilles.chabrier@ens-lyon.fr* ◄
► **Team members** ► *France Allard, research director; Marie-Christine Artru, full professor; Isabelle Baraffe, research director; Gilles Chabrier, research director; Benoit Commerçon, PhD student; Bern Freytag, postdoctoral fellow; Jean-François Gonzalez, associate professor; Alberic Joos, PhD student; Guillaume Laibe, PhD student; Jeremy Leconte, PhD student; Gérard Massacrier, research associate; Cédric Mulet-Marquis, postdoctoral fellow; François Soubiran, PhD student; Christophe Winisdoerffer, associate professor*◄ ***www-obs.univ-lyon1.fr***

► **The main research interests of the ENS-Lyon theoretical astrophysics group include the physics of compact objects** (dense plasmas; structure, evolution, spectral energy distribution of compact objects: neutron stars, white dwarfs, low-mass stars, brown dwarfs, planets), galactic physics (gravitational microlensing, galactic structure, galactic dark matter), the hydrodynamics of compact objects (coalescence of white dwarfs and neutron stars, evolution of compact binaries, stability of stars) and the study of hydrodynamic processes in astrophysics (star and planet formation, protoplanetary disks, instabilities and stellar pulsations, turbulence, MHD) with multi-dimensional numerical simulations. The underlying guideline in these different topics is the understanding of physical processes in astrophysics. These research fields involve a variety of domains in physics, mainly statistical physics, atomic physics and hydrodynamics. Over the years, different fields of research have been developed including (chronologically):

- fundamental physics: hydrodynamics; statistical physics of dense matter; matter-radiation interaction,
- planetary and stellar astrophysics: structure and evolution of compact objects: white dwarfs, neutron stars, low-mass stars, brown dwarfs, solar and extrasolar gaseous planets; characterization of Earth-like extrasolar planets; stellar seismology; star and planet formation,
- galactic physics and cosmology: stellar initial mass function; gravitational microlensing; galactic structure; galactic missing mass; primordial stars.



The figure below illustrates the spatial projection of the gravitational collapse of a rotating sphere (protostellar core) with 3D hydrodynamic simulations, and the formation and fragmentation of a central accretion disk, leading eventually to the formation of a binary stellar system.

Density map from a numerical simulation using the 3D AMR MHD code RAMSES. This simulation presents the gravitational collapse of an initially uniform sphere in solid rotation with no magnetic field included at different time steps. In this particular case, we observe the formation and fragmentation of a central accretion disc (Commerçon et al., A&A, 2008) ►

Recent scientific award recipients:

►Isabelle Baraffe: Gauss professorship, Göttingen Academy of Science, 2005; Johann Wempe Prize, 2004 (Germany).
►Gilles Chabrier: CNRS silver medal, 2006; Johann Wempe Prize, 2004 (Germany).

Selected publications:

►Chabrier, G., Gallardo, J., Baraffe, I., Evolution of low-mass star and brown dwarf eclipsing binaries, 2007, Astron. & Astroph., 472, 17
►Chabrier, G. & Baraffe, I., Heat Transport in Giant (Exo)planets: A New Perspective, 2007, Astroph. J., 661, L81
►Mulet-Marquis, C., Glatzel, W., Baraffe, I., Winisdoerffer, C., Nonradial oscillations in classical Cepheids: the problem revisited, 2007, Astron. & Astroph., 465, 937
►Hennebelle P., Chabrier G., Analytical theory for the Initial Mass Function, 2008 Astroph. J., 684, 395

►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

► **Director** ► ***Laurent Schaeffer,*** *Research director - laurent.schaeffer@ens-lyon.fr* ◄
► **Total personnel** ► *148* ◄
► **Partners** ◄ CNRS, University Lyon 1, Hospitals of Lyon ◄
► **Web** ◄ http://www.ens-lyon.fr/LBMC/web/nav/ ◄

► The Laboratory of Molecular Biology of the Cell (LBMC) studies the main questions of modern molecular and cellular biology: genetic and epigenetic regulation of gene expression and genome stability, oncogenesis, intercellular communication and intracellular signalling, cytoskeleton organisation, cell cycle, differentiation and cell death, energy metabolism and regulation of growth and longevity.
Having access to appropriate model systems is essential for investigating and developing new functional approaches. The Laboratory has incorporated or developed world class expertise with mouse, zebra fish, drosophila, caenorhabditis elegans and yeast in addition to numerous cell models.

The LBMC currently comprises 148 people, spread out over 13 independent research teams, developing individual research topics. The recruitment of new teams is primarily dictated by scientific excellence and integrates the fact that the laboratory aims to cover the main fields of eukaryotic cell biology (except plant biology) so as to encourage complementarity in research teams.

In the field of public health, the LBMC possesses strong links with the hospital sector resulting in collaborative biomedical and clinical research programs. The LBMC works to establish a research continuum from the elucidation of fundamental cellular mechanisms to the understanding of the dysfunctions at the origin of human pathologies, mainly in the fields of oncology and neuromuscular disorders. In 2007, the LBMC created an extension in the nearby Hospital of Lyon Sud to develop translational research in oncology. Three research groups are localized there.

On the socio-economic level, the LBMC encourages the emergence of biotechnology companies based on discoveries and expertises of the laboratory. From the past, one can cite: i) Genoway, involved in the development of transgenic animal models; ii) Vivalis, which develops the technology of chicken embryonal stem cells for biotechnological applications; iii) Aptanomics which uses the peptide aptamer technology to create novel therapeutic molecules against cancer; iv) Phylogene, which develops methods of identification and authentification of food, using DNA and proteins.

CURRENT RESEARCH TOPICS
Fundamental cellular processes

RELATED FIELDS
Molecular and cellular biology

AREAS OF APPLICATION
Cancer, neuromuscular disorders

INDUSTRIAL PARTNERS
See text

EQUIPMENT
Technical platforms of the IFR 128 (confocal microscopy, video time lapse, mass spectrometry, ...)

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►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

►Cellular and Organismal Aging Lab◄

► **Team leader** ► ***Hugo Aguilaniu*** - *hugo.aguilaniu@ens-lyon.fr* ◄
► **Team members** ► *Hugo Aguilaniu, research associate first class; Yiqun Chen, PhD student; Paola Fabrizio, research associate first class; Jérôme Goudeau, PhD student; Esther Mollereau, technician; Mehrnaz Shamalnasab, PhD student.*◄

www.ens-lyon.fr/LBMC/web/nav/listeArt.php?rub=11&rub2=39

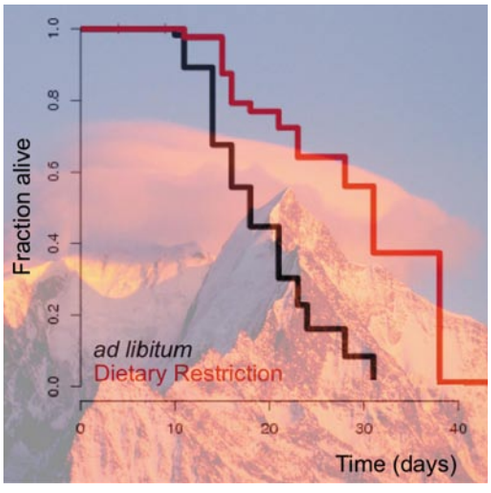
► **Our group uses Caenorhabditis elegans, Saccharomyces cerevisiae and mice to investigate the biological basis of the aging process.**

Dietary Restriction

Food intake and longevity are closely intertwined. It is popular wisdom that eating should be "balanced". But how to define the point at which food intake is indeed "balanced" became source of debate when McCay showed in 1935 that Dietary Restriction (DR; diminution of daily food intake without reaching malnutrition) significantly prolongs life span. Importantly this increase is accompanied by a significant decrease of all aging-related diseases including cancer, neurodegeneration and obesity (metabolic syndrome). Finding new genetic determinants of DR that will be of biomedical use is at the center of our group's interests.

Reproduction and aging

Germline Stem Cells (GSC) proliferation was recently shown to affect both longevity and fat storage (Hsin et al, Nature, 1999, Wang et al, Science, 2009). Interestingly, one of the predictions of the disposable soma theory of aging is that lowering reproductive costs could promote longevity (Kirkwood, Nature, 1977). Our lab uses genetic and biochemistry to find the molecular actors involved in these trade-offs. We believe that the role of the germline on fat and longevity will be conserved. In fact, impairing the reproductive apparatus (menopause, etc..) almost always results in major metabolic shifts in higher vertebrates. Our lab uses the power of genetic of Caenorhabditis elegans to find genetic determinants of these shifts with the goal of finding new therapeutic strategies.



Lifespan extension obtained on wild type nematode (C. elegans) simply by diminishing the daily food intake (dietary restriction: DR). Animals fed ad libitum are depicted in black (Mean lifespan of 18 days) while animals submitted to DR (depicted in red) live up 30 days. Moreover, DR animals are healthier and less prone to age related diseases. ►

From old to young

Numbers of biological parameters change in an age dependent manner. Our group studies the mechanisms allowing the resetting of "aging markers" at the time of reproduction. How can a reproductive (middle-aged) organism create a young individual remains an open question? In other words, we want to understand what it takes to make young individuals out of older ones. Interestingly, among all parameters that are reset to ensure proper rejuvenation, we want to find on these that are critical for lowering age-related diseases. We hope that our approach will open new biomedical strategies to cure age-related diseases.

Selected publications:

►Wei M, Fabrizio P, Hu J, Ge H, Cheng C, Li L, Longo VD. Life span extension by calorie restriction depends on Rim15 and transcription factors downstream of Ras/PKA, Tor, and Sch9. PLoS Genet. 2008 Jan;4(1)

►Panowski SH, Wolff S, Aguilaniu H, Durieux J, Dillin A. PHA-4/Foxa mediates diet-restriction-induced longevity of C. elegans. Nature. 2007 May 31;447(7144):550-5

►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

►Chromatin dynamics and DNA repair◄

► ***Dimitar Angelov,*** *Research Director CNRS - Dimitar.Anguelov@ens-lyon.fr* ◄
► **Team members** ► *Elsa Bensimon, Engineer; John Lalith Charles Richard, PhD student; Imtiaz Nisar Lone, PhD student; Manu Shukla, postdoctoral fellow; Sajad Hussain Syed, PhD student.*◄

► **The chromatin acts as a barrier to several vital cellular processes including transcription and repair. Nucleosome and chromatin structure, and thus DNA accessibility,** may be altered by the incorporation of linker histones, histone variants, and transcription regulators. They can also be altered by the post-translational modification of histone tails, and the action of ATP-dependent remodeling factors and histone chaperones.

Our goal is to investigate the physico-chemical and functional properties of chromatin, and to understand in molecular detail the fundamental question of how transcription and repair take place. We are particularly interested in changes that occur in nucleosomes upon incorporation of histone variants. We are currently investigating the mechanisms by which different ATP-dependent chromatin remodeling complexes, alone or in conjunction with histone chaperones, generate structural alterations in chromatin making it accessible to transcription and repair factors. We are also interested in how DNA binding proteins (transcription factors, repair proteins, etc.) search and recognize their DNA targets in the context of naked DNA, mono-nucleosomes, relaxed or condensed chromatin.

We are currently employing a combinational approach using conventional biochemistry and molecular biology in conjunction with a wide range of physical-chemistry techniques including cryo-electron microscopy and atomic force microscopy in collaboration with researchers at Lyon and Grenoble. For high-resolution dynamics studies we have developed the novel UV laser biphotonic DNA-protein footprinting and covalent crosslinking (Laser ChIP) approach. We are also applying the laser induced chemistry to study propagation of thermal induced structural fluctuations within DNA.

Selected publications:

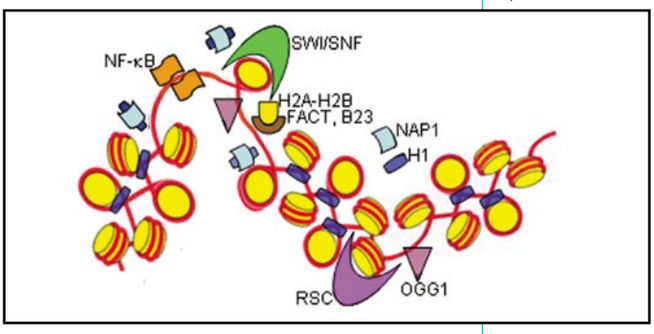
►Peyrard M, Lopez SC, Angelov D (2007) Fluctuations in the DNA double helix. European Physical Journal-Special Topics 147, 173-189.

►Menoni H, Gasparutto D, Hamiche A, Dimitrov S, Cadet J, Bouvet P, Angelov D (2007) SWI/SNF stimulates base excision repair of conventional nucleosome. Mol. Cell. Biol. 27, 5949-5926.

►Amiard S, Doudeau M, Pinte S, Poulet A, Lenain C, Moskalenko C, Angelov D, Hug N, Vindigni A, Bouvet P, Paoletti J, Gilson E, Giraud-Panis M-J (2007) A topological mechanism for TRF2-enhanced strand invasion. Nature Str. Mol. Biol. 14, 147-154.

►S. H. Syed, M. Boulard, M. Shukla, T. Gautier, A. Travers, J. Bednar, C. Faivre-Moskalenko, S. Dimitrov and D. Angelov (2009) The incorporation of the novel histone variant H2AL2 confers unusual structural and functional properties of the nucleosome. Nucleic Acids Res. 37, 4684-95.

"Breathing" of the Chromatin.
▼



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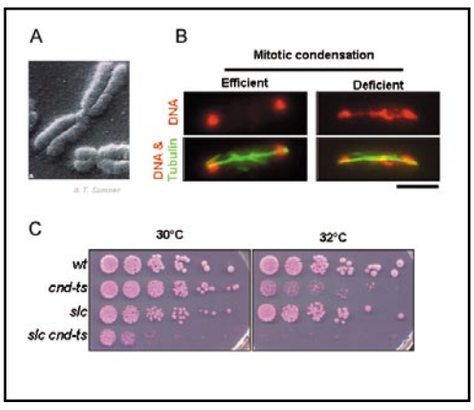
►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

►Chromosome Architecture and Functional Dynamic◄

► **Team leader** ► ***Pascal Bernard,*** *research associate first class CNRS - pascal.bernard@ens-lyon.fr* ◄
► **Team members** ► *Pascal Bernard, CNRS, Research Associate First Class; Xavier Robellet, CNRS, postdoctoral fellow.* ◄
http://www.ens-lyon.fr/LBMC/web/nav/listeArt.php?rub=11&rub2=53

►**Duplicated chromosomes must be segregated accurately during nuclear divisions.** Chromosome gain or loss can lead to miscarriages or congenital disorders, and is also suspected to be a driving force in some oncogenic processes. The overall goal of our research is to understand mitotic chromosome assembly and segregation by using the fission yeast Schizosaccharomyces pombe as a model organism.

Upon mitotic entry, entangled chromatin fibres condense into highly structured mitotic chromosomes. Condensin and topoisomerase II (Topo II) are two chromosomal enzymes essential for the assembly of a fully functional mitotic chromosome. Both abundantly bind to chromatin in prophase and dissociates (in part) in telophase. Condensin is also implicated in several processes during interphase, such as DNA damage signalling and repair, transcriptional silencing and nuclear compartmentalization of chromatin. Thus, condensin impinges on multiple pathways that preserve the integrity of the genetic text and/or ensure its accurate expression. Paradoxically, the mechanisms by which condensin binds to chromatin and leads to its condensation in a regulated manner, as well as the molecular bases of its interphase functions are poorly characterised. Furthermore, chromosomes condense somewhat when condensin and/or Topo II are impaired, implying the existence of other, unidentified condensation factors. Their identification and characterisation are of paramount importance for deciphering the molecular mechanisms of chromosome architecture and functional dynamics. In order to uncover new condensation factors, we have selected mutants that are viable when condensin is active but die when it is partly defective. Our main objective now is to characterise these molecules with respect to mitotic chromosome condensation and segregation, condensin association with chromatin and/or DNA metabolism in interphase.



A. Human mitotic chromosome. *Sister chromatids (replication products) and heterochromatic centromeres are visible.* **B. Defective condensation disrupts chromosome segregation in anaphase.** *Two fission yeast cells in anaphase are shown. DNA (red) was stained with DAPI and the mitotic spindle (green) detected by indirect immunofluorescence. Chromosomes segregate to opposite spindle poles when condensation is efficient (left panel). In contrast, impaired condensation disrupts chromosome separation and chromatin bridges appear. Bar: 5 microns.* **C. Genetics for identifying new condensation factors.** *To identify new condensation factors, we search for slc mutations: mutations that are synthetically lethal with condensin. Here, serial spotting assay shows what is synthetically lethal. We serially diluted yeast strains and spotted them on solid media. Then we incubated them at the indicated temperatures. wt: wild type control. cnd-ts: thermosensitive condensin mutant. At 30°C and 32°C, cnd-ts and slc single mutant strain are viable whereas the double mutant cnd-ts slc is dead.* ►

Selected publications :

►Bernard P, Schmidt CK, Vaur S, Dheur S, Drogat J, Genier S, Ekwall K, Uhlmann F, Javerzat JP. Cell-cycle regulation of cohesin stability along fission yeast chromosomes. EMBO J. 2008 Jan 9;27(1):111-21.

►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

►Assembly of chromatin and ribosome biogenesis◄

► **Team leader** ► **Philippe Bouvet,** *Professor - pbouvet@ens-lyon.fr* ◄

► **Team members** ► *Sadhan Das, PhD Student; Hélène Delage, Technician; Ali Massoudi, Postdoctoral fellow; Benoit Moindrot, PhD Student; Fabien Mongelard, Assistant Professor; Karine Monnier, Postdoctoral fellow; Rodrigo Pinto, Postdoctoral fellow; Cong Rong, PhD Student.* ◄

► **Profound alterations of the nuclear compartment are found in cancer cells. In particular,** hypertrophy of the nucleolus is one of the criteria used by pathologists to identify malignant cells. The nucleolus is the site of synthesis of ribosomal RNA (rRNA) and of the assembly of the ribonucleic particles involved in the synthesis of the proteins, the ribosomes. The biogenesis of the ribosomes is a process very important for the cell. Indeed, the synthesis of rRNA corresponds to about 40% of the transcriptional activity of the cell, and rRNA represents about 80% of total cellular RNA. The synthesis of ribosomes is very much linked to cell proliferation and is regulated during the cell cycle. The molecular mechanisms which regulate the assembly of ribosomes and their production in accordance with the need of the cell are still largely unknown.

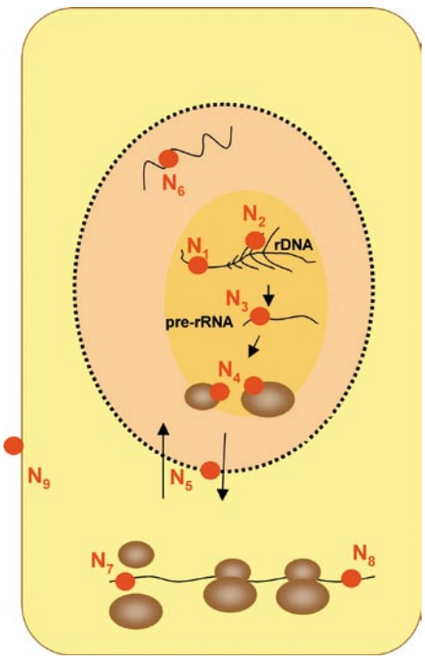
Our team studies this problem by characterizing a major nucleolar protein, nucleolin. We have previously shown that nucleolin possess a histone chaperone activity and that it may regulate the activity of some chromatin remodelling factors. Using biochemical and genetic approaches (knock out of nucleolin gene in DT40 cells, siRNAs) we are studying the molecular mechanisms that involve nucleolin in the regulation of chromatin dynamics, cell cycle regulation and in the transcription of ribosomal genes.

Selected publications:

►MONGELARD F., BOUVET P. Nucleolin: a multifaceted protein. Trends in Cell Biology, 2007, 17,80-6.

►UGRINOVA I., MONIER K., IVALDI C., THIRY M., STORCK S., MONGELARD F., BOUVET P. Inactivation of nucleolin led to nucleolar disruption, cell cycle arrest and defects in centrosome duplication. BMC Mol Biol. 2007, 8: 66.

►CALLÉ A., UGRINOVA I., EPSTEIN A.L., BOUVET P., DIAZ JJ, GRECO A. Nucleolin is required for an efficient herpes simplex virus type 1 infection. J. Virol., 2008, 82: 4762-4773.



Our team is interested is interested in understanding the function of chromatin structure and dynamics in the regulation of ribosome biogenesis. We study in particular, Nucleolin, which is present in several cellular compartments. In pink is represented the nucleus and in orange the nucleolar compartment. The red dots indicate the different nucleolin localizations. Association of nucleolin with nucleolar chromatin (rDNA) (N1) could be involved in the regulation of chromatin structure and RNA polymerase I transcription. (N2) Nucleolin on nascent pre-rRNA transcript participate to pre-rRNA folding. (N3) Maturation at the first processing site, and pre-rRNA assembly with ribosomal proteins (N4). (N5) Shuttling of nucleolin between the nucleus and the cytoplasm. (N6) Association of Nucleolin with genes transcribed by RNAP II and with messenger RNAs (N7), with functions going from the regulation of translation to mRNA stability (N8). (N9) Nucleolin on the cell membrane with potential roles in cell migration and adhesion and virus infection.
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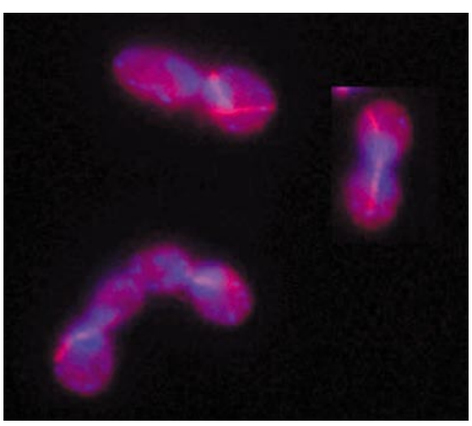
►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

►Telomeres: cell cycle checkpoints◄

► **Team leader** ► ***Michel Charbonneau*** *- michel.charbonneau@ens-lyon.fr* ◄
► **Team members** ► *Michel Charbonneau, research director second class; Nathalie Grandin, research associate first class.* ◄

► **Cells respond to DNA or mitotic spindle damage by activating specific pathways,** know as mitotic checkpoints, which halt the cell cycle to allow for possible repair. We are currently studying the molecular mechanisms at the origin of the control of the cell cycle in eukaryotes, and their deregulation in damaged cells using the yeast Saccharomyces cerevisiae as a model system. This genetic system allows for a thorough analysis of protein-protein interactions and protein modifications (for instance, by phosphorylation) that are important for impinging on cell cycle progression. These studies have profound implications in cancer research, as the checkpoint proteins have been very well conserved during evolution and most tumor cells exhibit mutations in checkpoint proteins.
In separate projects, we study — also in yeast — the protection mechanisms of the telomeres (the extremities of the linear chromosomes made of repeated DNA sequences surrounded by telomeric proteins) against degradation by nucleolytic attack. We also study how telomerase, the reverse transcriptase specialized in telomere replication, is recruited at the telomeres to maintain them at a constant size, a process needed to prevent chromosome degradation and ensure genome stability. We are also implicated in studying the so-called ALT (Alternative Lengthening of Telomeres) pathway, in which homologous recombination maintains telomere integrity in the absence of telomerase, a process that is responsible for the emergence of tumor cells in a subset of cancers.



Chromosomal DNA and mitotic spindle in checkpoint-arrested telomerase-deficient yeast mutant cells ►

Selected publications:

►Grandin, N. et Charbonneau, M. (2007). Control of the yeast telomeric senescence survival pathways of recombination by the Mec1 and Mec3 DNA damage sensors and RPA. Nucl. Acids Res. 35, 822-838.
►Grandin, N. et Charbonneau, M. (2007). Mrc1, a non-essential DNA replication protein, is required for telomere end protection following loss of capping by Cdc13, Yku or telomerase. Mol. Genet. Genomics 277, 685-699.
►Grandin, N. et Charbonneau, M. (2008). Protection against chromosome degradation at the telomeres. Biochimie 90, 41-59.

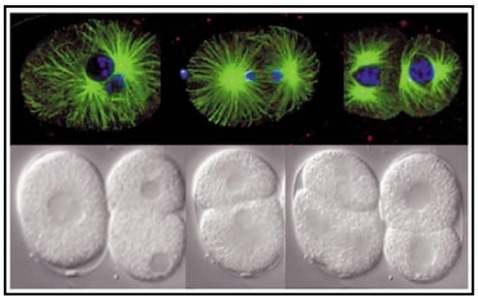
►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

►Plasticity and Evolution of cell division◄

► **Team leader** ► ***Marie Delattre,*** *Research Associate Second Class - marie.delattre@ens-lyon.fr* ◄
► **Team members** ► *Selena Bodennec, postdoctoral fellow CNRS.* ◄

► **Most biological systems remain stable while facing environmental variations, intrinsic noise and genetic modifications.** This capacity to buffer perturbations, or robustness, is thought to help the diversification of biological processes. Although these modifications remain cryptic or silent, they constitute a pool of potential variations and reflect the diversity of life. Despite this fundamental property of biological systems, robustness is understudied and cryptic evolution largely under-estimated. What is the extent of diversification? What are the constraints imposed on a given mechanism? How many perturbations can one system handle?

Our goal is to unravel these questions at the cellular level, by studying a simple and well-described system: the first asymmetric division of the Caenorhabditis elegans embryo. We aim to reveal the plasticity of mechanisms and the diversity of equivalent solutions underlying this cell division by submitting cells to various perturbations, and by comparing different species and strains. We chose the C. elegans' one-cell stage embryo because it is a powerful genetic and molecular model to decipher fundamental biological questions, transposable to metazoans. Secondly, a range of established molecular tools will allow us to rapidly identify mechanistic and quantitative variations between strains and environments. Lastly, several nematode species, displaying the same experimental advantages as C. elegans, are also currently available for our use.



◄*One and two cell stages nematode embryos in Nomarski optics or fluorescent microscopy.*

Our work will allow us to establish rules on constraints and plasticity imposed on cellular processes in metazoans in general. We hope this project will also help us understand how cells lose their robustness to perturbations in certain conditions, such as cancer.

Selected publications:

►Delattre, M., Canard, C., and Gonczy, P. (2006). Sequential protein recruitment in C. elegans centriole formation. Curr Biol 16, 1844-1849.
►Delattre, M., and Felix, M.A. (2009). The evolutionary context of robust and redundant cell biological mechanisms. Bioessays 31, 537-545.

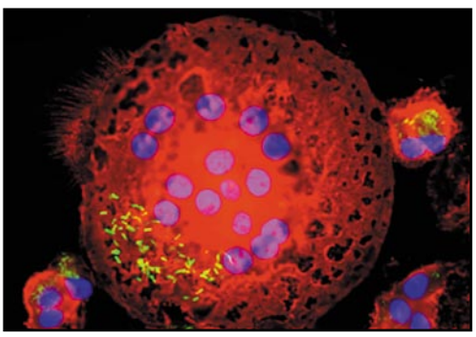
►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

►Dendritic Cells & Immune Plasticity◄

► **Team leader** ► ***Christine Delprat,*** *Full Professor, PhD, HDR Lyon 1 university - christine.delprat@ens-lyon.fr* ◄
► **Team members** ► *Alexandre Belot, MD, PhD student; Nathalie Bissay, technician; Bachar Ismail, PhD student; Carine Maisse, postdoctoral fellow; Selma Olsson, MD, PhD Student (Co-tutorship Karolinska Institutet, Stockholm, Sweden).* ◄
www.ens-lyon.fr/LBMC

► **Our general research focus is molecular and cellular immunology and related diseases** studying mechanisms regulating acquisition, hypersensitivity or impairment of immune functions and their consequences on cancer development and host integrity of humans and mice.

We investigate the role of interleukin-17A in myeloid cell survival, fusion and differentiation into aggressive tissue-destructive giant cells in the immune system as well as novel therapeutic agents able to regulate granuloma formation with giant cells. We perform cell biology and molecular studies of immune cells from healthy donors, but also from patients developing chronic inflammatory disease such as rheumatoid arthritis, granulomatous cancer such as Hodgkin's Disease, or a rare but aggressive disease of unknown etiology, called Langerhans Cell Histiocytosis.



Dendritic cell-derived multinucleated giant cell infected by recombinant Mycobacterium-GFP (green) showing high HLA-DR expression (red) and 15 hoescht-stained nuclei (blue). ►

Another aspect of our work concerns host-pathogen interactions between myeloid giant cells and Mycobacteria. To increase our knowledge on Mycobacterium pathogenicity, we compare the outcome of Mycobacterium various strains such as avium, bovis/BCG and tuberculosis facing to immune cells in different microenvironments. Characterization of cancer cell control mechanisms following BCG-therapy of bladder cancer will hopefully not only give us dynamic information on anti-Mycobacterium immune response in humans, but also open new avenue on long-term and chronic cancer cell control by the immune system.

Our team welcomes people fond of fruitful interactions between fundamental immunology and medicine, in order to increase basic scientific knowledge where we need to invent new therapeutic tracks.

Selected publications:

►Coury F., Annels N., Rivollier A., Olsson S., Santoro A., Speziani C., Azocar O., Flacher M., Djebali S., Brytting M., Egeler R.M., *Rabourdin-Combe C., *Henter J. I.*Arico M. & Delprat C. *equally contribution. Langerhans cell histiocytosis reveals a new IL-17A-dependent pathway of dendritic cell fusion. Nat Med, 2008. Jan;14(1):81-87.

►Speziani C., Rivollier A., Coury F., Mazzorana M., Azocar O., Flacher M., Tebib J., Jurdic P., Rabourdin-Combe C. & Delprat C. Murine dendritic cell transdifferentiation into osteoclasts is differentially regulated by innate and adaptive cytokines. Eur J Immunol, 2007. Mar;37(3):747-57.

►Rivollier A., Perrin-Cocon L., Luche S., Diemer D., Strub J.M., Hanau D., van Dorsselaer A., Lotteau V., Rabourdin-Combe C., Rabilloud T.& Servet-Delprat C. High expression of antioxidant proteins in dendritic cells : possible implications in atherosclerosis Mol. Cell. Proteomics 2006 Apr;5(4):726-36.

►*Rivollier A, *Mazzorana M, Tebib J, Piperno M, Aitsiselmi T, Rabourdin-Combe C, Jurdic P and Servet-Delprat C. Dendritic. Cell transdifferentiation into osteoclasts: a novel pathway sustained by the rheumatoid arthritis microenvironment. Blood. 2004. 104(13) : 4029-4037. These authors contributed equally to the work.

►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

► Telomeric and Epigenetic regulation◄

► **Team leader** ► **Eric Gilson** - *Eric.Gilson@ens-lyon.fr* ◄

► **Team members** ► *Eric Gilson, hospital and university professor, UCBL HCL; Pauline Abdallah, PhD student; Adeline Augereau, PhD student; Amadou Bah, PhD student; Serge Bauwens, research engineer, CNRS; Manon Bonneton, PhD student; Amina Boussouar, PhD student; Marie-Josèphe Giraud-Panis, research associate first class, CNRS; Renée Grataroli-Meunier, research associate first class, INSERM; Mélanie Koelblen, PhD student; Catherine Koering, research engineer, CNRS; Claire Leger-Falandry, HCL researcher; Frédérique Magdinier, research associate first class, INSERM; Sabrina Pisano, postdoctoral fellow; Anais Poulet, PhD student; Adélaïde Saint-Leger, PhD student, Erica Salvati, postdoctoral fellow; Caroline Schluth-Bolard, PhD student; Teresa Teixeira, research associate first class, CNRS; Jing Ye, PhD student.* ◄

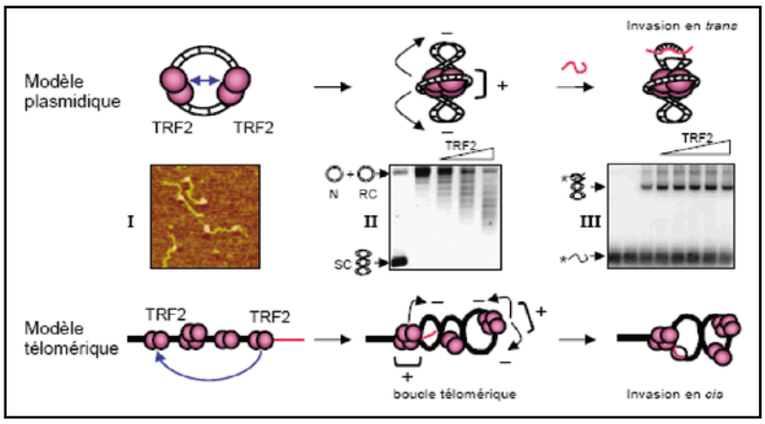
http://www.enslyon.fr/LBMC/web/nav/listeArt.php?id=52&rub=11&rub2=15

► **Telomeres have often been considered as DNA repeats of a certain length depending on the presence of a particular reverse transcriptase, the telomerase.**

In the past, the work of the team contributed to broadening this view by identifying the structure and function of various telomeric chromatin factors in yeast and human cells. The major objective of our recent research was to provide further mechanisms and molecular tools that describe telomeres as integrated and dynamic structures, both for basic research and medical applications.

In brief, our recent advances in this field concern the following topics.

- Mechanisms of telomere length homeostasis
- Mechanisms of yeast senescence
- Mechanisms by which TRF2 remodels the conformation of telomeric DNA : t-loop and Holliday junction.
- Identification and characterization of Apollo, a 5'-exonuclease interacting with TRF2 and protecting telomere from DNA repair.
- Telomeric heterochromatin, subtelomeric insulation and facio-scapulo-humeral dystrophy (FSHD).
- Telomere and cancer



◄*An unexpected twist at the end : right-handed wrapping of DNA around TRF2 favors strand invasion*

►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

►Genetic Expression Control and Viral Oncogenesis◄

► **Team leader** ► ***Pierre Jalinot,*** *Research Director, Second Class - pjalinot@ens-lyon.fr* ◄
► **Team members** ► *Gilbert Brun, professor; Vincent Mocquet, postdoctoral fellow; Christelle Morris, research associate, first class; Julia Neusiedler, PhD student; Jean-Philippe Robin, engineer; Armelle Roisin, engineer.* ◄ *www.ens-lyon.fr/LBMC*

► **In the early 1980s, the first retrovirus infecting humans was discovered in cells of a patient suffering from adult T-cell leukemia.** The discovery of the Human Adult T-cell Leukemia Virus type 1 (HTLV-1) was followed a few years later by the discovery of the Human Immunodeficiency Virus type 1 (HIV-1). These viruses express regulatory proteins that enhance proviral transcription or favour the movement of incompletely spliced viral RNAs towards the cytoplasm. These viral factors are also able to profoundly perturb key cellular regulatory pathways.

By performing a two hybrid screen we have identified several new cellular targets of the HTLV-1 Tax protein, of which transforming activity is well-established. In particular we have shown that Tax interacts with the INT6 protein that is involved in mice models for mammary tumour development. The INT6 protein is required in human cells for genome stability and for correct mitotis completion. In addition we have recently shown that INT6 is also important in the degradation of specific cellular RNAs. Intriguingly, INT6 is present is various protein complexes, including the eIF3 translation initiation factor, the COP9 signalosome and the 26S proteasome. Our team is engaged in various studies to understand how INT6 intervenes in the control of genome stability and how altering INT6 participates in cellular transformation.

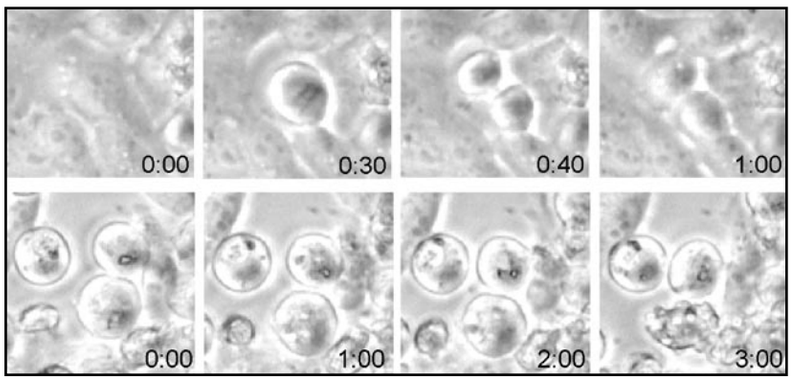
With a more applied approach, our team also works on technological means to block the activity of specific intracellular viral or cellular proteins by association with small hybrid proteins named SHP (patent FR04/02479) or by inducing their degradation.

Selected publications :

►Buchsbaum, S., Morris, C., Bochard, V., and Jalinot, P. Human INT6 interacts with MCM7 and regulates its stability during S phase of the cell cycle. Oncogene. (2007) 35: 5132-44.

►Morris C, Wittmann J, Jäck H-M, Jalinot P. Human INT6/eIF3e is required for nonsense-mediated mRNA decay. EMBO Rep. (2007) 6: 596-602.

►Terme, J. M., Wencker, M., Favre-Bonvin, A., Bex, F., Gazzolo, L., Duc Dodon, M., and Jalinot, P. (2008). Cross talk between expression of the human T-cell leukemia virus type 1 Tax transactivator and the oncogenic bHLH transcription factor TAL1. J Virol 82, 7913-7922.



This figure shows the requirement of INT6 for mitosis. The top panels correspond to a mitosis in normal HeLa cells followed by time-lapse microscopy. The numbers on the right indicate times (h : min). The bottom panels show what is observed in HeLa cells, where the INT6 protein has been suppressed by RNA interference. The duration of mitosis is increased and mitotic catastrophe is observed. ►

►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

►Apoptosis and neurogenetics◄

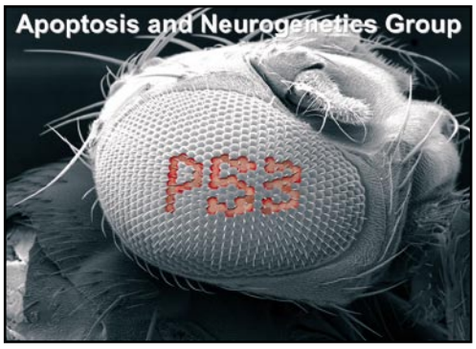
► **Team leader** ► **Bertrand Mollereau,** *professor - bertrand.mollereau@ens-lyon.fr* ◄
► **Team members** ► *Gilles Chatelain, engineer; Marie-Laure Dichtel-Danjoy, postdoctoral researcher; Pierre Dourlen, postdoctoral researcher; Antone Fouillet, post-doctoral researcher; Clémence Levet, PhD student, Bertrand Mollereau, Professor; Stéphane Vincent, Assistant Professor ENS.* ◄
www.ens-lyon.fr/LBMC/ApoDroso

► Mechanisms of cell death in Drosophila

Apoptosis is a form of physiological cell death that is essential for normal development and homeostasis. Apoptosis needs to be tightly regulated, and its deregulation may lead to cancer (lack of apoptosis) or degeneration (excess of apoptosis). Models to study apoptosis in Drosophila are diverse due to the powerful genetic tools in Drosophila and the numerous roles played by apoptosis in its development. Apoptosis in Drosophila not only controls cell proliferation, elimination of damaged or developmentally confused cells but also organ size and the architecture of the tissues (Mollereau, B. in press).

To study the mechanisms controlling cell death in a terminally differentiated neuron, we have established a neurodegenerative model in differentiated Drosophila photoreceptor cells. Using dominant modifier and recessive screens, we have isolated several candidate genes, in which mutations enhance or suppress cell death. Among those genes, we have characterized the role of cytochrome-c-d in the regulation of apoptosis in the retina (Mendes et al. 2006). Our results argue in favor of a role of cytochrome-c-d in the execution of apoptosis and feed the debate on the importance of the mitochondria in Drosophila apoptosis.

We also found mutations that are associated with the accumulation of unfolded/misfolded proteins in the endoplasmic reticulum (ER). In response to ER stress, the cells activate an unfolded protein response (UPR) to cope with the accumulation of unfolded/misfolded proteins in the ER. Severe ER stress can lead to apoptosis and is associated with degenerative pathologies. However, the ER-based mechanisms that regulate the molecular switch between death and survival are poorly understood.



◄ *The Drosophila eye as a model for neurodegenerative diseases. A Drosophila eye is visualized under scanning electron microscopy. The expression of Drosophila homolog of P53 induces neuron degeneration.*

We found that a moderate ER stress protects photoreceptor neurons from various apoptotic stimuli in the Drosophila adult retina. We show that a specific ER-mediated signal acts negatively on caspase-dependent cell death and promotes anti-oxidant defenses. We propose that ER-mediated survival is responsible for the late onset of neurodegenerative diseases. We are pursuing the characterization of the genes isolated in the screens with a particular focus on the roles of ER stress and autophagy on apoptosis.

Publications

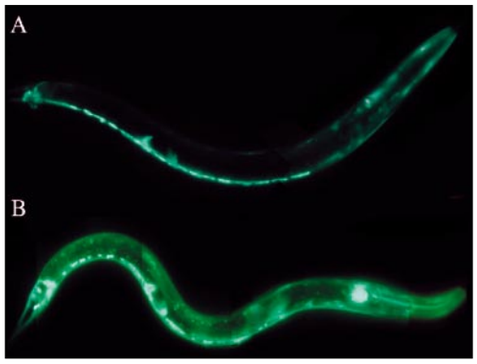
►Mollereau, B. and Domingos, P. (2005) Photoreceptor differentiation†: From immature neurons to functional photoreceptors. Developmental Dynamics. 232, 585-92.
►Mendes, C., Arama, E., Brown, S., Bergmann, A., Scherr, H., Srivastava, M., Steller, H. and Mollereau B. (2006). Cytochrome-c-d regulates developmental-induced apoptosis in Drosophila retina. Embo Reports 7 : 933-39
►Mendes C., Levet, C., Chatelain, G. , Dourlen, P., Gambis, A., Ryoo, H.D., Steller, H. and Mollereau, B. (2009). ER stress protects from neurodegeneration in Drosophila. Embo Journal 28, 1296-1307.
►Mollereau, B. (In press). Cell death: what can we learn from flies? Apoptosis.

►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

►Epigenetic regulation in development◄

► **Team leader** ► ***Francesca Palladino,*** *research director - Francesca.palladino@ens-lyon.fr* ◄
► **Team members** ► *Cécile Bedet, Postdoctoral fellow; Sonia Schott, technician; Yu Xue, Postdoctoral fellow.* ◄ *www.ens-lyon.fr/LBMC/web/nav*

► **The heritability of epigenetic profiles insures the maintenance of developmental and differentiation programs,** and alterations in these profiles can result in profound and diverse effects on normal development. However, how chromatin states are assembled and propagated during development is not well understood. We are using the nematode C. elegans to address this question. HP1 proteins are important players in the epigenetic regulation of gene expression, and we have shown that the C. elegans HP1 homologue HPL-2 acts in vulval development with other chromatin factors to prevent ectopic growth factor signaling. Using microarray analysis we have identified additional HPL-2 target genes: among these we find cell cycle regulators, components of the extracellular matrix, and interestingly, genes involved in stress response. Genetic analysis suggests that hpl-2 may in fact play a role in stress response and longevity. We are using chromatin immunoprecipitation (ChIP) analysis to identify direct targets and to dissect the molecular mechanism of HPL-2 recruitment and function. This analysis is complemented by "ChIP on chip" data in collaboration with the NIH funded modENCODE genomic project. Epigenetic regulation involves the coordinated activity of different factors, and we have shown that HPL-2 and the SET-2 H3K4 histone methyltransferase play antagonistic roles in post-embryonic development. We are now using a combination of genetic, molecular and biochemical approaches to understand the molecular basis of this antagonism. The genetic interactions and the developmental functions identified for these proteins in C. elegans will contribute to a better understanding of epigenetic networks in mammals.



HPL-2 regulates lag-2 expression. lag-2 encodes a ligand of LIN-12/Notch. A lag-2::GFP reporter shows strong ectopic expression in hpl-2 mutant worms (B) compared to WT (A). ►

Publications

►Simonet T., Dulermo R., Schott S., Ramos F., and Palladino F. Antagonistic functions of SET-2/SET1 and HPL/HP1 proteins in C. elegans development Dev Biol. 2007 Dec 1;312(1):367-83.
►Schott S., Ramos F., Coustham V and Palladino F. HPL-2/HP1 prevents inappropriate vulval induction in C. elegans by acting in both HYP7 and Vulval Precursor Cells. Genetics 2009 Feb;181(2):797-801
►Masse I., Molin L., Mouchiroud L., Vanhems P.,Palladino F., Billaud M. and Solari F. 2008 A Novel Role for the SMG-1 Kinase in Lifespan and Oxidative Stress Resistance in Caenorhabditis elegans. PLoS ONE. 2008 Oct 6;3(10):e3354.

►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

►Differentiation & Cell Cycle◄

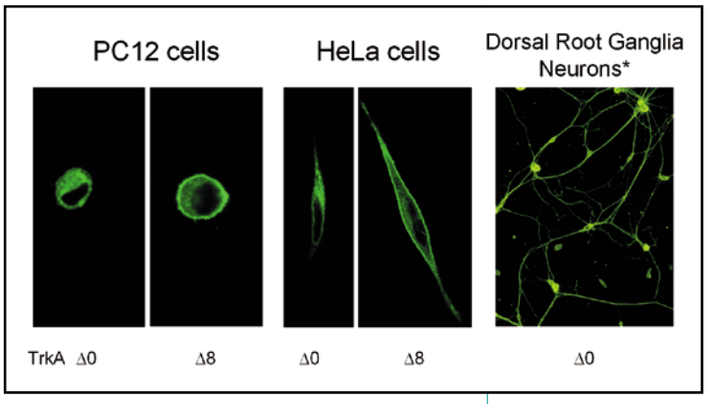
► **Team leader** ► ***Brian B. Rudkin,*** *research director, CNRS - bbrudkin@ens-lyon.fr* ◄
► **Team members** ► *Véronique Baumle, PhD Student; David Cluet PhD Engineer; Silvia Dibenedetto, PhD Student (Co-supervision University Modena, Italy); Yin Di Ding, PhD Student, (Co-supervision East China Normal University (ECNU), Shanghai, China); Emeline Drouin, Engineer; Ambre Spencer, PhD Student (Co-supervision ECNU, Shanghai, China); Yan Zhang, PhD Student (Co-supervision ECNU, Shanghai, China); Martin Spichty, research associate, CNRS; Lingli Yu, PhD student (Co-supervision ECNU, Shangai, China).* ◄

► **Our general research focus is molecular and cellular neurobiology**, as well as related cancers. We study signaling pathways that regulate proliferation, differentiation and apoptosis. Several model cellular and animal systems (*e.g.* Drosophila, Mouse) are implemented.

Signaling via neurotrophic factor receptors can stimulate different cellular processes depending on cell type and context. Our group constructed and characterized TrkA-EGFP chimera and observed the intracellular traffic in quasi real-time. We implemented Proteomics approaches to identify partners of TrkA in cancer and neuronal cell types. By investigating the chronolocalization of the ligand receptor complex and associated proteins, we aim to highlight similarities and differences in signaling between cancer and neuronal cells.

Another aspect of our work concerns small combinatorial protein tools called «peptide aptamers», which we use to study and perturb signaling pathways. Peptide aptamers act as mini-antibodies. They bind to specific sites on the target and selectively modulate certain functions. They consist of a protein scaffold (Thioredexin) into which a variable sequence of fixed length (*e.g.* 20 aa) is introduced in phase. The peptide aptamers are selected either against a specific target using two hybrid technology in Yeast or *via* functional selection in various cell types from bacteria to mammalian cells.

Our team performed functional selections and identified active aptamers that slow cell proliferation or prevent Bax-induced cell death. The targets of the peptide aptamers were identified by yeast two hybrid. This offers potential means to regulate these cellular processes with implications for cancer and neurodegeneration. We have also begun studies *in vivo*, which have so far yielded promising results.



Expression of NGF receptor TrkA-EGFP Chimera
Expression plasmids for full length (ΔO) or truncated (Δ8) TrkA-EGFP were transfected into PC12 Cells, HeLa Cells or Dorsal Root Ganglia neurons (Only ΔO). Note the differential localisation of the truncated receptor vs full length. We are studying which motifs and partners are participating in the trafficking of the TrkA receptor as a function of cell cycle and signalling complex cytolocalisation.
**Collaboration with YUAN ChongGang East China Normal University, Shanghai, China.*

Publications

►Bardou, C., Borie, C., Bickle, M., Rudkin, B.B. and Colas, P. (2009). Peptide Aptamers for Small Molecule Drug Discovery. Meth Mol. Biol. 535:373-388

►Com, E., Lagadec, C., Page, A., El Yazidi-Belkoura, I., Slomianny, C., Spencer, A., Hammache, D., Rudkin, B. B. and Hubert Hondermarck. (2007). TrkA signaling in breast cancer cells involves the DNA-dependent protein kinase subunit Ku70 to prevent apoptosis. Mol Cell Proteomics 6:1842-1854 E-Pub 2007 July 7

►de Chassey, B., Mikaelian, I., Mathieu, A.-L., Bickle, M., Olivier, D., Nègre, D., Cosset, F.-L., Rudkin, B.B. and Colas, P. (2007). An antiproliferative genetic screening identifies a peptide aptamer that targets calcineurin and upregulates its activity. Mol Cell Proteomics 6:451-459, E-Pub 2006 Dec 4

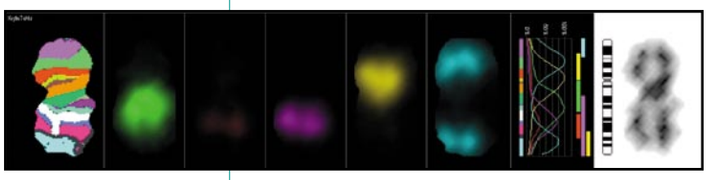
►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

► Indolent B-cell Proliferations◄

►**Team leader** ► ***Gilles Salles,*** *Professor - gilles.salles@chu-lyon.fr* ◄
► **Team members** ► *Lucile Baseggio, research associate; Françoise Berger, full professor; Evelyne Callet-Bauchu, associate professor; Régine Cattalo, engineer; Amel Chebel, engineer; Wei Wen Chien, PhD student; Bertrand Coiffier, full professor; Pascale Felman, research associate; Martine French, research associate; Hervé Ghesquières, PhD student; Sandrine Hayette, engineer; Tagrid Kaddar, PhD student; Jean-Pierre Magaud, full professor; Nicolas Rachinel, postdoctoral fellow; Gilles Salles, full professor; Alexandra Traverse-Glehen, associate professor; Aurélie Verney, technician.* ◄

► **Our team examines since several years the clinical, pathological and biological features of a subset of B-lymphocytes derived malignancies** that includes several lymphoma subtypes (lymphocytic, marginal zone, follicular and mantle cell lymphomas) and chronic lymphocytic leukaemia (CLL). Our work is supported by strong and active interactions between the clinico-pathological and the biological expertises. We have characterized several features of these malignancies at the morphological, immunological, cytogenetic and molecular levels. Further recent developments of our research include (1) the relationship between normal and malignant B-cell differentiation in those models; (2) the role cellular senescence and cell death in these malignancies, with the exploration of p16INK and telomerase pathways. New approaches will be developed such as high density array CGH and SNPs arrays, as the well as the identification and functional characterization of microRNA whose expression is deregulated in these tumors.

Cytogenetic banding of chromosome 7 in splenic marginal zone lymphoma ▼



Publications

►Chebel A, Bauwens S, Gerland LM, Belleville A, Urbanowicz I, de Climens AR, Tourneur Y, Chien WW, Catallo R, Salles G, Gilson E, Ffrench M. Telomere uncapping during in vitro T-lymphocyte senescence. Aging Cell. 2008 Dec 11. [Epub ahead of print]

►Poncet D, Belleville A, t'kint de Roodenbeke C, Roborel de Climens A, Ben Simon E, Merle-Beral H, Callet-Bauchu E, Salles G, Sabatier L, Delic J, Gilson E. Changes in the expression of telomere maintenance genes suggest global telomere dysfunction in B-chronic lymphocytic leukemia. Blood. 2008 Feb 15;111(4):2388-91.

►Traverse-Glehen A, Baseggio L, Bauchu EC, Morel D, Gazzo S, Ffrench M, Verney A, Rolland D, Thieblemont C, Magaud JP, Salles G, Coiffier B, Berger F, Felman P. Splenic red pulp lymphoma with numerous basophilic villous lymphocytes: a distinct clinicopathologic and molecular entity? Blood. 2008 Feb 15;111(4):2253-60.

►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

►LBMC - Team Laurent Schaeffer ◄

► **Team leader** ► ***Laurent Schaeffer,*** *Research director, CNRS* ◄

► **Team members** ► *Dominique Baas, associate professor, UCBL; Pierre Copin, PhD student; Emilie Delaune-Henry, postdoctoral fellow; Alice Fornari, PhD student; Yann-Gaël Gangloff, research associate second class, CNRS; Evelyne Goillot, research associate first class, CNRS; Alexandre Guiraud, PhD student; Vincent Moncollin, research associate first class, INSERM; Veronique Morel, research associate second class, CNRS; Marielle Pasdeloup, engineer; Valérie Risson, research engineer, CNRS; Jean-Luc Thomas, research engineer, INRA; Aurelia Vernay, EPHE student; Alessio Zanardi, postdoctoral fellow; Michele Zoli, visiting professor.* ◄

► **Innervated skeletal muscle constitutes a model system of communication between two distinct cellular partners.** Our team has elucidated general mechanisms through the study of the neuromuscular synapse—an ideal tool for studying the mechanisms by which a presynaptic neuron controls the differentiation and function of a post-synaptic cell.

RESEARCH THEMES

Epigenetic regulation of synaptic gene expression by motor innervation:

The different post translational modifications of the histone N-terminal tails constitute an epigenetic code that can be selectively recognized by transcription factors. This process highlights answers at the transcription level.

We study the histone code in the neuromuscular and central nervous system and identify the chromatin modifying factors which control:

- The activation of synaptic gene expression by neural factors.
- The repression of synaptic gene expression in extra synaptic regions of muscle fibre by electrical activity caused by motor innervation.
- Plasticity in the central nervous system

The PI3K pathway in skeletal muscle:

We study the role of CKIP-1 (Casein Kinase Interacting Protein 1) in the response to promyogenic stimuli at the neuromuscular junction. CKIP-1 is controlled by the PI3 kinase pathway. We study the role of CKIP-1 during development, both in transgenic mice and zebra fish models.

Role of mTOR in muscle differenciation and plasticity

The serine/threonine kinase mTOR is a molecular integrator of different intra and extra cellular signals that performs numerous functions. We have generated a conditional knock-out of mTOR in the skeletal muscle of mice. These animals develop a severe muscle dystrophy, thus providing a unique tool to address mTOR functions in vivo.

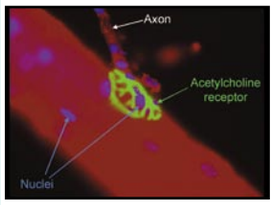
Regulation of skeletal muscle atrophy

We have identified HDAC6 as a key player in skeletal muscle atrophy. This protein is a new therapeutic target to limit atrophy.

Congenital myasthenic syndromes (CMS)

CMS are diseases of the neurotransmission at the neuromuscular junction. We characterise mutations in new genes causing CMS, and study the pathophysiological mechanism using mouse models.

The neuromuscular synapse visualized by staining of the acetylcholine receptor with a-bungarotoxin (in green).



Publications

►Ravel Chapuis A., Vandromme M., Thomas JL. and Schaeffer L. (2007) Post synaptic chromatin is under neural control at the neuromuscular junction. /EMBO J./ 21;26(4):1117-28.

►Dupuis L., Gonzales de Agular JL., Echaniz-laguna A., Eschbach J., Rene F., Oudart H., Halter B., Huze C., Schaeffer L., Bouillaud F. and Loeffler JP. (2009). Muscle mitochondrial uncoupling dismantles neuromuscular junction and triggers distal degeneration of motor neurons. /PLOS One/ 2009;4(4):e5390.

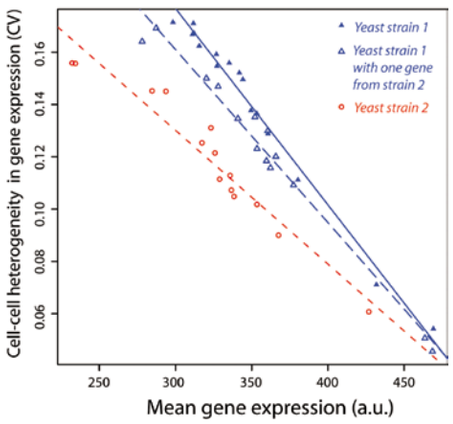
►Huzé C, Bauché S, Richard P, Chevessier F, Goillot E, Gaudon K, Ben Ammar A, Chaboud A, Grosjean I, Lecuyer HA, Bernard V, Rouche A, Alexandri N, Kuntzer T, Fardeau M, Fournier E, Brancaccio A, Rüegg MA, Koenig J, Eymard B, Schaeffer L, Hantaï D. (2009) Identification of an agrin mutation that causes congenital myasthenia and affects synapse function. /Am J Hum Genet./ Aug;85(2):155-67.

►MOLECULAR BIOLOGY OF THE CELL LABORATORY◄

►Genetics of Intra-Species Variations◄

► **Team leader** ► ***Gaël Yvert,*** *Research Associate First Class - gael.yvert@ens-lyon.fr* ◄
► **Team members** ► *Hélène Bottin, Technician; Steffen Fehrmann, PhD Student; Jean-Baptiste Veyrieras, Visiting Scientist* ◄ ***http://www.ens-lyon.fr/LBMC/gisv***

► **Despite the exciting burst that genetics have experienced for the past decades,** very little is known about the genetic architecture of common traits. This frustration is due to the complexity by which genotypic variation drives phenotypic diversity. Created in April 2005, our group mines into this complexity by studying molecular and cellular traits in a single-cell microorganism commonly used in laboratories : the baker's yeast Saccharomyces cerevisiae. This system offers numerous advantages : a very well annotated genome, a high recombination rate, easy manipulation of genes in their chromosomal context, and access to a large variety of strains from distant origins (from bread making to wine fermentations all over the world). In addition, the DNA microarray technology now offers the possibility to monitor thousands of molecular traits and to easily build dense genetic maps of natural allelic variations.



Genetic variation in gene expression stochasticity. Each dot represents a population of 15,000 isogenic yeast cells from genetic background 1 (filled blue triangles) or 2 (open red circles) expressing a fluorescent protein. Mean gene expression of the population is reported on the horizontal axis, while the vertical axis reports the coefficient of variation across the population which reflects cell-to-cell heterogeneity. This heterogeneity is higher in background 1 than in background 2, and this difference is reduced when "repairing" a particular gene of strain 1 (open blue triangles). ►

Using crosses between divergent strains, we are able to dissect the control of cellular morphology, epigenetic regulations or fermentation capacities of industrial strains. We also found natural genetic variation in the level of stochasticity of gene expression : when the expression of a single gene is quantitated in individual cells, the cell-to-cell variability can differ from one genetic background to another (see figure). Applying quantitative genetics to a cross between such strains can reveal the regulators of this heterogeneity. Notably we found that efficiency of transcriptional elongation is a key factor contributing to stochasticity.

Publications

►ANSEL J, BOTTIN H, RODRIGUEZ-BELTRAN C, DAMON C, NAGARAJAN M, FEHRMANN S, FRANCOIS J AND YVERT G. Cell-to-cell stochastic variation in gene expression is a complex genetic trait. PLoS Genetics, 2008, 4(4): e1000049.

►NOGAMI S, OHYA Y AND YVERT G. Genetic Complexity and Quantitative Trait Loci Mapping of Yeast Morphological Traits. PLoS Genetics, 2007, 3(2):e31.

►MARULLO P, AIGLE M, BELY M, MASNEUF-POMAREDE I, DURRENS P, DUBOURDIEU D AND YVERT G. Single QTL Mapping and Nucleotide Level Resolution of a Physiological Trait in Wine Saccharomyces cerevisiae Strains. FEMS Yeast Research, 2007, 7(6) :941-952.

►CHEMISTRY LABORATORY◄

► **Director** ► *Philippe Sautet, Research Director - Philippe.Sautet@ens-lyon.fr* ◄
► **Total personnel** ► *90* ◄
► **Partners** ◄ *CNRS* ◄
► **Web** ◄ *http://www.ens-lyon.fr/CHIMIE/* ◄

► The chemistry laboratory has a range of specialties in organic, inorganic and physical chemistry and develops research projects at the frontiers with biology, material sciences and physics. The research themes hence cover a large spectrum of expertise in chemistry, joining organic and inorganic syntheses together with a specific highlight on characterization and modeling.
The scientific projects of the laboratory are centered on three themes. The first one concerns the synthesis by organic or coordination chemistry approaches of new and complex molecules with potential applications in life science. This theme, which has significantly developed in the last years in the laboratory, is in collaboration with groups in biochemistry and biology. One part deals with molecules for biological characterization and diagnostic with the design of "intelligent" contrast agents for Magnetic Resonance Imaging, the development of bio-probes for Xenon NMR, and of chromophores active in the infra-red range where biological systems are transparent. In addition, a transdisciplinary project, combining organic synthesis, numerical simulations and biochemical assays, aims at constructing molecules which would inhibit the aspartic protease, a key process in the replication of the HIV virus.
The second theme concerns the design of molecules for innovative multi-functional materials. Molecules and nanoobjects for molecular recognition are synthesized, allowing the construction of materials by self assembling. Another aspect deals with molecules with optical or/and magnetic properties, with new chromophores and spin transition complexes. Optical limitation in the infra-red range, and optical commutation are among the specific targets for the applications. Finally porous solids are created following an hybrid organic-inorganic route, with post-synthesis hydrophobation and controlled distribution of catalytically active sites.
The third research theme is centered on theoretical approaches and numerical simulations for complex chemical systems. In the last year, the strong expertise of the laboratory on the simulation of processes related to heterogeneous catalysis has been confirmed, with a special emphasis on the understanding of catalytic surfaces in realistic pressures of gas, of complex reaction networks at surfaces and of the properties of confined fluids in porous media. It has also allowed strengthening the calculation of magnetic properties of coordination complexes, from precise ab initio approaches and phenomenological models. Finally a new direction has emerged with the simulation of enzymatic sites, their reactivity with substrates and their deactivation by specific inhibitors.
The scientific results have appeared in more than 150 articles in major international journals for the period 2007-2008.

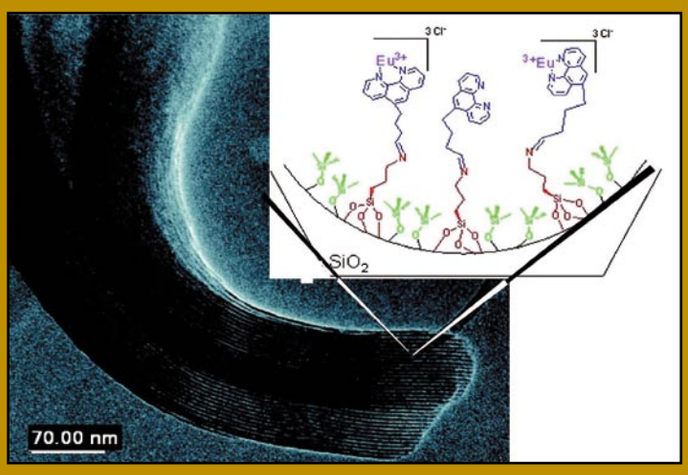
CURRENT RESEARCH TOPICS
Molecules for life science, Molecules for materials, theory and simulations

RELATED FIELDS
Contrast agents and biosensors, optoelectronic devices, porous materials, Quantum chemistry and statistical Physics

AREAS OF APPLICATION
Heterogeneous catalysis, Environment and energy, Medical Imaging, Telecommunications, Molecular electronics

INDUSTRIAL PARTNERS
IFP, TOTAL, CEA, Thales

EQUIPMENT
Liquid NMR, EPR, Magnetometer, Analytical (LCMS, HPLC), Spectroscopy (Fluorescence, IR, UV, DSC), Parallel computers



► *Functionnalization of the internal surface of mesostructured silica with europium complexes.*

►Chemistry For Optics (CFO)◄

► **Team leader** ► ***Chantal Andraud,*** *Research Director CNRS - Chantal.andraud@ens-lyon.fr* ◄
► **Team members** ► *Quentin Bellier, PhD student; Pierre-Antoine Bouit, PhD student; Adrien Bourdolle, PhD student; Yann Bretonnière, research associate, CNRS; Florence Darbourg, PhD student; Wissam Dayoub, postdoctoral fellow; Thibault Gallavardin, PhD student; Julien Massin, PhD student; Olivier Maury, research associate, CNRS.* ◄

► **This group engineers molecules for different applications related to optics and nonlinear optics.** Some applications include telecommunications (electro-optic modulation), biology (cell imaging, the measurement of membrane potential variations in neurones, sensing oxygen in living cells, phototherapy), and the protection of ocular and optical sensors through optical limiting.

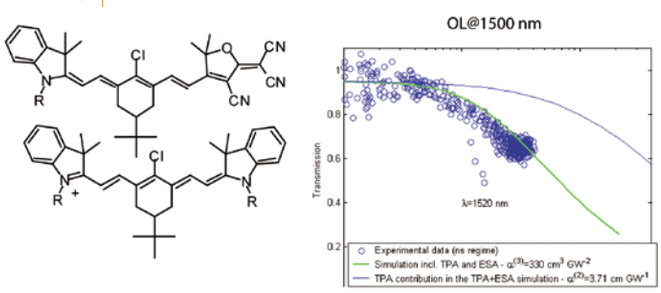
These applications use the second harmonic generation (SHG) and /or two-photon absorption (TPA) processes with specific constraints for molecules (absorption, solubility...) depending on the target field.

We design different families of molecules such as linear and dendritic oligomers, coordination complexes for transition metals or lanthanides, and finally, linear or octupolar conjugated push-pull molecules. In order to optimise molecules, we perform theoretical calculations to interpret and predict their properties.

In their final stages, these systems can be grafted on different solid supports such as sol-gel matrices, metallic or sol-gel nanoparticles.

This research field is at the interface of chemistry, physics and biology and requires close collaboration with partners all over France and the world.

Optical limiting properties at telecommunication wavelengths of heptamethine dyes. ▼



Selected publications:

►Near IR Nonlinear Absorbing Chromophores with Optical Limiting Properties at Telecommunication Wavelengths P.-A. Bouit, G. Wetzel, G. Berginc, B. Loiseaux, L. Toupet, P. Feneyrou, Y. Bretonnière, K. Kamada, O. Maury, C. Andraud Chem. Mat. 2007, 19, 5325-533.

►Long-Lived Two-Photon Excited Luminescence of Water Soluble Europium Complex: Applications in Biological Imaging using Two-Photon Scanning Microscopy A. Picot, A. D'Aléo, P. L. Baldeck, A. Grishine, A. Duperray, C. Andraud, O. Maury J. Am. Chem. Soc. 2008, 130, 1532-1533.

►Excitonicly Coupled Oligomers and Dendrimers for Two-Photon Absorption C. Andraud, R. Fortrie, C. Barsu, O. Stéphan, H. Chermette, P. L. Baldeck Adv. Polym. Sci. 2008, 214, 149-203.

►Two-photon absorption related properties of functionalized BODIPY dyes in the infrared range up to telecommunications wavelengths P.-A. Bouit, K. Kamada, P. Feneyrou, G. Berginc, L. Toupet, O. Maury, C. Andraud Adv. Mat. 2009, 21, 1151ñ1154.

►CHEMISTRY LABORATORY◄

►Hybrid Material◄

► **Team leader** ► ***Laurent Bonneviot,*** *Full Professor - laurent.bonneviot@ens-lyon.fr* ◄
► **Team members** ► *Belén Albela, associate professor; Feifei Gao, postdoctoral fellow ; Marion Giraud, assistant professor ; Hodna Kassab, PhD student; Wenjuan Zhou, PhD student.* ◄

► **Our group develops a bio-inspired approach for designing multifunctional heterogeneous catalyst adsorbents, membranes for more environmental friendly chemical processes.**

Gas or liquid phase molecules react on specific sites of the surface of solids in which both molecular diffusion and molecular structure controls are needed. To take into account both constrains, we develop novel synthetic methodologies to molecularly modify the internal surface of ordered nanoporous silicas. Hierarchical control of porosity (Bonneviot et al. J. Porous Solids 2007,), nano-filtration by membranes (Hamad et al, 2008) and confinement effect (Peyrard et al, Eu. J. Phys. D, 2005) are important points. Nonetheless, our main effort is devoted to the molecular surface engineering. Functionalization is obtained by reacting specific organosiloxanes with surface hydroxyl groups. We have investigated the distance between the latter functions (Collaboration with Pr. Yoshitake of Yokohama National University, Japan; Miyajima et al., J. Materials Chemistry, 2007). Nonetheless, the heart of our expertise resides in the "Molecular Stencil Patterning", a novel methodology invented by us to isolate a given function by another one using a step wise surface "pavement" technique. Quaternary ammonium ions are used as self-organizing mask on the surface during the grafting of a first function (hydrophobic). Then, the mask is removed and a second function is grafted. Accordingly, one may immobilized complexes Cu(II) or Eu(III) mimicking the environment of metal sites in enzymes (figure, Abry et al. 2009a et b). Such materials are active and selective at room temperature in oxidation reaction, working in water like enzymes and in addition, they can be recycled.

Specific tools

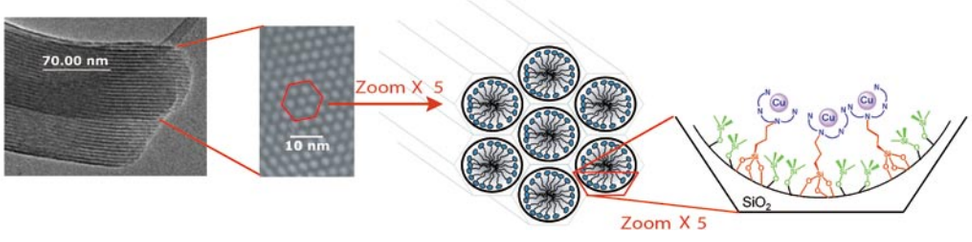
Solid state NMR, Electron Paramagnetic Resonance, X-ray Absorption Spectroscopy, Dynamic Light Scattering, autoclave reactors.

Selected publications:

►B. Hamad, A. Alshebani, M. Pera-Titus, S. Wang, M.Torres, B. Albela, L. Bonneviot S. Miachon, J.-A. Dalmon, «Synthesis and characterization of MCM-41 (LUS) nanocomposites », Microporous Mesoporous Mater., 115, 40-50, 2008.

►S. Abry, A. Thibaud, B. Albela, P. Delichere , F. Banse, L. Bonneviot, «Design of grafted copper complex in mesoporous silica in defined coordination, hydrophobic and confinement states», New J. Chem., 33, 484-496, 2009a.

►S. Abry, F. Lux, B. Albela, A. Artigas-Miquel , S. Nicolas, B. Jarry, P.Perriat,, G. Lemercier, L. Bonneviot, «Europium(III) complex probing distribution of functions grafted using molecular stencil patterning in 2D hexagonal mesostructured porous silica», Chem. Mater., 21, 2349-2359, 2009b..



►CHEMISTRY LABORATORY◄

►Electronic Phenomena in Inorganic Compounds◄

► **Team leader** ► ***Dr. Serguei A. Borshch*** - *borchtch@ens-lyon.fr* ◄
► **Team members** ► *Marie-Laure Bonnet, PhD student; Dr. Boris Le Guennic; Dr. Galina S. Matouzenko; Mikael Kepenekian, PhD student; Dr. Vincent Robert; Jean-Baptiste Rota, PhD student; Alexander Verat, postdoctoral fellow.* ◄ ***http://www.ens-lyon.fr/CHIMIE/Fr/Groupes/PECI/index.html***

► **Current research themes :**

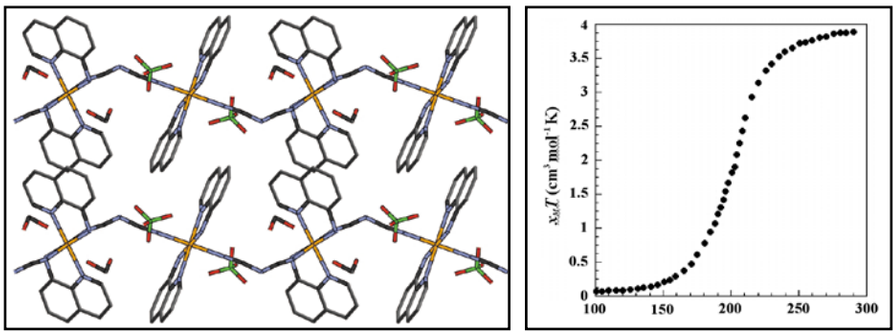
1. The synthesis and physico-chemical studies of new mononuclear, binuclear and polymeric compounds with spin crossover behavior: use in information storage and display devices. The analysis of cooperative interactions and photoinduced effects.
2. Quantum-chemical studies of molecular magnets based on ab intio, density functional and phenomenological methods. Quantitative and qualitative characterization of interactions between spin carriers and magnetostructural correlations.
3. Intermolecular electron transfer in mixed-valence clusters and complexes with valence tautomerism. The microscopic analysis of the multistability phenomena.

Selected publications:

►Le Guennic B., Borshch S. A., Robert V. Prussian Blue Analogue CsFe[Cr(CN)6] as a Matrix for the Fe(II) Spin Crossover Inorganic Chemistry, 2007, 46, 11106-11111.

►Genre C., Jeanneu E., Bousseksou A., Luneau D., Borshch S. A., Matouzenko G. S. First dicyanamide-bridged spin crossover coordination polymer: synthesis, structural, magnetic and spectroscopic studies Chemistry-A European Journal, 2008, 14, 697-705.

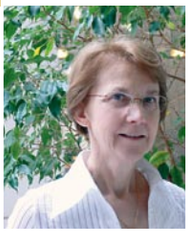
►Rota, J.B., Norel, L., Train, C., Ben Amor, N., Maynau, D., Robert, V. Inspection of the Duality of a Verdazyl-Based Radical in Transition Metal Complexes: A π* Donor Ligand and a Magnetic Partner Journal of the American Chemical Society 2008, 130, 10380-10385.



► *Structural and magnetic properties of the first dicyanamide-bridged spin crossover polymer.*

►CHEMISTRY LABORATORY◄

►Reactivity, catalysis and spectroscopy◄



► **Team leader** ► ***Françoise Delbecq,*** *researcher, CNRS - francoise.delbecq@ens-lyon.fr* ◄
► **Team members** ► *Marie-Laure Bocquet, Research Associate First Class; Paul Fleurat-Lessard, Associate Professor; Elise Dumont, Associate Professor; David Loffreda, Research Associate First Class; Françoise Delbecq, Research Associate First Class; Philippe Sautet, Research Director; François Lux, Graduate Teaching Assistant; Carine Michel, Graduate Teaching Assistant; Asma Aloui; Florian Auneau; Rodrigo Ferreira; Slimane Laref; Bin Wang; Raphaël Wischert; Nicolas Chéron, PhD students; Fabrizio Cinquini; Bradley Dickson, Postdoctoral fellows; Xavier Rozanska, Associate researcher.* ◄

www.ens-lyon.fr/CHIMIE/Fr/Groupes/RCS/RCS_home.html

► **The main research field of the team is the theoretical description of the reactivity in heterogeneous and homogeneous catalysis.** The heterogeneous catalysts can be pure metals, metallic alloys, metal particles, chiral inductors and organometallic complexes deposited on supports like oxides. The studies of reactivity focus essentially on selective or enantioselective reactions with the aim of finding the origin of the catalyst selectivity to a given product. An important aspect that is growing up is the introduction of the solvation, temperature and pressure effects and the consideration of metal supported particles, which allows a more realistic description of the reactivity.

The Inelastic Electron Tunneling Spectroscopy (IETS) images acquired with the Scanning Tunneling Microscope permits a chemical characterization of adsorbed molecules complementary to their topographic STM imaging. The modeling of IETS that begins to be developed in our group, is a promising tool for quantitative identification of intermediates in heterogeneous catalysis.

The field of the biological systems is also explored. We combine a quantum approach and a classical approach to study the enzymatic reactivity. We are presently investigating a new family of inhibitors for the HIV-PR1 protease.

The team also includes a research axis in methodology: it takes part to the effort of several international teams to develop new methods for exploring the free energy surface. So it will be possible to reproduce experimental conditions in our simulations.

In 2008, the team has published 19 papers in international journals (including J. Am. Chem. Soc., Angewandte Chemie, Phys. Rev. Letters) and has given 8 invited conferences. It develops several national and international collaborations (Lausanne, Bonn, Berlin, Munich, Barcelona, Caracas, Riverside).

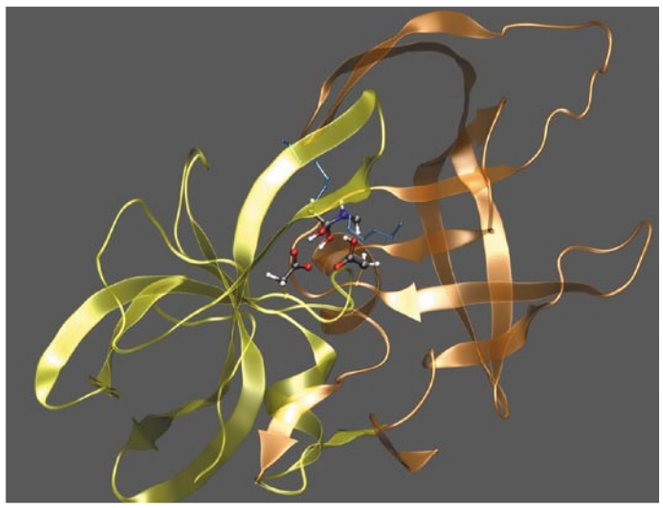
Selected publications:

►Joubert J., Delbecq F., Sautet P., Thieuleux C., Taoufik M., Blanc F., Copéret C., Thivolle-Cazat J., Basset J.-M. Synthesis, characterization and catalytic properties of γ-Al_2O_3 supported zirconium hydrides through a combined use of surface organometallic chemistry and periodic calculations. Organometallics, 2007, 26, pp. 3329-3335.

►B. Wang, M.-L. Bocquet, S. Marchini, S. Gunther, J. Wintterlin, Chemical origin of a graphene Moiré overlayer on Ru(0001), Phys. Chem. Chem. Phys. 2008, 10, 3530.

►Dupont C., Loffreda D., Delbecq F., Jugnet Y. Vibrational study of CO chemisorption on the Pt3Sn(111)-(2x2) surface. J. Phys. Chem C, 2007, 111, pp. 8524-8531.

Modeling of the VIH aspartic protease complexed with its substrate.



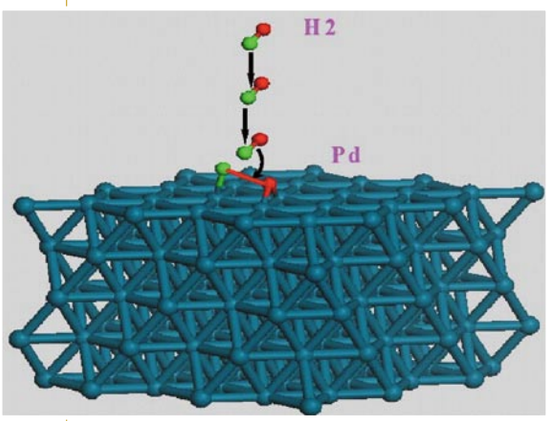
►CHEMISTRY LABORATORY◄

►Kinetics and Structure◄

► **Team leader** ► ***Wei Dong, Research Director*** *- Wei.Dong@ens-lyon.fr* ◄
► **Team members** ► *Wei Dong, research director; Max Kolb, research director; Vincent Krakoviack, associate professor; Taras Patshan, postdoctoral fellow; Yang Xiao, postdoctoral fellow; Wei Chen, PhD student; Laurent Gueudre, PhD student.* ◄

► **Our research efforts focus on two main themes:**
1) fluids confined in porous media;
2) surface reaction dynamics.

Recently, we have made important progress in studying glass transition and fluid adsorption in random porous media. The mode-coupling theory was extended to study very slow dynamics of confined fluids. This is the first theoretical approach based on a microscopic description which helps explore the diverse factors that influence the dynamic behaviours of confined fluids. Some new models have been proposed for describing the fluid adsorption in porous materials with sponge-like pore structure. We have developed a theoretical approach based on integral equations for these new models. We have also derived a first analytical and highly accurate equation of state by extending the scaled particle theory to confined fluids.



Dynamic process of the dissociation of a H2 molecule on a Pd(111) surface. ▼

Nowadays, the molecular dynamics (MD) method is widely used for studying complex non reacting systems. However, modelling complex large reacting systems remains a big challenge. The main obstacle is the difficulty for describing the processes taking place at different length and time scales accurately. Despite the remarkable advances in quantum mechanics methods and progress in computational hardwares, the application domain of the ab initio simulations is still quite limited. The usual force fields that are widely used for MD simulations do not allow us to describe chemical reactions. The simulations based on reactive force fields constitute an emerging alternative for studying complex reacting systems. We are developing an approach based on reactive force fields which allows us to study the reaction dynamics of complex systems in heterogeneous catalysis, e.g., on supported catalysts.

Selected publications:

►DONG W., KRAKOVIACK V., ZHAO S.L. Fluids confined in porous media: A soft-sponge model. J. Phys. Chem. C 111, 15910, (2007).
►KRAKOVIACK V. Mode-coupling theory for the slow collective dynamics of fluids adsorbed in disordered porous media. Phys. Rev. E 75, 031503, (2007).
►MATINEZ A.E., DONG W., BUSNENGO H.F. Comparative study of H2 adsorption on W(100)-c(2x2) Cu and W(100): Surface alloying effects. Appl. Surf. Sci. 254, 82, (2007).

►CHEMISTRY LABORATORY◄

►Supramolecular chemistry and stereochemistry◄

► **Team leader** ► ***Jean-Pierre Dutasta*** *- dutasta@ens-lyon.fr* ◄
► **Team members** ► *Nelly Batail, PhD student; Annissa Bendjeriou, postdoctoral researcher; Thierry Brotin, research associate first class; Véronique Dufaud, research associate first class; Marie Genelot, PhD student; Laure Guy, engineer ENS Lyon; Steven Harthong, PhD student; Alexandre Martinez, associate professor; Pascal Raytchev, PhD student; Antoine Stopin, PhD student; Jérôme Vachon, graduate teaching assistant.* ◄

www.ens-lyon.fr/CHIMIE/Fr/Groupes/page_groupe_supra/homegroupe.html

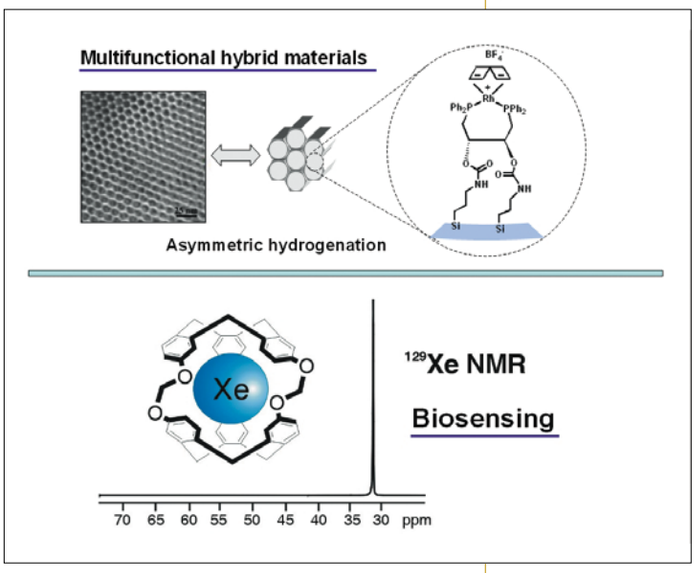
►**The first topic developed in our group concerns the host-guest molecular recognition processes and the fundamental aspects of molecular chirality.** We are particularly interested in (hemi)cryptophane and phosphonate cavitand molecules for the detection of cationic and neutral guests. Recent investigations in the functionalization of these molecular receptors open the route to the preparation of useful new molecules, for example, for the encapsulation of noble gases for bio-medical applications in NMR imaging (MRI). Our group is deeply involved in a bio-sensor project for the recognition of biomedical targets by MRI. The chemistry of these molecules, their transformation, their functionalization, their complexation properties and their chiroptical properties are developed in our group. The resolution of enantiomers is actively developed in close relation with industry. Other research projects are devoted to the design of chiral molecules for application in supramolecular catalysis or optics. The second theme concerns the extension of such concepts to multifunctional mesoporous hybrid materials. Thus, molecular scale processes such as host-guest relationships or chemical reactions at a catalytic site are not considered in isolation: processes involving larger scales of the material (characteristics or complementary functional groups in proximity to the key site, molecular transport within the solid, thermal conductivity of the solid, etc.) are taken into account and are considered in an integrated manner, starting from the conception of the material through the synthesis of the solid to its post-synthetic modification.

Selected publications:

►A cryptophane core optimized for xenon encapsulation. H. A. Fogarty, P. Berthault, T. Brotin, G. Huber, H. Desvaux and J.-P. Dutasta, J. Am. Chem. Soc. 2007, 129, 10332.

►A cryptophane biosensor for the detection of specific nucleotide targets through xenon-NMR spectroscopy. V. Roy, T. Brotin, J.-P. Dutasta, M.-H. Charles, T. Delair, F. Mallet, G. Huber, H. Desvaux, Y. Boulard and, P. Berthault, ChemPhysChem, 2007, 8, 2082.

►Organized Surface Functional Groups: Cooperative Catalysis via Thiol/Sulfonic Acid Pairing Margelefsky, Eric L., Zeidan, Ryan K., Dufaud, Veronique, Davis, Mark E. J. Am. Chem. Soc. 2007, 129, 13691.



The top of the picture shows the structure of a newly designed porous material for asymmetric hydrogenation. The bottom of the picture represents the xenon. cryptophane-111 complex and its characteristic ^{129}Xe NMR spectrum.

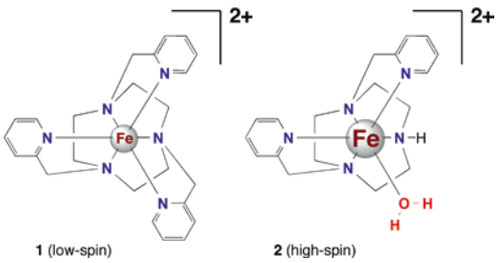
►CHEMISTRY LABORATORY◄

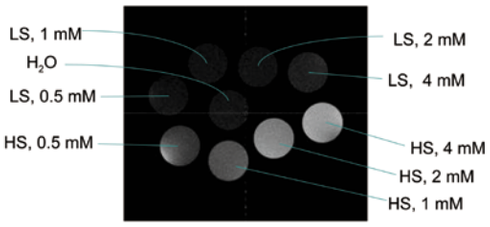
►Bioorganic chemistry◄

► **Team leader** ► ***Jens Hasserodt,*** *full professor - jens.hasserodt@ens-lyon.fr* ◄
► **Team members** ► *Frédéric Avenier, postdoctoral fellow; Philippe Maurin, associate professor; Delphine Pitrat, technician; Akhilesh Singh, postdoctoral fellow; Oliver Thorn-Seshold, PhD student; Fayçal Touti, PhD student; Charlène Valmalle, assistant professor; Michael Waibel, PhD student.* ◄

► **Our research comprises two distinct projects firmly planted in the field of synthetic chemistry but with significant relevance for the discipline of molecular and cellular biology.** In one case, we continue to explore a rare chemical group interaction, the tertiary amine-carbonyl interaction, for (a) its utility in the design of novel enzyme inhibitors, and (b) for its capacity to replace the all-important hydrogen bond in the design of short bio-mimetic oligomer sequences that reliably fold in aqueous/physiological media, in contrast to accepted knowledge that short peptide or peptidomimetic sequences (that rely on H-bonding for folding) usually exist as random-coil populations without any distinct super-structure. Novel biomimetic foldamer systems may serve for the discovery of sequences that inhibit protein-protein interactions, a rapidly growing field of research.

Our second principal project aims to develop a molecular probe for the detection of a specific enzymatic activity (e.g. one generated by a reporter gene) in the living organism by MRI. Current design efforts by competing groups are hampered by their use of the paramagnetic metal ion Gadolinium that is popular principally for its high magnetic moment. Gd-based contrast agents for MRI are always paramagnetic, and therefore always generate a signal, no matter the constitution of its surrounding cage. One may therefore only hope to design a probe for a biochemical activity that changes its signal from «on» to a little more «on». We propose an iron(II)-based design that principally allows for the design of a probe that acts in an «off-ON» mode.





Selected publications:

► Stavila V., Allali M., Canaple L., Stortz Y., Franc C., Maurin P., Beuf O., Dufay O., Samarut J., Janier M., Hasserodt J., Significant relaxivity gap between a low-spin and a high-spin iron(II) complex of structural similarity: an attractive off/on system for the potential design of responsive MRI probes New. J. Chem. 2008, 32, pp. 428-435 ; as of april 3rd 2008, promoted by the editorial office as a hot article. http://dx.doi.org/10.1039/b715254j

►Stavila, V.; Stortz, Y.; Franc, C.; Pitrat, D.; Maurin, P.; Hasserodt, J. "Effective repression of the fragmentation of a hexadentate ligand bearing an auto-immolable pendant arm by iron coordination" Eur. J. Inorg. Chem. 2008, 25, 3943-3947. http://dx.doi.org/10.1002/ejic.200800419

►Waibel, M.; Pitrat, D.; Hasserodt J. , "On the Inhibition of HIV-1 Protease by Hydrazino-ureas Displaying the N-C=O Interaction", Bioorg. Med. Chem. 2009, 17, 3671-3679. http://dx.doi.org/10.1016/j.bmc.2009.03.059.

►CHEMISTRY LABORATORY◄

►POM4 (Magnetic and Optical properties of Molecules and Molecular Materials)◄

► **Team leader** ► ***Gilles Lemercier,*** *associate professor - gilles.lemercier@ens-lyon.fr* ◄
► **Team members** ► *Christophe Aronica, assistant professor; Mickaël Four, PhD student.* ◄
Equipe en migration vers l'Université de Reims
http://www.univ-reims.fr/ICMR

► **Our main focus is on the fundamental and more applied studies of the optical and magnetic properties of molecules** (or even a synergy of both), coordination complexes and related molecular materials (obtained, for example, by the functionalization of surfaces such as Au or Silica). In this rapidly growing interdisciplinary area, we are first involved in the design and synthesis of new ligands for optics and nonlinear optics along three main lines (see figure below):

1. New ligands and related coordination complexes (especially Ru(II) complexes) for their fundamental interests (collaborations for calculations) and applications (biological imagery, dioxygen probes and PDT for example) due to their optical properties (absorption and emission wavelength, excited-state lifetimes).

2. Rare-earth (especially Eu(III)) complexes as optical probes; the associated ligands are designed to be grafted on different materials (via collaboration to functionalize the internal surface of the channels of mesostructured LUS type silica, for example) or to lead to an auto-organization on graphite or gold surfaces for STM studies (in collaboration with CEA initiated by ACI "NanoDELO").

3. Investigation of the interplay of magnetic and nonlinear optical (NLO) properties in variable size multifunctional molecular assemblies. Our project is to build a paramagnetic metallic center whose coordination sphere is substituted by a Π-delocalized system being the site of charge transfer processes. Indeed, this study addresses both interests which are fundamental in nature and applications in commutation or the fine tuning of the properties of molecular materials.

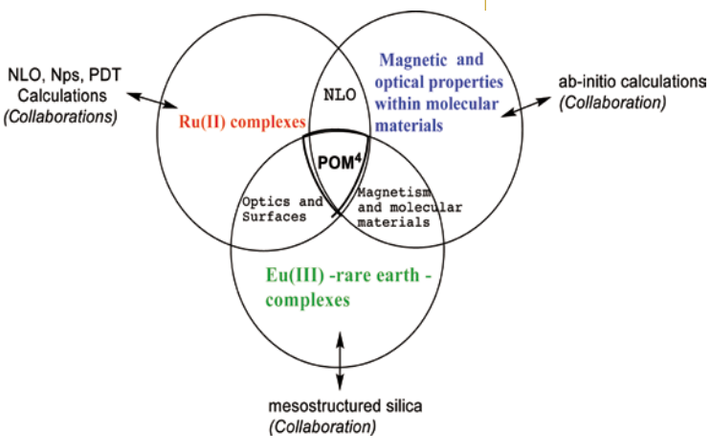
Selected publications:

►C. BOCA, M. FOUR, A. BONNE, B. VAN DER SANDEN, S. ASTILEAN P. L. BALDECK, G. LEMERCIER, An Ethylene-Glycol Decorated Ruthenium(II) Complex for Two-Photon Photodynamic Therapy (PDT); Chem. Commun. 2009, DOI: 10.1039/b907143a

►S. ABRY, F. LUX, B. ALBELA, A. ARTIGAS-MIQUEL, S. NICOLAS, B. JARRY, P. PERRIAT, G.LEMERCIER, L. BONNEVIOT, Europium(III) Complex Probing Distribution of Functions Grafted using Molecular Stencil Patterning in 2D Hexagonal Mesostructured Porous Silica Chem. Mat. 2009, 21, 2349-2359.

►C. ARONICA, A. VENANCIO-MARQUES, J. CHAUVIN, V. ROBERT, G. LEMERCIER, A Rational Design of Catechol based Compounds: Experimental and Theoretical study of Optical Properties»., Chem. Eur. J. 2009, 15, 5047-5055.

Main interests and research subjects developed in the POM4 group.



►CENTER FOR HIGH FIELD NMR - CRMN◄

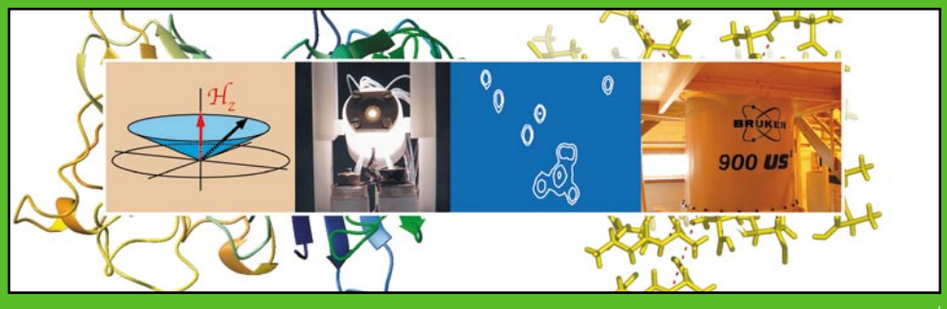
► **Director** ► **Pierre Toulhoat,** *senior researcher;* **Lyndon Emsley,** *professor - crmn@ens-lyon.fr* ◄
► **Total personnel** ► *21* ◄
► **Partners** ◄ *ENS Lyon, CNRS, UCB Lyon 1* ◄
► **Web** ◄ *www.ens-lyon.fr/crmn et www.ralf-nmr.fr* ◄

The Center for High Field NMR in Lyon (CRMN) provides an optimum environment to foster accelerated development of state-of-the-art NMR, in view of developing sophisticated new materials and of overcoming important hurdles in modern biology and medicine. The CRMN has a unique range of equipment including several high resolution spectrometers operating at multiple fields up to 1 GHz, supported by an expert technical staff and research groups dedicated to the development and application of novel, state-of-the-art spectroscopic and computational methodology in NMR.

We are specialized in developing the NMR technique itself. Our staff members are all well established figures in the international NMR community. Much of their work is related to providing the technical and methodological developments at the heart of NMR that allow other research groups to make breakthroughs in applications problems. Nevertheless, they have all made recent contributions themselves to applications, with high impact discoveries. The extremely wide range of the areas covered by these applications is one of the most important factors in the strength of the center.

For example, the Lyon group, working with scientists at MIT and CPE-Lyon, recently showed that surface supported metathesis catalysts have the same mechanism and efficiency of action as their solution counterparts, but that they are significantly more robust when on the surface. In different work, with IBCP-Lyon, they showed for first time that microcrystalline samples allow NMR to probe the details of the water-protein interactions that stabilize protein structures and control folding and unfolding processes. In yet another area, the Lyon group showed, in work with Pines in Berkeley, that high-resolution structural information can be obtained from structurally disordered systems, opening up a new and potentially rich area of application. Finally, in collaboration with geneticists in Lyon we were able to us NMR to provide metabolic markers to discriminate between different genetically modified strains of the model animal C. elegans that were otherwise apparently identical. This allows us also to understand the metabolic consequences of such genetic changes.

In addition to in house research, the CRMN runs a European Large Scale Facility for NMR, offering the European scientific community a unique environment for the study of diverse problems in biological, chemical, physical, and medical sciences by NMR.



▲ *Understanding the physics of nuclear spins leads to the development of new NMR experiments using sophisticated instrumentation, which in turn can solve problems in a wide range of application areas.*

CURRENT RESEARCH TOPICS
Developing new methods for high-field NMR spectroscopy; Systems biology, notably in relation to cancer; Characterization of surface species active in catalysis; Crystallography by NMR; Structure and dynamics of proteins

AREAS OF APPLICATION
Drug development, diagnostics, sustainable development, etc.

INDUSTRIAL PARTNERS
Bruker, the pharmaceutical industry

EQUIPMENT
NMR spectrometers operating in the range from 500 MHz to 1 GHz.

Selected publications:

►S. Laage, A. Lesage, L. Emsley, I. Bertini, I. Felli, R. Pierattelli and G. Pintacuda, ìTransverse Dephasing Optimized Homonuclear J-Decoupling in Solid-State NMR Spectroscopy of Uniformly 13C-Labeled Proteins,î J. Am. Chem. Soc. 131, 10816 (2009).

►B.J. Blaise, J. Giacomotto, B. Elena, M.-E. Dumas, P. Toulhoat, L. SÈgalat and L. Emsley ìMetabotyping of Caenorhabditis elegans reveals latent phenotypes,î Proc. Natl. Acad. Sci. USA 104, 19808 (2007).

►P. Felgines Avenier, M. Taoufik, A. Lesage, A. Baudouin, A. De Mallmann, L. Veyre, J.-M. Basset, L. Emsley, and E.A. Quadrelli, ìDinitrogen Dissociation on an Isolated Surface by a Single Tantalum Atom,îScience 317, 1056 (2007).

►COMPLEX SYSTEMS INSTITUTE - IXXI◄

► **Director** ► **Pablo Jensen,** *senior researcher - pablo.jensen@ens-lyon.fr* ◄
► **Total personnel** ► *40* ◄
► **Partners** ◄ *CNRS, INRIA, IRD, ENS Lyon et LSH, INSA Lyon, Univ. J. Fourier Grenoble, Univ. Lyon 1, Univ. Lyon 2* ◄
► **Web** ◄ *http://ixxi.fr* ◄

IXXI promotes interdisciplinary collaboration in the modeling of complex systems. It gathers 230 scientists from several fields (mainly computer science, mathematics and physics) and universities in the Rhône-Alpes region. Our building hosts 40 residents, with large discussion areas, IXXI partners are: CNRS, INRIA, IRD, ENS Lyon et LSH, INSA Lyon, Univ. J. Fourier Grenoble, Univ. Lyon 1, and Univ. Lyon 2.
The interdisciplinary research on the modeling of complex systems is carried out in three complementary ways:

- Basic research on tools. Computer science, mathematics and physics: cellular automata, point processes, etc.
- Modeling of specific complex systems. Medical applications, systems biology, social systems, etc.
  – The spread of nosocomial infections
  – The robustness and variation in evolution: digital genetic models
  – The localization of retail activities
- Epistemology of complex systems. Through seminars and a project on the history of "complex systems" we want to better understand what complex systems modeling is and what its main strengths and limitations are.

IXXI promotes interdisciplinary research in three steps:

- Organizing events to favor networking.
  – seminars, schools, IXXI days, IXXI letter;
- Supporting innovative projects, events.
  – original, interdisciplinary, inter-institutions
  – accept that some "fail"
  – light administration (2 pages), 5000 euros
- Helping maturation of successful projects
  – help obtaining national and European money
  – hosting projects in our facilities

In September 2008 we are opening the first truly interdisciplinary Master in complex systems modeling. It will draw students mainly from three basic disciplines: computer science, math and physics. They will receive a wide culture in complex systems modeling by combining the three approaches while keeping their anchorage in their own discipline.
How?

– advanced courses in their own discipline,
– introductions to the other two,
– modeling methodology and epistemology,
– interdisciplinary lectures on specific topics (e.g. dynamical systems by a physicist, a computer scientist and a mathematician).

CURRENT RESEARCH TOPICS
Complex systems modeling, complex networks, systems biology, social systems, medical applications, etc.

AREAS OF APPLICATION
Medicine, genomics, environment, society

INDUSTRIAL PARTNERS
OSLO Software (4 place Danton, 69003 LYON), CCI du Rhône

Selected publications:

►Auger, P; de la Parra, RB; Poggiale, JC, et al. Aggregation of variables and applications to population dynamics. Structured population models in biology and epidemiology 2008, 1936, pp. 209-263.
►Pablo Jensen, Jean-Baptiste Rouquier, Pablo Kreimer and Yves Croissant. Scientists who engage with society perform better academically. Science and Public Policy 2008, 35(7), pp. 527-541.

◄
We are developing tools such as dynamical clustering to analyze millions of trips made by rental bicycles (Vélo'V), to learn about social rhythms, travel strategies, urban life, etc.

►COMPUTER SCIENCE LABORATORY - LIP◄

► **Director** ► **Gilles Villard,** *Senior Researcher CNRS - directeur.lip@ens-lyon.fr* ◄
► **Total personnel** ► *131* ◄
► **Partners** ◄ *CNRS, INRIA, UCB Lyon 1* ◄
► **Web** ◄ *http://www.ens-lyon.fr/LIP* ◄

► The Computer Science Lab gathers 45 permanent faculties and researchers from CNRS, with 40PhD students, and 36 temporary scientific people on various projects. Research is developped on several key topics of the discipline with the help of an administrative and technical staff of 5 engineers and 5 assisting people. LIP members are highly involved in teaching within the University of Lyon.

Through the years, the Lab has evolved with †the creation of new research teams and he evolution of the research axes of existing teams. The laboratory is currently organized around six projects-teams, among which 4 are joint with INRIA.

Through algorithmic and software developments at every levels, an important strength of LIP research is to conciliate both fundamental aspects, and advances closer to technology evolutions. On the fundamental side this goes from complexity and models of computation, to semantics and formal proving, and to mathematical computation and a wide spectrum of algorithmic questions. On directions ahead for technology evolution and efficient use of computing means, the LIP is involved in computer arithmetic and computer algebra, grid and cloud computing, peer-to-peer systems, protocols and software for networks and internet of the future, embedded computing systems, FPGA computing and web technologies.

Most teams participate to high performance experiments, and to validation and transfer of their results through the development of software/hardware libraries and platforms (arithmetic operators, compilers, toolboxes for the deployment of client-server applications over the grid, complex system simulation, high performance network protocols, ...).

Other key points are multi-disciplinary investments and industrial research and collaborations. The LIP laboratory has for instance assisted to the creation of ambitious projects such as the Grid5000 project and the Complex System Institute. The role of research with the industrial world is often emphasized such as through the Competitivity Cluster Minalogic, Nano2012, or the INRIA-Bell-Labs common lab.

CURRENT RESEARCH TOPICS
Computer Arithmetic, Compilation and Embedded Computing Systems, Models of Computation and Complexity, Programs and Proofs, Algorithms and Scheduling for Distributed Heterogeneous Platforms, Optimized Protocols and Software for High Performance Networks

RELATED FIELDS
Algorithmic, Fundamental Computer Science, Software & Hardware design

AREAS OF APPLICATION
Fundamental computer science; Efficiency, Reliability and Security of Computing and Communicating Systems; High Performance Computing (Grids and Clouds); Mathematical Computing; Complex systems; Life Science Applications

INDUSTRIAL PARTNERS
IBM, Intel, STMicroelectronics, Alcatel-Lucent, ...

EQUIPMENT
PC clusters, Grid'5000 nodes, workstations

► *Grid'5000 clusters for large scale high performance computing*

►COMPUTER SCIENCE LABORATORY - LIP◄

►Compsys: compilation and embedded computing systems◄

► **Team leader** ► ***Alain Darte,*** *senior researcher - alain.darte@ens-lyon.fr* ◄
► **Team members** ► *Christophe Alias, research associate; Benoit Boissinot, PhD student; Quentin Colombet, engineer; Alain Darte, senior researcher; Paul Feautrier, full professor; Laure Gonnord-Danthony, postdoctoral fellow; Alexandru Plesco, PhD student; Fabrice Rastello, research associate; Caroline Suter, assistant.* ◄ ***www.ens-lyon.fr/LIP/COMPSYS/***

► **The objective of Compsys is to adapt and to extend code optimization techniques primarily designed for compilers/parallelizers for high-performance computing** to the special case of embedded computing systems. In particular, Compsys works on micro-code optimizations for specialized processors, and on high-level synthesis of hardware accelerators. The main characteristic of Compsys is its focus on combinatorial optimization problems (graph algorithms, linear programming, polyhedra) coming from code optimization problems arising in this field (register allocation, cache optimization, memory allocation, scheduling, optimizations for power, automatic generation of software/hardware interface, etc.) and the validation of techniques developed in compilation tools. Our recent achievements and current developments are:

• the study of a new approach for register allocation - in two steps - with a spilling phase (optimization of loads and stores) followed by an assignment phase including register coalescing (optimization of register-to-register moves), complexity study: developments of heuristics and algorithms, extension to just-in-time compilation, all aspects developed in a strong collaboration with the STMicroelectronics compiler group;

Example of colored interference graph with affinities for register allocation. ►

• the introduction of new mathematical tools (related to critical lattices) to optimize the memory reuse for multi-dimensional arrays and theoretical as well as software developments (software tool Cl@k) with integration in a source-to-source program transformations environment (software tool Bee);

• the development of methodologies for systems on chip, scheduling strategies for synthesis tools, prototypes of high-level synthesis tools including high-level program transformations, developments of software/hardware interfaces, etc.

Compsys visibility in the embedded computing systems and compiler design communities is acknowledged by its participation in program committees of conferences such as ASAP, CASES, DATE, CC, PLDI, and in the editorial board of ACM Transactions on Embedded Computing Systems. Compsys is also member of HIPEAC, European network of excellence on High-Performance Embedded Architecture and Compilation. Our main industrial partner is STMicroelectronics (both in compilation and high-level synthesis).

Selected publications:

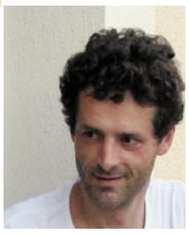
►Christophe Alias, Fabrice Baray, and Alain Darte. An Implementation of Lattice-Based Memory Reuse in the Source-to-Source translator Rose. In ACM SIGPLAN/SIGBED Conference on Languages, Compilers, and Tools for Embedded Systems (LCTES'07), San Diego, USA, June 2007.

►Florent Bouchez, Alain Darte, and Fabrice Rastello. On the Complexity of Register Coalescing. In International Symposium on Code Generation and Optimization (CGO'07), March 2007. IEEE Computer Society Press. Best paper award.

►Paul Feautrier. Les Compilateurs. In Jean-Eric Pin, editor, Encyclopédie de l'Informatique. Vuibert, 2007.

►COMPUTER SCIENCE LABORATORY - LIP◄

►Arénaire. Computer arithmetic◄



►**Team leader** ► ***Florent de Dinechin,*** *associate professor, ENSL - florent.de.dinechin@ens-lyon.fr* ◄
► **Team members** ► *Nicolas Brisebarre, research associate, CNRS; Marie Buillas, Administrative staff; Sylvain Chevillard, PhD student; Guillaume Hanrot, professor, ENSL; Claude-Pierre Jeannerod, research associate, INRIA; Mioara Joldes, PhD student; Jingyan Jourdan Lu, PhD student; Vincent Lefèvre, research associate, INRIA; Nicolas Louvet, associate professor, UCBL; Micaela Mayero, associate professor; Ivan Morel, PhD student; Christophe Mouilleron, PhD student; Jean-Michel Muller, research director, CNRS; Hong Diep Nguyen, PhD student; Andrew Novocin, post-doctoral fellow, INRIA; Adrien Panhaleux, PhD student; Bogdan Pasca, PhD student; Nathalie Revol, research associate, INRIA; Guillaume Revy, PhD student; Damien Stehlé, research associate, CNRS; Honoré Takeugming, engineer, ENSL; Serge Torres, engineer, ENSL; Alvaro Vasquez, post-doctoral fellow, INRIA; Gilles Villard, research director, CNRS.*◄

www.ens-lyon.fr/LIP/Arenaire

► **How can numbers be represented in a computer?** How does a computer perform addition or multiplication, how does it evaluate a sine or an exponential? Can we get the result faster? Can we get a more accurate result? Is it possible to obtain the exact result, or is it possible to prove how many digits are correct? In general, how can the quality and reliability of our computing environment be improved, and at what cost? These are the questions that drive research in computer arithmetic.

Arénaire strives to cover computer arithmetic at large. We work with integers, finite fields used in cryptography, and computer approximations to real numbers. Our collective expertise ranges from the design of hardware operators to multiple-precision software and computer algebra, from the four basic operations to elementary functions and linear algebra operators, from the mathematics of approximation to lattice reduction algorithms. We target embedded processors, reconfigurable circuits, high-performance computers. We work on operator design, on tools to automate this design, on the mathematics needed by these tools, on proving the quality of the operators. Improving computing may mean getting more accurate results, or getting them more quickly, or at a lower hardware cost, or using less memory, or with lower power consumption.

Arénaire also participates to the standardization of computer arithmetic and develops established libraries and software tools. STMicroelectronics and Alcatel-Lucent France are two examples of our laboratory's industrial collaborations.

Selected publications:

► Jean-Michel Muller, Nicolas Brisebarre, Florent de Dinechin, Claude-Pierre Jeannerod, Vincent Lefèvre, Guillaume Melquiond, Nathalie Revol, Damien Stehlé, and Serge Torres. Handbook of Floating-Point Arithmetic. Birkhauser Boston, 2009.

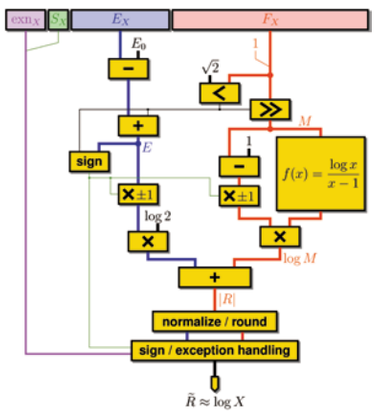
► Jean-Luc Beuchat, Nicolas Brisebarre, Jé rémie Detrey, Eiji Okamoto, Masaaki Shirase, and Tsuyoshi Takagi. Algorithms and arithmetic operators for computing the t pairing in characteristic three. IEEE Transactions on Computers, 57(11):14541468, November 2008.

► Phong Q. Nguyen and Damien Stehlé. Low-dimensional lattice basis reduction revisited. ACM Transactions on Algorithms, 2009.

► J.-LPeter Kornerup, Christoph Quirin Lauter, Vincent Lefèvre, Nicolas Louvet, and Jean-Michel Muller. Computingcorrectly rounded integer powers in floating-point arithmetic. ACM Transactions on Mathematical Software, 37(1), 2009.

► Alin Bostan, Claude-Pierre Jeannerod, and Eric Schost. Solving structured linear systems with large displacement rank. Theoretical Computer Science, 407(1:3):155-181, November 2008.

► Jérémie Detrey and Florent de Dinechin. Parameterized floating-point logarithm and exponential functions for FPGAs. Microprocessors and Microsystems, Special Issue on FPGA-based Reconfigurable Computing, 31(8):537545, December 2007.



A hardware floating-point logarithm. ◄

►COMPUTER SCIENCE LABORATORY - LIP◄

►MC2 – MODELS OF COMPUTATION AND COMPLEXITY◄

► **TEAM LEADER** ► ***Pascal Koiran,*** *professor - pascal.koiran@ens-lyon.fr* ◄
► **TEAM MEMBERS** ► *Florent Becker, PhD student; Jorge Beltran, expert engineer; Eric Boix, engineer CNRS; Irénée Briquel, PhD student; Gian Chiquillo, expert engineer; Bruno Grenet, PhD student; Arnaud Grignard, expert engineer; Laurent Jouhet, PhD student; Camilo La Rota, expert engineer; Mathieu Malaterre, expert engineer; Mathlide Noual, PhD student; Natacha Portier, associate professor; Damien Regnault, PhD student; Eric Remila, associate professor; Julien Robert, PhD student; Jean-Baptiste Rouquier, PhD student; Eric Thierry, associate professor; Ricardo Uribe, expert engineer.* ◄
www.ens-lyon.fr/LIP/MC2/

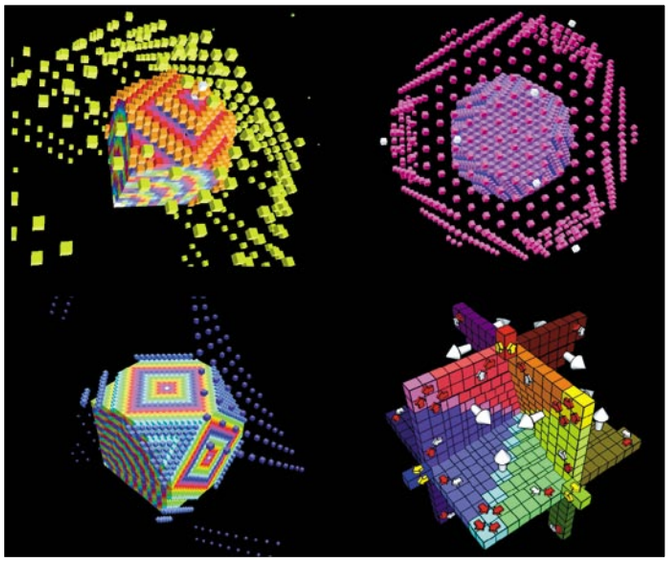
► **COMPUTATIONAL COMPLEXITY IS ONE OF THE MAIN INTERESTS OF OUR RESEARCH GROUP.** Our work centers on the design and analysis of efficient algorithms for a variety of problems—scheduling, tiling, navigation in large networks, and performance analysis of communication networks—with the development of algorithmic tools for network calculus.

We also study more theoretical questions: lower bounds, complexity classes, Kolmogorov complexity, etc. The goal here is to understand what the minimal resources required are (for instance, in computing time) for solving a given problem. These questions are studied for a number of different computation models: probabilistic, quantum, algebraic, or timed models, models with a finite or infinite state space, parallel models (networks of threshold automata, cellular automata), and synchronous or asynchronous models. Due to the richness of their dynamical behavior, some of these models (e.g., cellular automata) are also studied from a dynamical systems point of view.

Our work on complex systems benefits from our experience in discrete models. The complex systems that we study may be of human origin (social networks, the Internet, peer-to-peer systems, self-assembly of nanomaterials) or biological origin (gene regulation networks, morphogenesis of Arabidopsis Thaliana).

Our team also coordinates the European project Morphex and is developing, within this project, a generic platform for the modeling of complex systems.

Time optimal self-assembly of nano-cubes with the corresponding directions of information propagation within the nano-artefact. ▼

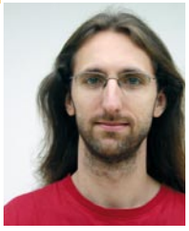


SELECTED PUBLICATIONS :

►An Algorithmic Toolbox for Network Calculus. A. Bouillard and E. Thierry.
Discrete Event Dynamic Systems, volume 18, issue 1, pages 3-49, 2008.
►P. Koiran, V. Nesme and N. Portier. The quantum query complexity of Abelian hidden subgroup problems. Theoretical Computer Science, 380:115-126, 2007 (special issue about ICALP 2005).
►M. Morvan, E. Rémila, E. Thierry, A note on the structure of spaces of domino tilings, Discrete Mathematics (2007) vol. 307, p. 769-773.

►COMPUTER SCIENCE LABORATORY - LIP◄

►PLUME◄



► **TEAM LEADER** ► ***Olivier Laurent,*** *CNRS researcher - Olivier.laurent@ens-lyon.fr* ◄
► **TEAM MEMBERS** ► *Philippe Audebaud, associate professor; Romain Demangeon, PhD student; Jean Duprat, associate professor; Daniel Hirschkoff, associate professor; Pierre Lescanne, professor; Aurélien; Pardon, PhD student; Patrick Baillot, CNRS researcher; Marc Lasson, PhD student; Barbara Petit, PhD student; Colin Riba, associate professor.* ◄

► **THE PLUME TEAM APPLIES METHODS FROM MATHEMATICAL LOGIC TO GUARANTEE THE CORRECTNESS OF COMPUTER SOFTWARE.** More precisely, we treat programs as formally defined mathematical entities, over which formal reasoning and verification can be constructed on machine.

Part of the team's work is aimed at building programming language theories to give a precise understanding of challenging programming constructs. We develop methods of formal reasoning related to probabilistic algorithms, expressed in dedicated programming languages. We also work on formal models for concurrent and distributed programming, using process algebras like pi-calculus.

As expressed by the Curry-Howard correspondence, proofs and programs are essentially the same mathematical objects. The process of typing a program can be related to the elaboration of a proof, and the process of putting this proof in canonical form can be related to the execution of the corresponding program. Systems for automated deduction, such as Coq (developed at INRIA), incarnate this correspondence by allowing the user to specify and mechanically check program properties as well as mathematical theories. Members of the Plume team use Coq for both formal mathematical development and program verification. Significant effort also goes into broadening the Curry-Howard correspondence. We want to deepen the understanding of the operational accounts of proofs in sequent calculus. We also work on applying recent developments in linear logic, realizability, games semantics, and implicit complexity to the formal program certification in order to obtain richer forms of guarantees for larger classes of programs.

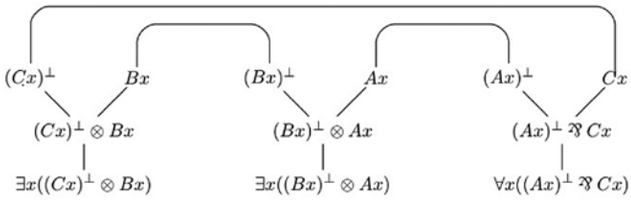
SELECTED PUBLICATIONS:

►HIRSCHKOFF D., POUS D. A Distribution Law for CCS and a New Congruence Result for the pi-Calculus. Proceedings of FoSSaCS, LNCS vol. 4423, 2007, pp. 228-242.

►DOUGHERTY D., GHILEZAN S., LESCANNE P. Characterizing strong normalization in the Curien-Herbelin symmetric lambda calculus: Extending the Coppo-Dezani heritage. Theoretical Computer Science 398(1-3), 2008, pp. 114-128.

►AUDEBAUD Ph., PAULIN C. Proofs of randomized algorithms in Coq. Science of Computer Programming 74(8), 2009, pp. 568-589.

►BAILLOT P., MAZZA D. Linear Logic by Levels and Bounded Time Complexity. To appear in Theoretical Computer Science, 2009.



Toute preuve est un un réseau de preuve,

tout réseau de preuve est un programme,

donc toute preuve est un programme.

►COMPUTER SCIENCE LABORATORY - LIP◄

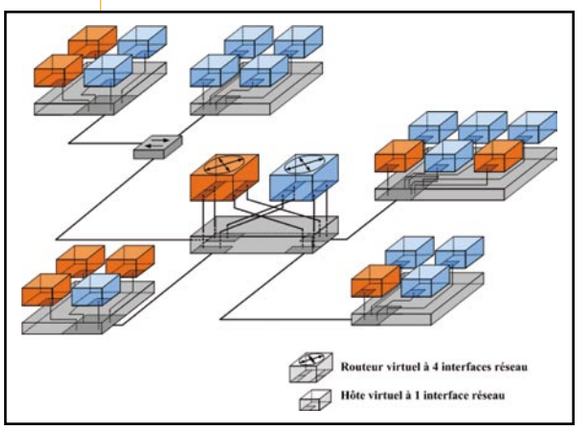
►RESO◄

► **TEAM LEADER** ► ***Pascale Vicat-Blanc Primet, research director*** *- pascale.primet@inria.fr* ◄
► **TEAM MEMBERS** ► *Fabienne Anhalt, PhD student; Thomas Begin, associate professor; Andreea Chis, PhD student; Eric Fleury, full professor; Jean-Patrick Gelas, associate professor; Olivier Glück, associate professor; Paulo Goncalves, research associate first class; Olivier Gremillet, postdoctoral fellow; Isabelle Guérin Lassous, full professor; Pierre-Solen Guichard, postdoctoral fellow; Romaric Guillier, PhD student; Ludovic Hablot, PhD student; Guilherme Koslovski, PhD student; Laurent Lefèvre, research associate first class; Patrick Loiseau, PhD student; Jean-Christophe Mignot, engineer; Dinil Mon Divakaran, PhD student; Anne-Cecile Orgerie, PhD student; Sébastien Soudan, PhD student; Rémi Vannier, PhD student; Pascale Vicat-Blanc Primet, research director.* ◄ ***www.ens-lyon.fr/LIP/***

► **RESO STUDIES PROTOCOLS AND COMMUNICATION & TRAFFIC MODELING ISSUES IN HIGH SPEED WIRED AND MESH NETWORKS IN THE CONTEXT OF THE FUTURE INTERNET.** The current Internet stack (TCP/IP) and its associated simple network management protocol are not consistent with the evolution of the network infrastructure components (optical and wireless technologies) and their use by emerging important end user applications. For example, very high rates (40 gigabits or 10 gigabits) induce a protocol processing power that may consume lots of energy. In a large scale virtual and integrated computing intensive distributed environment, network performance and reliability requirements are very high and can strongly influence the performance of the whole system and applications. The "bursty" traffic of emerging applications is not well modeled by classical statistical distributions that were valid in the early days of the Internet.

RESO research areas concern the design of protocols for the Future Internet, performance optimization and measurement, end to end quality of service studies, bandwidth sharing and congestion control, traffic measurement and modeling, network and system interaction, communication libraries and interfaces, static and dynamic analysis of interaction networks, and wireless networks. Approaches that we propose are based on programmable and autonomous networks, flow-aware and traffic-aware networking, virtualization, overlays, scheduling, measurement-based control, protocol and function offloading, and data path analysis and shortening. To better understand and model a phenomenon as well as to validate our proposals, we adopt a methodology combining theory and experimental analysis based on measurement, prototype development and large scale testbed deployment. RESO regroups members of two INRIA project teams EPI RESO and EPI A4RES. RESO actively participates in the joint laboratory INRIA-Bell Labs (Alcatel-Lucent laboratories) launched in 2007. The team is part of the European Euro-NF (network of the future) network of excellence and several european (IST) and national (ANR) projects. RESO has an associated-team with AIST in Japan. We also collaborate with France-Telecom, Hitachi and Myricom. We are participating in the design and deployment of international and national grid platforms (Grid5000/ Aladdin, LCG) based on very high speed networks (GEANT, RENATER). We also participate in standard bodies like Open Grid Forum, IRTF and IETF.

Network elements virtualisation. ▼



SELECTED PUBLICATIONS:

►SOUDAN S., CHEN Binbin, PRIMET VICAT-BLANC Pascale, Flow Scheduling and endpoint rate control in GridNetworks, Future Generation Computer Systems - Special issue on networks for Grid applications, September 2008 (to appear), Elsevier.
►SARR C., CHAUDET C., CHELIUS G. and GUERIN LASSOUS I., Bandwidth Estimation for IEEE 802.11-based Ad Hoc Networks, IEEE Transactions on Mobile Computing, Vol.7, No. 8, August 2008.
►SCHERRER Antoine, BORGNAT Pierre, FLEURY Eric, GUILLAUME Jean-Loup, and ROBARDET Céline, Analysis and Simulation of Dynamic Interaction Networks, Computer Network, 2008 (to appear), Elsevier.

►COMPUTER SCIENCE LABORATORY - LIP◄

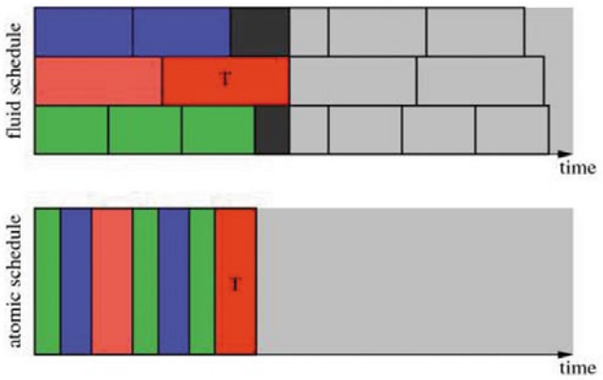
►GRAAL Algorithms and scheduling for distributed heterogeneous platforms◄

► **Team leader** ► **Frédéric Vivien,** *research associate - frederic.vivien@inria.fr* ◄

► **Team members** ► *Nicolas Bard, engineer; Leila Ben Saad, PhD student; Anne Benoit, associate professor; Julien Bigot, PhD student; Laurent Bobelin, postdoctoral fellow; Hinde Bouziane, graduate teaching assistant; Yves Caniou, associate professor; Eddy Caron, associate professor; Aurélien Cedeyn, engineer; Ghislain Charrier, PhD student; Indranil Chowdhury, postdoctoral fellow; Benjamin Depardon, PhD student; Frédéric Desprez, research director; Fanny Dufossé, PhD student; Gilles Fedak, research associate; Matthieu Gallet, PhD student; Jean-Sébastien Gay, PhD student; Haiwu He, engineer; Michail Heymann, postdoctoral fellow; Benjamin Isnard, engineer; Mathias Jacquelin, PhD student; Jean-Yves L'Excellent, research associate; Gaël Le Mahec, graduate teaching assistant; David Loureiro, engineer; Loris Marchal, research associate; Clément Mathieu, engineer; Christian Pérez, research associate; Franck Petit, visiting professor; Vincent Pichon, PhD student; Veronika Rehn-Sonigo, PhD student; Clément Rezvoy, PhD student; Yves Robert, full professor; Bing Tang, visiting PhD student; Bernard Tourancheau, full professor; Bora Uçar, research associate; Wang Yu, visiting PhD student.* ◄ ***http://graal.ens-lyon.fr***

► **New computing platforms are no longer monolithic.** They consist of collections of computers which can be scattered across an administrative domain, a country, or even the world. Such platforms can be built by the interconnection of computing centers, each holding clusters typically gathering several dozens of multi-processor nodes. They can also be made up by individual machines joining a Peer-to-Peer system. In all cases, the set of computational resources is heterogeneous: the processors have different computing speeds and memory capabilities. The computers from different sites are interconnected by wide-area network links and the platforms are often volatile: computers may join or leave them at any time, or may break down.

Deploying highly demanding applications on such platforms is called Grid computing. The efficient use of Grids poses new challenges. In this context, we address fundamental algorithmic and scheduling problems that have received little attention so far. An enormous effort has been devoted to enable Grid computing by addressing interconnection and security problems, or by building middlewares. However, we believe that many projects have failed to study fundamental problems such as the complexity of problems and algorithms, and scheduling heuristics. Also theoretical results are rarely validated on available (software) platforms.



▲ *Properties of dominant schedules when scheduling bag-of-task applications.*

The GRAAL research team tackles two main challenges for the widespread use of heterogeneous distributed platforms: the development of environments that will ease their use (in a seamless way) and the design and evaluation of new algorithmic approaches for applications using such platforms. The team works on three themes: scheduling strategies and algorithm design; parallel sparse direct solvers; network enabled servers.

Selected publications:

►BENOIT A., ROBERT Y., Mapping pipeline skeletons onto heterogeneous platforms, Journal of Parallel and Distributed Computing, 68(6), 2008.

►CARON E., DESPREZ F., TEDESCHI C., Enhancing Computational Grids with Peer-to-Peer technology for Large Scale Service Discovery, Journal of Grid Computing, 3, 2007.

►EARTH SCIENCE LABORATORY - LST◄

► **Director** ► *Gilles Dromart, professor - directeur.lst@ens-lyon.fr* ◄
► **Total personnel** ► *52* ◄
► **Partners** ◄ *CNRS, UCB Lyon 1* ◄
► **Web** ◄ *http://geologie.ens-lyon.fr/LST/* ◄

► The LST Earth sciences laboratory was created in 1987. At first research at the laboratory focused on classical geological methods before being expanded towards geophysics, geochemistry, remote sensing and mineral physics with applications to more diverse topics ranging from the formation of the solar system, the planets and their evolution to the latest addition at the turn of the last century, geomicrobiology. The scientific activities of the laboratory are now divided into four major themes: the formation of the solar system, surface dynamics of the Earth and planets, internal dynamics of the Earth and planets, and interactions between minerals and living organisms.

Various approaches are used: physics and numerical modeling of natural processes, geology, remote sensing, analytical imaging and tomography, multi-collection ICP mass spectrometry, vibrational spectroscopy, high-pressure experimentation. Fundamental advances in these topics are based on instrumental and analytical developments, on the high quality equipment in the laboratory and on large instruments such as synchrotrons. The laboratory's research teams are particularly well known for the elaboration of isotopic methods in geo- and cosmo-chemistry, in situ chemical and structural probes for Deep Earth mineralogy and the characterization of extraterrestrial matter, physical modeling of global planetary processes and image processing in geodynamics and tectonics. The laboratory is involved in applying this scientific progress to the current societal concerns centered on environmental and natural hazards; new isotopic methods, developed for dating and deciphering the details of the steps in the formation of the solar system or to study the Earth's convection, find applications in pollutant tracking and the remote sensing of landslides is performed using techniques that serve to study the surface of Mars.

The laboratory's research activity is transferred to higher education through the implication of its researchers in teaching Earth science at the Master's level and also through their involvement in the Master of Physics and Chemistry. Former Master and PhD students typically pursue academic careers in research centers and universities in France and, for a growing number, in foreign institutions, or occupy positions in the research and development sectors of large industrial groups. Researchers also participate in the training of future high school teachers, thereby ensuring the percolation of the latest conceptual advances in Earth and planetary sciences to all levels of public education.

CURRENT RESEARCH TOPICS
The geochemical budget of planets; Earth mantle dynamics; Earth lithosphere dynamics, early Earth, Earth material under extreme P,T conditions, exobiology, life under extreme conditions

AREAS OF APPLICATION
The properties and behavior of materials, natural hazards, global change, CO_2 sequestration

INDUSTRIAL PARTNERS
CNES, IFP, BRGM, Ciments Lafarge

EQUIPMENT
MC-ICP-MS and LA-ICP-MS, Raman spectroscopy, high pressure presses

►
Field view of the Fortescue/Hamersley Groups in the northwest of Western Australia, a kilometer thick sequence of Archaean (i.e. 2.8-2.4 Ga) mafic and felsic volcanic and associated sedimentary rocks which unconformably overlies Pilbara Craton granite–greenstones (courtesy of Nicolas Coltice). Study of the Pilbara Basins, including low-temperature thermo-chronology and sedimentology, aims at better designing the numerical modeling of the general landmass emergence which occurred at the Archaean-Proterozoic transition. Thermo-mechanical models that are currently developed take into account mantle cooling, crustal accretion and hypsometric curves, and should help predict the maximal elevation of Archaean hinterlands and the onset of modern erosion/transport/sedimentation cycles on Earth.

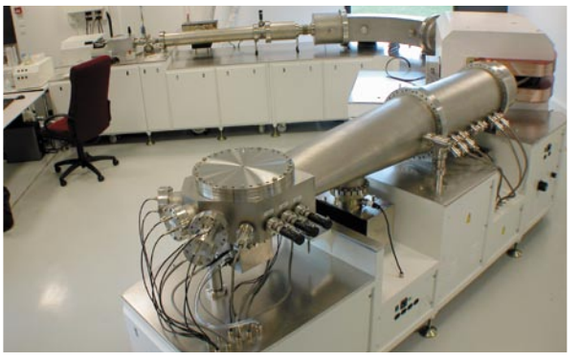
►EARTH SCIENCE LABORATORY - LST◄

►Geochemistry and cosmochemistry◄

► **Team leader** ► ***Francis Albarède,*** *professor - francis.albarede@ens-lyon.fr* ◄
► **Team members** ► *Janne Blichert-Toft, senior scientist; Philippe Télouk, senior technical staff; Sylvain Pichat, junior faculty; Vincent Balter, junior scientist; Ghylaine Quitté junior scientist; Emmanuelle Albalat, junior technical staff ; Chantal Douchet, junior technical staff; Aline Lamboux, junior technical staff; Martin Guitreau, PhD student; Marie-Laure Pons, PhD student.* ◄

► **The oldest field of interest of our group is the long-term dynamics of the terrestrial mantle and the growth of continents,** particularly the most ancient rocks on Earth. The last ten years have seen a revolution in the quality and throughput of isotopic data. Investigation the isotope compositions of neodymium, hafnium, and lead in mid-ocean ridge basalts and Hawaiian volcanoes provided us with an unprecendented map of the mantle reaching the surface and cast new light on the dynamics of mantle mixing. We dated the oldest objects of the solar system, known as refractory inclusions, at 4568.5 million years, demonstrated that 30 million years after the birth of the solar system, the Earthís core had formed and the upper mantle was largely molten (magma ocean). We also demonstrated that continental crust appeared in the first hundreds of millions of years and argued that the formation of the first continients and the appearance of life were companion events. We also revised the age of the Martian surface by dating Martian meteorites and obtained an old age of 4.0 billion years superseding the accepted age of 180 million years. Our original investigations on the isotopes of some elements (copper, zinc, nickel, iron) are opening new perspectives on the condensation of the Solar Nebula.

The ENS Lyon's Nu 1700: the largest ICP MS in the world. ▼



We are also developing new istopic tools and concepts relevant to the environment, such as the stable isotopes of comer, zinc, iron and, the uranium-series geochemistry of oceanic sediments, to the isotope composition of metals in biological material and to the dating of human fossils.

Our group is actively involved in analytical and instrumental development and is recognized as a CNRS national facility. We received the first commercial multiple-collector inductively-coupled plasma mass spectrometer in 1994 and a large radius ICP-MS in May 2008, the third mass spectrometer of that type in the world.

Selected publications:

►Hafnium isotopes in Jack Hills zircons and the formation of the Hadean crust
Author(s): Blichert-Toft J, Albarede F
Source: EARTH AND PLANETARY SCIENCE LETTERS
Volume: 265 Issue: 3-4 Pages: 686-702 Published: JAN 30 2008

►U-Pb dating of fossil enamel from the Swartkrans Pleistocene hominid site, South Africa
Author(s): Balter V, Blichert-Toft J, Braga J, et al.
Source: EARTH AND PLANETARY SCIENCE LETTERS
Volume: 267 Issue: 1-2 Pages: 236-246 Published: MAR 1 2008

►Tungsten and nickel isotopes in two enstatite achondrites: Itqiy and Zaklodzie
Author(s): Quitte G, Zanda B
Source: METEORITICS & PLANETARY SCIENCE
Volume: 42 Pages: A128-A128 Supplement: Suppl. S Published: AUG 2007

►Francis Albarède. Volatile accretion history of the terrestrial planets and dynamic implications. Nature, 2009 (In press).

►EARTH SCIENCE LABORATORY - LST◄

►Dynamics of the surface of the Earth and planets◄

► **Team leader** ► ***Pascal Allemand*** *- allemand@univ-lyon1.fr* ◄
► **Team members** ► *Pascal Allemand, full professor; Gilles Dromart, full professor; Emilie Gardin, PhD student; Philippe Grandjean, technician; Marie-Paule Guinet, technician; Yves Langlois, associate professor; Philippe Hervé Leloup, research director; Gweltaz Maheo, associate professor; Cathy Quantin, associate professor; Pierre Thomas, full professor.* ◄ ***http://geologie.ens-lyon.fr/LST/***

► **The surface of a planetary body is the place where internal and external processes meet and interact.** Our work is aimed at understanding and modeling the relationships between these two kinds of dynamics through remote sensing, field geology, geomorphologic analysis and measurements of sedimentary flux at various scales in space and time. The planet Mars is investigated through the multi-spectral and hyperspectral images acquired by current orbiters. Dune dynamics is explored to restore the recent climatic variations driven by the oscillation of the planet's axis. The sedimentary record is analyzed both in terms of geometry and mineralogical content in order to reconstruct climatic conditions.

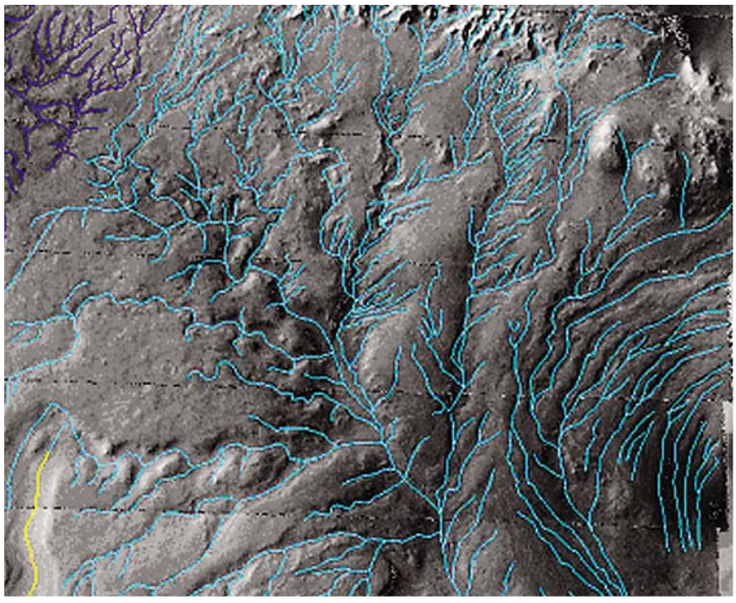
The dynamics of earth relief evolution are studied through the cases of mountain building in the Alps and the Himalayas. These studies combine field geology, the analysis of structures and microstructures, petrology, multi-method geochronology, and geomorphology. This allows us to retrieve the rock depth-temperature-deformation-time history and ranges structural and topographic evolution at geological time scales. The dynamics of relief development is investigated on the island of Guadeloupe from the scale of the climatic event to the scale of tectonic uplift. The practical objectives of this project are to produce and validate methods in the localization, prevision and characterization of landslides and mud and debris flows using remote sensing data of high and very high resolution and in situ measurements of water and solid flows in rivers.

Selected publications:

►Quantin C., Mangold N., Hartmann W.K., Allemand P. (2007) Possible long-term decline in impact rates 1: Martian geological data, Icarus 186, 1–10.

►Maheo G., Leloup P., Valli F., et al. (2007) Post 4 Ma initiation of normal faulting in southern Tibet. Constraints from the Kung Co Half-Graben. Earth and Planetary Science Letters, 256, 233-243.

►Dromart G., Quantin C. & Broucke O. (2007) Stratigraphic architectures spotted in Southern Melas Chasma, Valles Marineris, Mars. Geology, 3, 363-366.



The Dinggye active normal fault, South Tibet. The active uplift of the Ama Drime range (6730m) is attested by the morphology of its eastern topographic flank that exhibits typical triangular facets approximately 500 m high. Petrographic data suggest that the total exhumation of the range has a magnitude of about 50 km for the last 17 million years. ▼

►EARTH SCIENCE LABORATORY - LST◄

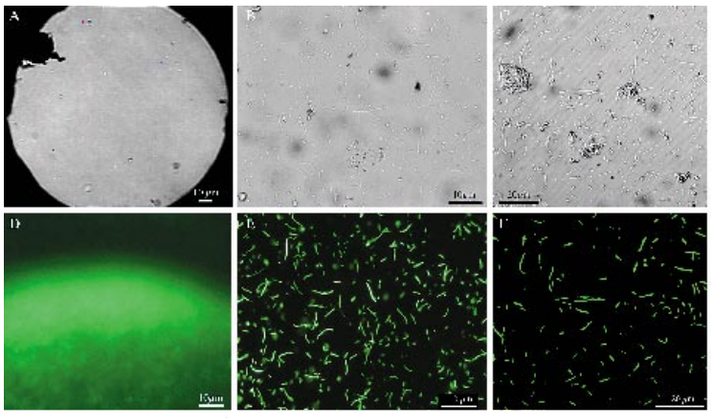
►Origin of life, and interactions between minerals and life◄

► **Team leader** ► ***Isabelle Daniel,*** *professor* ◄

► **Team members** ► *Anne-Marie Aucour, assistant professor; Vincent Balter, associate researcher; Chantal Douchet, assistant engineer; Gilles Dromart, professor; Laurence Lemelle, associate researcher; Philippe Oger, associate researcher; Sylvain Pichat, assistant professor; Bruno Reynard, senior researcher.* ◄

Progresses in imaging of microorganisms under high pressures in diamond anvil cells, from classical cells (left) to cells designed in the laboratory in classical (middle) or confocal (right) microscopie, in the visible (top) and in epifluorescence mode (bottom). Cell division can be followed in situ, as well as metabolism using X-ray or Raman spectroscopies. Oger et al. Development of a low-pressure diamond anvil cell and analytical tools to monitor microbial activities in situ under controlled P and T BBA 1764 (2006) 434-442 ▼

This theme is developed by a mixed group of biologists, geologists and physicists. We share our experimental skills to design and perform experiments dedicated to the recognition of the fingerprint of life in terrestrial and extra-terrestrial rocks. The case of extra-terrestrial rocks is of course related to the preparation of a spatial mission, which might bring back to Earth Martian rocks within the next decades. For instance, we use microscopic observations and spectroscopic methods such as fluorescence, or X-ray spectroscopy, to recognize bacteria at the surface of minerals, and to characterise the specific changes induced by the bacteria at the surface of minerals. In the frame of terrestrial issues, we attempt to estimate the limits for life within the depth of the Earth. Beyond the fundamental question, we also want to know how micro-organisms evolve with depth, and how important they are in the physical and chemical characteristics of rocks. This should help to recognize the early traces of life. Hence, we investigate by means of various spectroscopic tools the behaviour of live cells and of some cellular compounds of key interest as a function of pressure and temperature, in order to identify the changes that would affect the organic traces of life in the geological records. We also measure experimentally the isotope signature of selected elements involved in the metabolism of a large number of micro-organisms, in order to use that signature in rocks to reconstruct paleo-climates, and to look for biological signatures in old rocks. At a somewhat different scale, we also try to identify the relative role of micro-organisms in the porosity and permeability of carbonate rocks, which are key parameters to evaluate the quality of those rocks as oil reservoirs, and to infer the best process to recover as much oil as possible.



Selected publications:

►Daniel I., Oger P., Winter R. Origin of life and biochemistry under high pressure-conditions - Chemical Society Reviews 35 (2006) p. 858-875.

►Lemelle L., Labrot P., Salome M., Simionovici A., Viso M., Westall F. In situ imaging of organic sulphur in 800 My-old neoproterozoic microfossils by x-ray spectromicroscopy at the S K-edge. Organic Geochemistry 39, 2 (2008) p.188-202

►Balter V., Blichert-Toft J., Braga J., Telouk P., Thackeray F., Albarède F. U-Pb dating of fossil enamel from the Swartkrans Pleistocene hominid site, South Africa. Earth and Planetary Science Letters 267 (2008) p. 236-246

►EARTH SCIENCE LABORATORY - LST◄

►Dynamics of the Earth and Planetary interiors◄

► **Team leader** ► ***Yanick Ricard,*** *senior researcher* ◄

► **Team members** ► *Francis Albarède, professor; Thierry Alboussiere, researcher; Muriel Andreani, associate professor; Hervé Bertrand, associate professor; Janne Blichert-Toft, senior researcher; Paul Capiez, engineer; Hervé Cardon, engineer; Frédéric Chambat, associate professor; Nicolas Coltice, associate professor; Isabelle Daniel, professor; Eric Debayle, senior researcher; Chantal Douchet, engineer; Fabien Dubuffet, researcher; Caroline Fitoussi, researcher; Cécile Grigné, postdoctoral researcher; Hiroki Ichikawa, postdoctoral researcher; Stéphane Labrosse, professor; Jan Matas, researcher; Gilles Montagnac, engineer; Jean-Philippe Perillat, associate professor; Bruno Reynard, senior researcher; Philippe Telouk, engineer; Bertrand Van de Moortele, engineer; Lucile Bezacier, Mélanie Chollet, Nicolas Flament, Julien Monteux, Sylvain Petitgerard, Antoine Rozel, Martina Ulvrova PhD students.* ◄

► **The "geodynamic team" studies the forces acting in the Earth's interior on geological time scales. Our main focus is the Earth's mantle, which constitutes the outer 3000 km of our planet.** The mantle is solid for all rapid phenomena, but behaves as a highly viscous liquid on the very long time scale of geological processes. This layer is stirred by convective motions that occur with velocities of a few centimeters a year, and extract the heat stored at great depth or produced by the decay of radiogenic elements. The dynamics of the mantle is coupled with that of the liquid iron core in which the Earth's magnetic field is produced. The necessary conditions for this dynamo process provide information on the mantle's thermal regime. Near the surface, the mantle carries the lithosphere and the crust as well as controls the dynamics of plate tectonics. The forces that drive the mantle are responsible for the geological activity of the planet.

We try to understand the structure of the mantle from the anomalies of the Earth's gravity field, from the distribution of seismic velocities, and from the confrontation with mineralogical data measured in laboratories at mantle pressure and temperature.

We model the present day dynamics of the Earth and its evolution during the last billion years using simple physical models as well as high performance numerical simulations.

We want to understand why plate tectonics is so specific to our planet by comparing the dynamics of the Earth to that of the other solid planets.

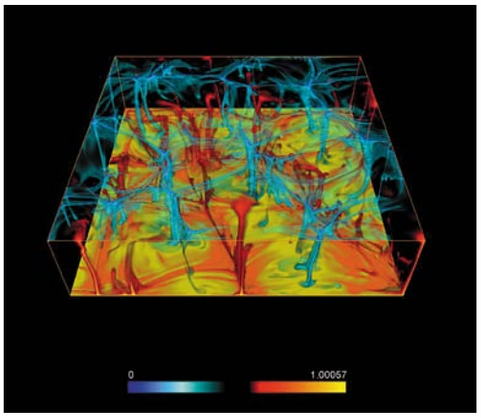
We also study the early stages of the history of the Earth when the primitive planet differentiated into mantle, core and early crust.

Selected publications:

►A crystallizing dense magma ocean at the base of the Earth's mantle
Author(s): Labrosse S, Hernlund JW, Coltice N
Source: NATURE Volume: 450 Issue: 7171 Pages: 866-869 Published: DEC 6 2007

►Global warming of the mantle at the origin of flood basalts over supercontinents
Author(s): Coltice N, Phillips BR, Bertrand H, et al.
Source: GEOLOGY Volume: 35 Issue: 5 Pages: 391-394 Published: MAY 2007

►High-pressure creep of serpentine, interseismic deformation, and initiation of subduction
Author(s): Hilairet N, Reynard B, Wang YB, et al.
Source: SCIENCE Volume: 318 Issue: 5858 Pages: 1910-1913 Published: DEC 21 2007



◄ *Model of convection in a box. The fluid is heated from the bottom and cooled from the surface. Thermal instabilities (hot in red, cold in blue) are rising from the bottom and sinking from the surface. The Earth's mantle undergoes this type of convective dynamics although it is not heated from its base but mostly cooled from its surface.*

►FUNCTIONAL GENOMICS INSTITUTE - IGFL◄

► **DIRECTOR** ► *Vincent Laudet, Professor - directeur.igfl@ens-lyon.fr* ◄
► **TOTAL PERSONNEL** ► *90* ◄
► **PARTNERS** ◄ *UCB Lyon 1, CNRS, INRA* ◄
► **WEB** ◄ *http://igfl.ens-lyon.fr/* ◄

► The IGFL is devoted to basic research in the field of integrative biology of animal models. Our aim is to understand the functions and the evolution of complex biological systems, to identify genetic regulatory networks and how these networks are operative during development and under physiological and/or pathological situations in the adult. We are also interested in determining how these networks were modified during evolution, for example during specific adaptations driven by natural selection or during complex events such as domestication. Although a basic research institute, the IGFL is nevertheless also concerned by the application of its research in health sciences and wants to contribute to a better knowledge of biodiversity. The scientific fields covered extends from functional genomics (nuclear receptor function at the organism level, metabolism, transcriptional regulation) to developmental biology (organogenesis of mineralized tissues such as bones and teeth, neurodevelopment, stem cells, sex determination and differentiation) and evolutionary genomics (sex evolution, genomics of adaptation, ancient DNA research, transposable elements). Several biological models are used by the IGFL teams depending on their relevance to the biological questions asked: mouse, rat, chicken, zebrafish or medaka are available but also tribolium, amphioxus, cave bear or platyfish, either as live stocks or through derivative materials. The IGFL hosts the national platform for paleogenetics which allows researchers in the field of ancient DNA to perform specific experiments in the best possible conditions.
The IGFL is organized in 9 independent research groups and will expand by attracting young talented group leaders. We are widely open at the international level through participations to several European programs (network of excellence or integrated projects) as well as by establishing long-term collaborations with several institutions in Europe, USA or Asia.

CURRENT RESEARCH TOPICS
Functional genomics, Development, Molecular endocrinology, Evolution

RELATED FIELDS
Cell differenciation, Experimental genetics, Paleogenetics

AREAS OF APPLICATION
Human Health, Biodiversity

INDUSTRIAL PARTNERS
Sanofi Aventis

EQUIPMENT
National Platform for Paleogenetics

►FUNCTIONAL GENOMICS INSTITUTE - IGFL◄

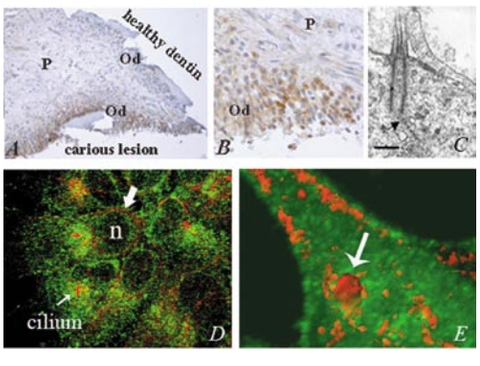
►Odontoblasts and dental tissue regeneration◄

► **Team leader** ► ***Françoise Bleicher,*** *Professor, Team leader's - francoise.bleicher@ens-lyon.fr* ◄
► **Team members** ► *Florence Carrouel, postdoctoral fellow; Marie-Lise Couble, engineer; Stéphanie Durand, graduate teaching assistant; Jean-Christophe Farges, professor; Jean-François Keller, PhD student; Nicolas Lehmann, graduate teaching assistant; Henry Magloire, professor; Marie-Jeanne Staquet, research associate; Dominique Seux, associate professor; Béatrice Thivichon-Prince, graduate teaching assistant.* ◄

► **Odontoblasts, located at the pulp/dentine interface and partly included in calcified tubules, are organized as a single layer of specialized cells** (in close contact with sensory axons) responsible for dentin formation. We are studying the role they play in tooth pain transmission and immune response under carious lesion.

Recent evidence for excitable properties suggests that odontoblasts may operate as sensor cells. Thus, dentinal tubules and odontoblast/nerve complexes represent a unique mechano-sensory system giving dentine forming cells a pivotal role in signal transduction. The mediators of mechano-transduction identified in odontoblasts include mechano-sensitive ion channels and primary cilium. The latter is essential for microenvironment sensing but its role in the control of odontoblast behaviour remains to be elucidated. Our project aims at unravelling the role of the primary cilium during dentinogenesis (control of tooth architecture) and transduction of pain, particularly in hypersensitive teeth.

Cariogenic bacteria trigger inflammatory and immune events in dental pulp, the molecular and cellular determinants of which remain largely unknown. We demonstrated that human odontoblasts are equipped to sense all kinds of pathogens that could enter the tooth. When activated by bacterial components, odontoblasts initiate an immune response by secreting cytokines, chemokines that recruit immature dendritic cells, while down-regulating their specialized function of dentin matrix synthesis. Clinically, the modulation of this response could prevent the apparition of irreversible inflammatory/immune damage in dental pulp. Our project aims at developing therapeutic agents able to limit odontoblast responses to cariogenic bacteria aggression. Development of such agents represents an innovative approach to the treatment of dental caries.



A: Immunolocalization of TLR2 in the dental pulp of carious human third molars. The odontoblast layer present under the carious lesion is stained whereas that under healthy dentin is not. B: Higher magnification showing staining of odontoblasts. C: Ultrastructure of a primary cilium in human cultured odontoblast. A filamentous structure with repeating dots is visible at the base of the cilium (arrow). D: Identification of primary cilium (thin arrow) in human cultured odontoblasts using acetylated a tubulin antibody (red). Large arrow shows the microtubule network connected to the cilium rootlet. Calcium ion channels of the neural form (Cav2.2) are concentrated at the base of the cilium (green). E: Confocal laser microscopy and 3D reconstruction of a primary cilium (arrow) emerging from a cultured odontoblast. ►

Selected publications:

►STAQUET MJ, DURAND SH, COLOMB E, ROMÉAS A, VINCENT C, BLEICHER F, LEBECQUE S, FARGES JC. Different roles of odontoblasts and fibroblasts in immunity. J Dent Res. 2008 Mar;87(3):256-61.

►CARROUEL F, COUBLE ML, VANBELLE C, STAQUET MJ, MAGLOIRE H, BLEICHER F. HUGO (FNDC3A): a new gene overexpressed in human odontoblasts. J Dent Res. 2008 Feb;87(2):131-6.

►Magloire, H., Couble, M.L., Thivichon-Prince, B., Maurin, J.C. and Bleicher, F. (2008) Odontoblast: a mechano-sensory cell. J Exp Zoolog B Mol Dev Evol. 2009 Jul 15;312B(5):416-24.

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►Functional Genomics of Reproduction◄

► **Team leader** ► ***Philippe Durand,*** *Research Director First Class - philippe.durand@ens-lyon.fr* ◄
► **Team members** ► *Philippe Durand, Research Director First Class; Bruno Barenton, Research Director Second Class; Frantz Bouhallier, PhD student; Hervé Lejeune, Full Professor; Guillaume Montillet, Engineer; Marie-Hélène Perrard, Research Associate First Class ; Ingrid Plotton, Associate Professor; Franca Raucci, Postdoctoral fellow; Jean-Pierre Rouault, Research Associate First Class.* ◄

► **During spermatogenesis, diploid spermatogonia divide mitotically several times to provide a population of spermatocytes** that proceed through meiosis to give birth to haploid spermatids ; these latter undergo, during spermiogenesis, a morphological differentiation leading to spermatozoa. Spermatogenesis requires the realization of a particular genetic program which occurs in a specific environment («niche»). Indeed, multiplication, differentiation and apoptosis of male germ cells are finely regulated by pituitary hormones (LH and FSH) and by a complex network of factors originating from both the somatic cells and the germ cells of the testis. Our project focuses on a genomic and a physiopathological approach of spermatogenesis with applications in human reproduction, toxicology and in the biotechnologies of reproduction in laboratory and farm animals.. Several aspects will be studied :

Numerous regulations occur during spermatogenesis; post-transcriptional control being very important. Our work seeks to establish the role and the functional relevance of some of these post-transcriptional controls by studying the role of miRNA.

In order to understand the role of the intratesticular factors, we will perform time and cell specific invalidation of the receptors of intratesticular factors, in vitro and in vivo, by the Cre/lox or RNAi approaches. This strategy will allow to by-pass the problem of the endogenous production of the factor..

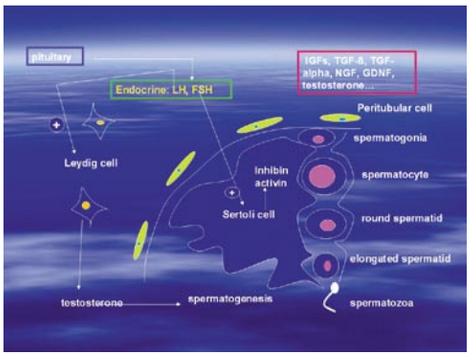
As for spermatogenesis disorders, our project relates to the quantification of regulatory factors of spermatogenesis in testicular biopsies of patients needing assisted reproduction, and to the realization of human spermatogenesis steps in vitro.

Selected publications:

►FROMENT P., VIGIER M., NÈGRE D., FONTAINE I., BEGHELLI J., COSSET F.L., HOLZENBERGER M., DURAND P. Inactivation of the insulin-like growth factor-1 receptor gene in primary Sertoli cells. Journal of Endocrinology, 2007, 194, 557-568.

►PERRARD M.H., VIGIER M., DAMESTOY A., CHAPAT C., SILANDRE D., RUDKIN B.B., DURAND P. Beta-nerve growth factor participates in an auto/paracrine pathway of regulation of the meiotic differentiation of rat spermatocytes. Journal of Cellular Physiology, 2007, 210, 51-62.

►GODET M., SABIDO O., GILLERON J., DURAND P. Meiotic progression of rat spermatocytes requires mitogen-activated protein kinases of Sertoli cells and close contacts between the germ cells and the Sertoli cells. Developmental Biology, 2008, 315, 173-188.



◄ *Regulation of spermatogenesis*

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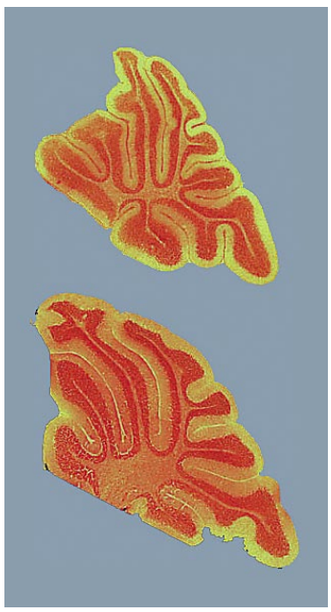
►Neurodéveloppement◄

► **Team leader** ► ***Frédéric Flamant*** *PHD - Frederic.flamant@ens-lyon.fr* ◄
► **Team members** ► *François Beby, PhD student; Fabrice Chatonnet, postdoctoral fellow; Teddy Fauquier, postdoctoral fellow; Frédéric Flamant, research director; Pierre Godement, research director; Romain Guyot, engineer; Frédéric Picou, PhD student; Sabine Richard, research associate.* ◄
http://igfl.ens-lyon.fr/les-equipes/equipe-3

► **The development of the central nervous system, and its late post-natal maturation, imply a complex network of genetic regulation and cellular interactions,** which are still poorly understood. The Neurodevelopment group studies the influence of thyroid hormone on development and function of the central nervous system. We use advanced mouse genetics methods to understand the various modes of action of thyroid hormone nuclear receptors during pre- and post-natal brain development. Detailed analysis of transgenic mice phenotype, at the molecular and cellular level, combined with controlled expression of receptors mutation, using the CRE/loxP genetic recombination system, allows up to identify primary consequences of these mutations. We hope that the identification of thyroid hormone receptors target genes will bring new insight on many aspects of brain development and function.



► *The upper image is a section of the cerebellum of a mutant mice expressing a mutated receptor for thyroid hormone. Compairison to wild-type littermate control (lower panel), reveal a number of alterations in neural cells proliferation and migration.*

Selected publications:

►QUIGNODON L, VINCENT S, WINTER H, SAMARUT J, FLAMANT F. A point mutation in the activation function 2 domain of thyroid hormone receptor alpha1 expressed after CRE-mediated recombination partially recapitulates hypothyroidism. Mol Endocrinol. 2007 Oct;21(10):2350-60.

►DKHISSI-BENYAHYA O, GRONFIER C, DE VANSSAY W, FLAMANT F, COOPER HM. Modeling the role of mid-wavelength cones in circadian responses to light.Neuron. 2007 Mar 1;53(5):677-87.

►FOSSAT N, LE GRENEUR C, BÉBY F, VINCENT S, GODEMENT P, CHATELAIN G, LAMONERIE T. A new GFP-tagged line reveals unexpected Otx2 protein localization in retinal photoreceptors. BMC Dev Biol. 2007 Nov 2;7:122.

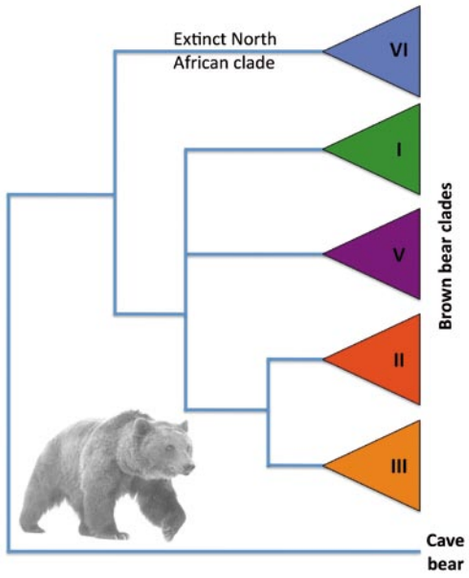
►FUNCTIONAL GENOMICS INSTITUTE - IGFL◄

►Paleogenetics and Molecular Evolution◄

► **Team leader** ► ***Catherine Hänni,*** *Research Director - catherine.hanni@ens-lyon.fr* ◄
► **Team members** ► *Olivier Chassaing, PhD student; Marilyne Duffraisse, Engineer; Benjamin Gillet, Engineer at the PALGENE platform; Sandrine Hughes, Research Associate first class; Mohamad Merheb, PhD student; Ludovic Orlando, Associate Professor; Maud Pionnier, PhD student.* ◄

http://igfl.ens-lyon.fr/les-equipes/equipe-4

► **The "Paleogenetics and Molecular Evolution" team is using and studying ancient DNA molecules to perform research in the field of molecular evolution and comparative genomics.** The team is involved in many research programs all using the genetic information retrieved from the past to better understand the evolutionary history of animal populations, extinct animal species but also human evolution trough time. Our most recent breakthrough focused on domestication of goats and sheep to better understand what were their wild progenitors and how the domesticated animals have spread in Europe during the Neolithic period. We are studying ancient brown and cave bears populations at the genetical level to see how climatic changes impact population dynamics, a question of immediate importance in these times of global warming. We are also interested in human evolution, with a special interest in our past relashioships with Neandertals. In a more methodological field of research, we enlarge the type of materials used to retrieve DNA (leather or organic remains found in amphora etc..).We developp new methods for analysing ancient DNA and this is a particularly important goal given that, thanks to high-throughput sequencing, ancient DNA research reaches the genomic scale. Our team is at the origin of the French National Platform for Paleogenetics, PALGENE, settled by the CNRS and ENS Lyon, and open to the scientific community.



◄ *Our team evidenced a recent lost of genetic diversity in brown bears. We identified a divergent and now extinct clade in North Africa by studying the mitochondrial DNA extracted from bear bones dated of 1,300 years BP and 7,500 years BP from two North African caves.*

Selected publications:

►Calvignac S., Terme J.M., Hensley S., Jalinot P., Greewood A., Hänni C. Ancient DNA identification of early 20th century Simian T-cell Leukemia Virus type 1 (STLV-1) from a museum specimen bone , Mol. Biol. Evol. 2008, 25 : 1093-1098

►Pagès M., Calvignac S., Klein C., Paris M., Hughes S., Hänni C. Combined analysis of fourteen nuclear genes refines the Ursidae phylogeny. Mol. Phylogenet. Evol., 2008, 47(1):73-83.

►Krause J., Orlando L., Serre D., Viola B., Prüfer K., Richards M.P., Hublin J.J., Hänni C., Derevianko A.P., Pääbo S. Neanderthals in central Asia and Siberia. Nature, 2007, 449(7164):902-4.

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►Cell biology and bone physiopathology◄

► **Team leader** ► ***Pierre Jurdic*** *- pjurdic@ens-lyon.fr* ◄
► **Team members** ► *Romain Dacquin, postdoctoral fellow; Elodie Decembre, assistant engineer CNRS; Chantal Domenget, engineer; Anne Claire Duchez, PhD student; Anne Gallois, PhD student; Irma Machuca, research assistant first class; Marlène Mazzorana, research assistant first class; Murthy Pandruvada, postdoctoral fellow.* ◄

► **We study bone physiology through human and murine models, using cell biology approaches**. Bone is a dynamic tissue formed during development, renewed during adult life and finally degraded when aging through the coordinated action of resorption by osteoclasts and formation by osteoblasts. Osteoclasts are cells of hematopoietic origin deriving from the monocytic lineage similarly to macrophages and immune dendritic cells (DC). We have defined three main topics†to decipher bone physiopathology:

- Osteoimmunology. We brought the first demonstration that DC can transdifferentiate into osteoclasts. Our results suggest that inflammatory conditions, such as in rheumatoid arthritis, potentiate transdifferentiation. Our goals are†1) to prove this hypothesis in rheumatoid arthritis murine models†; 2) to identify different osteoclast subpopulations.

Histological section of the diaphysis of a mouse femur. Bone is in black. ►

- Cytoskeleton dynamics. By using osteoclasts constitutively expressing actin fused to GFP, we have deciphered the dynamic organization of the actin cytoskeleton of osteoclasts adherent either onto glass or apatite mineral. We want to precise the molecular mechanisms implicated in osteoclast-mediated bone degradation.
- Signaling molecules. Due to several observations we have postulated that signaling molecules such as semaphorins could be implicated either in the osteoclast differentiation pathway or in bone physiology. We are currently testing this hypothesis using mice with semaphorin gene inactivation. We use histomorphomeyty analyses to better characterize the phenotype of mutant mice.

Selected publications:

►CHABADEL A., BANON-RODRIGUEZ I., CLUET D., WERHLE-HALLER B., GENOT E., JURDIC P., ANTON I., and SALTEL F. (2007). CD44 and _3 integrin organize two functionally distinct actin based domains in osteoclasts. Mol. Biol. Cell 18, 4899-4910.

►SALTEL F., CHABADEL A., BONNELYE E., and JURDIC P. (2008). Actin cytoskeletal organization in osteoclasts: a model to decipher transmigration and matrix degradation. Eur. J. Cell Biol. 87, 459-468. (review)

►GALLOIS A., LACHUER J., YVERT G., WIERINCKX A., BRUNET F., RABOURDIN-COMBE C., DELPRAT C., JURDIC P., and MAZZORANA M. (2009). Genome-wide expression analyses establish dendritic cells as a new osteoclast precursor able to generate bone-resorbing cells more efficiently than monocytes. J. Bone Min. Res. (in press).

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►Molecular Zoology◄

► **Team leader** ► ***Vincent Laudet,*** *Professor first class - vincent.laudet@ens-lyon.fr* ◄
► **Team members** ► *Gérard Benoit, Research Associate First Class; Laure Bernard, engineer; François Bonneton, associate professor; Florent Campo-Paysaa, PhD student; Jie Chen, PhD student; Pascale Chevret, research associate first class; Christelle Gobet, engineer; Anne Lambert, engineer; Ingrid Masse, postdoctoral fellow; Gabriel Markov, PhD student, Sophie Pantalacci, postdoctoral fellow; Mathilde Paris, PhD student; Michael Schubert, research associate second class; Marie Sémon, associate professor; Maria Theodosiou, postdoctoral fellow; Marie Tohme, PhD student; Gérard Triqueneaux, engineer; Philippe Veber, postdoctoral fellow.* ◄
http://igfl.ens-lyon.fr/les-equipes/equipe-6

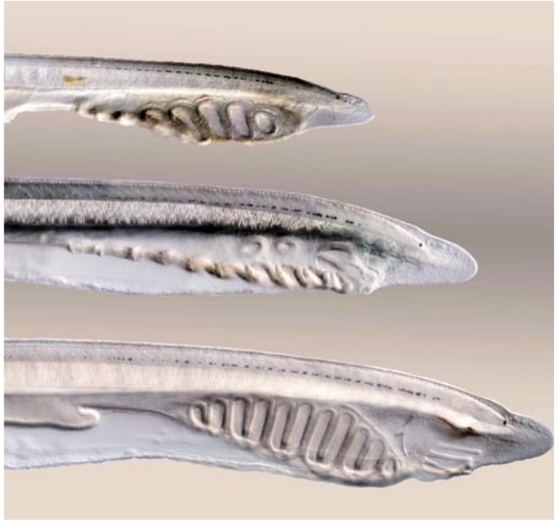
► **Our team use molecular and developmental biology to address basic evolutionary questions on two main issues.** We first study nuclear hormone receptors (mainly thyroid hormone receptors, retinoid receptors and estrogen receptors) at the evolutionary level by studying the main steps of their diversification (mainly at the level of ligand binding) as well as the role they played during evolution. We recently shown by studying an invertebrate chordate (the amphioxus; see picture) that metamorphosis regulated by thyroid hormones is present in all vertebrates. We also compare by a combination of functional analysis and target gene identification (« ChIP on chip ») the transcriptional network regulated by retinoid in several model systems (amphioxus, zebrafish, mouse). Our second main topic concerns the evolution of teeth. We use teeth in both rodents and fishes as a model system to identify genes that were targets of natural selection in controlling the shape of these complex structures. We are focusing on a specific pathway, the ectodysplasin (EDA) pathway that plays an important role in all ectodermal appendages (teeth, hairs, feathers, scale etc...). In rodent we study how changes in the regulation or biochemical activity of members of this pathway may have play a role in the tremendous diversification of teeth patterns actually observed in rodents. In fishes we have shown that retinoic acid are instrumental in pharyngeal teeth formation in the zebrafish. We are currently investigating if this signaling pathway has played a role in the loss of oral teeth and pharyngeal teeth diversification in Cypriniformes.

Selected publications:

►BERTRAND S., THISSE B., TAVARES R., SACHS L., CHAUMOT A., BARDET P-L., ESCRIVA H., DUFFRAISSE M., MARCHAND O., SAFI R., THISSE C., LAUDET V.. Unexpected novel relational links uncovered by extensive developmental profiling of nuclear receptor expression. PLOS Genetics, 2007, 3, e188.

►PANTALACCI S., CHAUMOT A., BENOIT G., SADIER A., DELSUC F., DOUZERY E. LAUDET V. How a signaling pathway evolved: conservation, evolutionary shifts and elaboration of the EDA pathway during vertebrate evolution. Mol Biol Evol. 2008, 25, 912-928.

►PARIS M., ESCRIVA H., SCHUBERT M., BRUNET F., BRTKO J., CIESELSKI F., ROECKLIN D., VIVAT-HANNAH V., JAMIN E.L., CRAVEDI J-P., SCANLAN T.S., RENAUD J-P., HOLLAND N.D. LAUDET V. Amphioxus metamorphosis and the origin of the thyroid hormone signalling pathway. Current Biology, 2008, 18, 825-830.



The cephalochordate amphioxus displays striking morphological modifications during metamorphosis. Premetamorphic larvae (top) are asymmetric and present only one gill-slit row on the right side of the body. During metamorphosis, conspicuous remodeling occurs—e.g., the appearance of a second gill-slit row on top of the first one, which migrates to the other side of the body. Our team have shown that thyroid hormones triggers this metamorphosis.
▼

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►Oncogenesis and Development◄

► **Team leader** ► ***Jacques Samarut,*** *Full Professor - jacques.samarut@enslyon.fr* ◄
► **Team members** ► *Nathalie Allioli, associate professor; Dogus Altintas, PhD student; Denise Aubert, engineer; Anne Marie Birot, engineer; Laurence Canaple, postdoctoral fellow; Damien Cureton, technician; Myriam Decaussin Petrucci, associate professor; Karine Gauthier, reasearch associate; Anne Mey, research associate; Julien Nadjar, technician; Michelina Plateroti, research associate; Patrick Ravel-Capuis, associate professor; Amélie Rezza, PhD student; Alain Ruffion, full professor; Maria Sirakov, postdoctoral fellow; Sandrine Thenot, research associate; Violaine Tribollet, technician; Maïa Veron, PhD student; Séverine Vincent, engineer; Virginie Vlaeminck-Guillem, associate professor.* ◄
http://igfl.ens-lyon.fr/

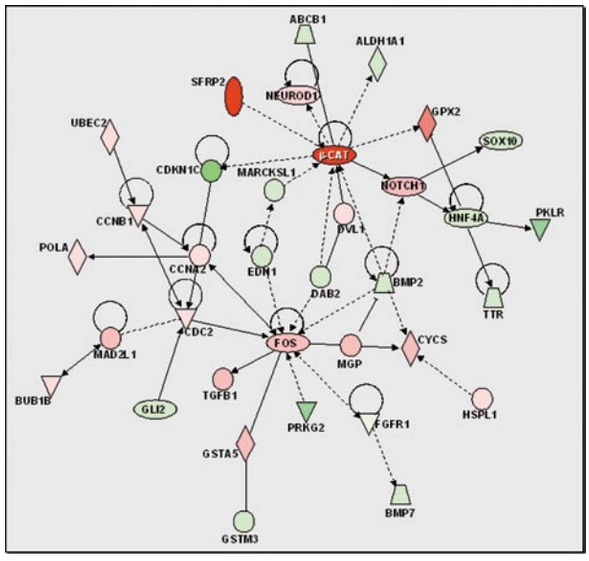
► Nuclear hormone receptors in normal and pathologic development.

Nuclear hormone receptors are major transcriptional regulators controlling essential functions in vertebrates. We are interested in the roles and mechanisms of action of both thyroid hormone and androgen receptors.

We are dissecting the respective functions of the various isoforms of thyroid hormone receptors in the development and homeostasis of tissues in the mouse using targeted mutant and transgenic mice together with genomic analyses. The functions we are investigating include intestine crypt homeostasis, glucose and lipid metabolism and atheroma development.

We are addressing the question of the roles of androgen receptors in human prostate tumor development. The approach consists in identifying target genes of the receptors in the chromatin of prostate cells and investigating the roles of these genes in prostate cell physiology.

Network of genes regulated by thyroid hormone through the TRa receptor in mouse intestine crypts. Scheme constructed from transcriptome analysis on laser microdissected crypts followed by Ingenuity Pathway Analysis. Activated genes are depicted in pink and red; repressed genes are depicted in green. Arrows and lines indicate functional relationships between genes. ▼



► Regulation of gene expression in embryonic stem cells and early embryo.

We are using pluripotent chicken embryonic stem cells to identify molecular mechanisms controlling chromatin organization and gene expression at the earliest steps of embryonic development. More specifically we analyze the role of the ENS-1 gene we have identified to be specifically expressed in pluripotent cells. The ENS-1 protein binds to the HP1γ protein and might control gene expression through contributing to chromatin organization. We are also investigating how expression of the ENS-1 genes is regulated in pluripotent stem cells and during early development of the chick embryo. The approaches consist in manipulating gene expression together with epigenetic studies in ES cells and early chick embryo.

Selected publications:

►Kress E, Rezza A, Nadjar J, Samarut J and Plateroti M (2009). The frizzled-related sFRP2 gene is a target of the Thyroid hormone Receptor alpha1 and activates b-catenin signaling in the intestinal epithelial progenitors . J. Biol. Chem. 284: 1234-1241.

►Lavial F., Acloque H., Bertocchini F., MacLeod D.J., Boast, S. Bachelard E., Montillet G., Thenot S., Sang H.M., Stern C.D., Samarut J., Pain B.2007. Chicken PouV, a homologue of Oct4, and Nanog regulate pluripotency in chicken embryonic stem cells. Development 134, 3549-3563.

►Papayanotu C, Mey A, Birot A-M, Saka Y, Boast S, Smith JC, Samarut J and Stern CD. 2008. A mechanism regulating the onset of Sox2 expression in the embryonic neural plate. Plos Biology 1: e2.

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►Physiopathology of orphan nuclear receptors◄

► **Team leader** ► ***Jean-marc Vanacker,*** *research director CNRS - jean-marc.vanacker@ens-lyon.fr* ◄
► **Team members** ► *Stéphanie Bianco, PhD student; Christelle Forcet, senior researcher CNRS; Marlène Gallet, Post-doc; Juliette Sailland, PhD student; Violaine Tribollet, engineer CNRS.* ◄

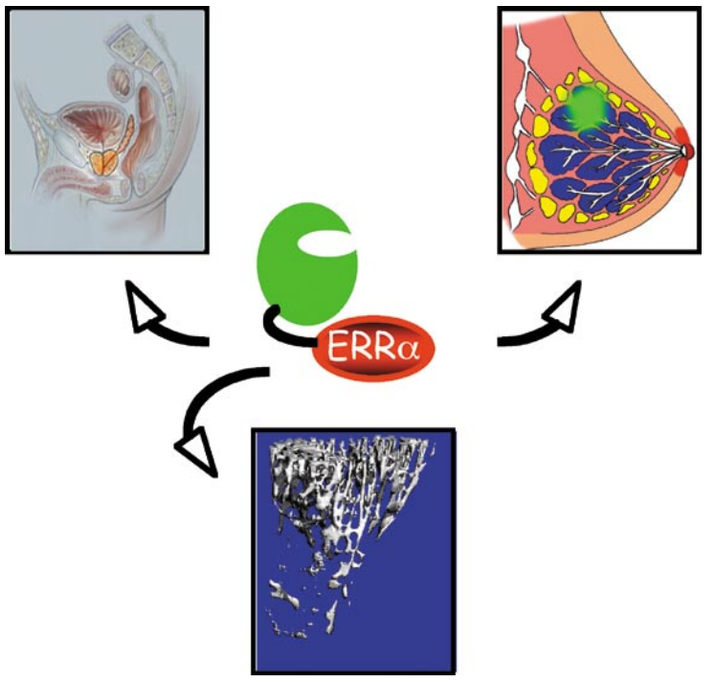
► **ERRα is an orphan (no natural ligand identified to date) member of the nuclear hormone receptor family** which cross-talks with both estrogen and androgen signalings, but is not regulated by these hormones. We study the role of this receptor as such and as an interference factor with hormonal signaling. This is performed in breast and prostate, two tissues in which hormonal (estrogenic and androgenic, respectively) signaling is instrumental. Furthermore, high expression of ERRα in various tumors (including those of breast and prostate) is correlated to a poor prognosis. We thus study the role of the receptor in cell proliferation and migration. In addition we study the functions of ERRα in bone, a tissue in which both estrogen and androgen are major actors.

Selected publications:

►Bianco S, Lanvin O, Tribollet V, Macari C, North S, Vanacker JM 2009 Modulating ERRalpha activity inhibits cell proliferation. J Biol Chem. 284:23286-23292

►Teyssier C, Bianco S, Lanvin O, Vanacker JM. 2008 The orphan nuclear receptor ERRα interferes with steroid signaling. Nucleic Acids Res. 36: 5350-5361

►Lanvin O, Bianco S, Kersual N, Chalbos D, Vanacker JM 2007 Potentiation of ICI182,780 (Fulvestrant)-induced Estrogen Receptor-α degradation by the Estrogen-Receptor Related Receptor-a inverse agonist XCT790. J. Biol. Chem. 282: 28328-28334.



◄ *Determining the functions of ERRα per se and as an interference factor in hormone-responsive tissues.*

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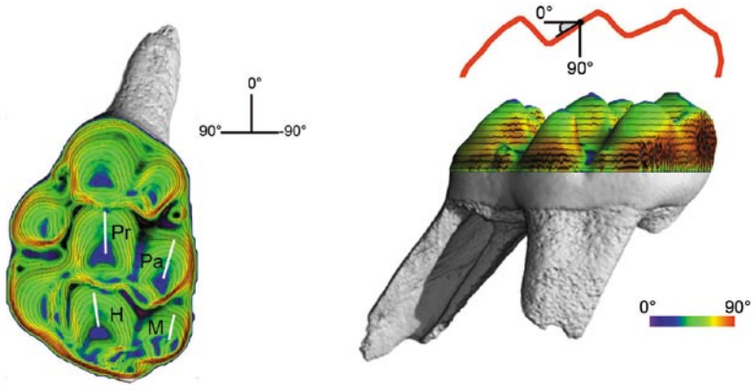
►Evo-Devo of Vertebrate Dentition◄

► **Team leader** ► ***Laurent Viriot,*** *Professor– Laurent.Viriot@ens-lyon.fr* ◄
► **Team members** ► *Antoine Louchart, postdoctoral fellow; Elodie Maitre, postdoctoral fellow; Joseph Nicolas, PhD student; Emmanuel Pasco, PhD student.* ◄

► **For decades, comparative dental anatomy revealed to be an unfailing resource of key characters for taxonomy, phylogeny and reconstruction of diet adaptations of extant and extinct vertebrates.** The biological question addressed by our team aims at better understanding the mechanisms that controlled tooth and dentition morphological changes over the course of evolution. We raised dental anatomy to the status of privileged model for Evo-Devo studies using a broad spectrum data going from field paleontology to developmental biology. The major assets of the team are (1) our expertise in dental comparative anatomy, (2) our competence in 3D imaging and morphometrics, and (3) the consideration of the fossil record as a crucial component of Evo-Devo investigations.



3D Morpho-topographic descriptors of a muroid tooth crown shape; (left) orientation of cusp slope, (right) crown flattening index. All images have been processed from X-Ray Syncrhrotron microtomography at the ESRF. ▼

Our 4 main research directions are:

- Morphogenesis and evolution of jugal teeth in rodents with a privileged target at identifying genes involved in the evolution of molar teeth in muroid rodents;
- Origin and evolution of the evergrowing incisors in rodents;
- Diversity of the pharyngeal dentition in Cypriniformes fish in relation to the pattern of expression of the retinoic acid;
- Mechanism of dental ever-replacement in vertebrates with crocodile dentition taken as a model.

Selected publications:

►LIHOREAU F., BOISSERIE J-R., VIRIOT L., COPPENS Y., LIKIUS A., MACKAYE H., TAFFOREAU P., VIGNAUD P., BRUNET M. (2006) Anthracothere dental anatomy reveals a late Miocene Chado-Libyan bioprovince. PNAS 103:8763-8767.

►LAZZARI V., CHARLES C., TAFFOREAU P., VIANEY M., AGUILAR J-P., JAEGER J-J., MICHAUX J., VIRIOT L. (2008) Mosaic Convergence of Rodent Dentitions. PLoS ONE 3(10):e3607.

►CHARLES C., PANTALACCI S., TAFFOREAU P., HEADON D., LAUDET V., VIRIOT L. (2009) Distinct impacts of Eda and Edar losses of function on mouse dentitions. PLoS ONE 4(4):e4985.

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►Vertebrate Evolutionary Genomics◄

► **Team leader** ► ***Jean-Nicolas Volff,*** *Professor - Jean-Nicolas.Volff@ens-lyon.fr* ◄
► **Team members** ► *Astrid Boehne, PhD student; Frédéric Brunet, Engineer; Delphine Galiana-Arnoux, Associate professor; Christina Schultheis, Postodoctoral fellow; Jean-Nicolas Volff, Full professor.* ◄ *http://igfl.ens-lyon.fr/les-equipes/equipe-9/*

►Teleost fish, which roughly make up half of extant vertebrate species, exhibit an amazing level of biodiversity affecting their morphology, ecology and behavior as well as most other aspects of their biology. This huge variability makes fish extremely attractive for the study of many biological questions, including those related to development and evolution. We are particularly interested in sex determination, reproduction and pigmentation, which are hypervariable characters in fish.

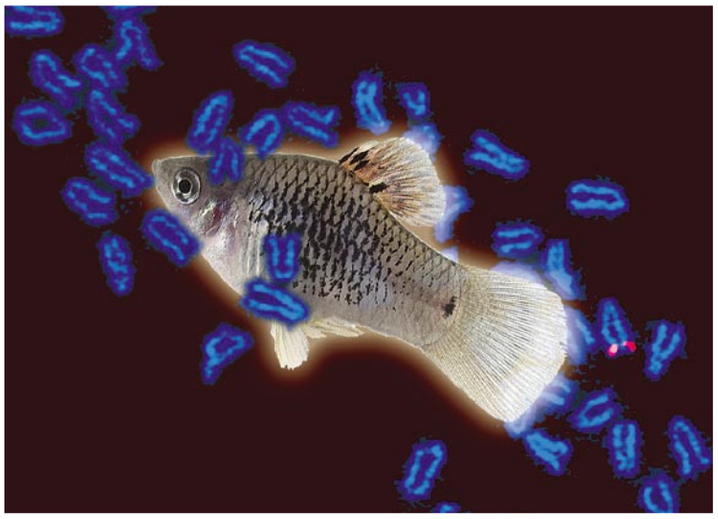
The genome sequences of the pufferfish species *Takifugu rubripes* (Fugu) and *Tetraodon nigroviridis*, the zebrafish *Danio rerio*, the medaka *Oryzias latipes* and the threespine stickleback *Gasterosteus aculeatus*, together with genomic data from various other fish species, have opened an important era of comparative genomics shedding a new light on the structure and evolution of vertebrate genomes. Comparative analyses based on fish genomes have for example revealed the ancestral bony vertebrate genome, confirmed the occurrence of at least one event of genome duplication in the early history of vertebrates and allowed the identification of conserved regulatory and coding sequences in the human genome. Based on this huge mass of information, as well as on our own sequencing projects, we aim to identify through comparative functional genomics peculiar evolutionary mechanisms driving biodiversity in fish. We principally use as models for our studies the platyfish *Xiphophorus maculatus* and the medaka *Oryzias latipes*.

Selected publications:

►BRAASCH I., SCHARTL M., VOLFF J.-N. Evolution of pigment synthesis pathways by gene and genome duplication in fish. BMC Evolutionary Biology, 2007, 7:74.

►VOLFF J.-N., NANDA I., SCHMID M., SCHARTL M. Governing sex determination in fish: repeated regulatory putsches and ephemeral dictators. Sexual Development, 2007, 1:85-99.

►BÖHNE A., BRUNET F., GALIANA-ARNOUX D., SCHULTHEIS C, VOLFF J.-N. Transposable elements as drivers of genomic and biological diversity in vertebrates. Chromosome Research, 2008, 16:203-215.



The platyfish Xiphophorus maculatus is used as a model to study the molecular and evolutionary basis of sex determination in fish. Genes localized on the sex chromosomes of the platyfish (here the Y chromosome is marked red) have been identified and their function is now analyzed in more detail. ▼

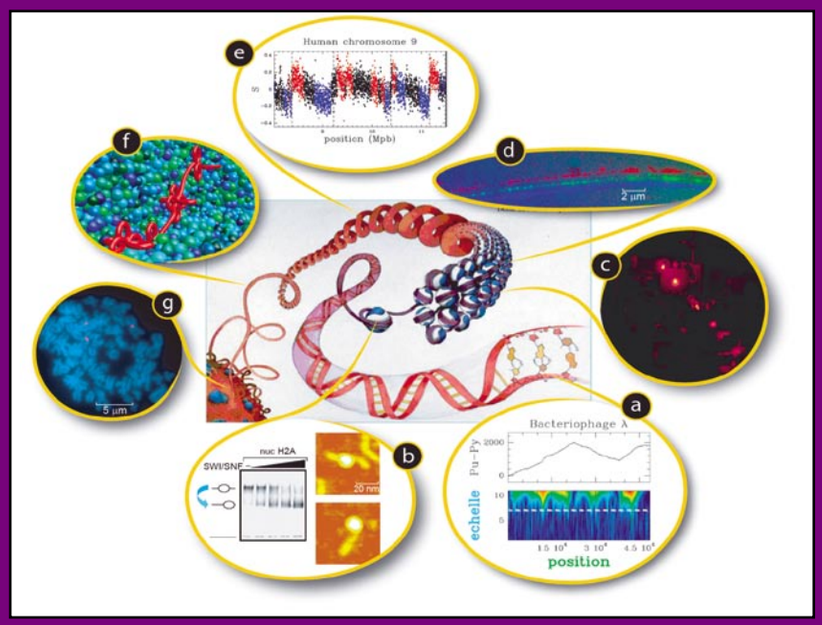
►JOLIOT-CURIE LABORATORY - LJC◄

► **Director** ► **Philippe Bouvet** - *pbouvet@ens-lyon.fr* ◄
► **Total personnel** ► *50* ◄
► **Partners** ◄ *CNRS* ◄
► **Web** ◄ *www.ens-lyon.fr/Joliot-Curie* ◄

► The goal of the Joliot-Curie laboratory is to favor the development of original approaches towards biological objects by researchers from all disciplines. These projects should use innovative, interdisciplinary and complementary approaches (physics, bioinformatics, chemistry, etc.) in addition to biological techniques.
The LJC gives researcher the opportunity to take an original approach to studying a biological object and to spend a period of time, usually three to five years, working in the laboratory elaborating these experiments. The researchers - from all disciplines - involved in these projects are expected to be physically located within the LJC but they remain under the administrative responsibility of their original laboratory.
The projects involved are selected by an international scientific committee based on their originality, interdisciplinarity and complementarities with research performed in other ENS Lyon laboratories. A call for new research projects is issued every year, open to any theme that addresses an important biological issue and requires a complementary, interdisciplinary approach.
The main research areas that are currently developed in the LJC touch on the structure and dynamics of nucleosome remodeling, the functional organization of the genome, the effect of sequence on the structure and dynamic of naked and nucleosomal DNA, the assembly of telomeric complexes, the interaction of the cell with its environment, the real-time tracking of single yeast cells, and the development of polymers for bi-Photon Fluorescence Imaging.

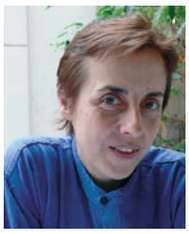
CURRENT RESEARCH TOPICS
Epigenetics, chromatin structure and dynamics, genome organization, the organization of the origin of DNA replication, telomere structure and assembly, single cell biophysics, polymers, cell imaging

EQUIPMENT
Atomic Force Microscopy (AFM), Total Internal Reflection Fluorescence microscope (TIRF), Scanning Surface Plasmon Microscopy (SSPM), Magnetic tweezer



► *Several of the Joliot-Curie Laboratory's projects have for objective the development of the tools necessary to better understand the structure and function of chromatin organization. This is done using a panel of biological, biophysical and bio-informatic techniques. Examples: bioinformatic analysis of genomes (a), chromatin dynamics using AFM and biochemistry (b), chromatin organization using biophysics (c), chromatin combing and the development of new fluorophore probes (d), bioinformatics (e), modeling (f), and cell biology (g).*

►JOLIOT-CURIE LABORATORY - LJC◄

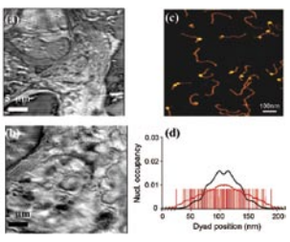


►The dynamics of biological molecules◄

► **Team leader** ► ***Françoise Argoul,*** *research director, CNRS - francoise.argoul@ens-lyon.fr* ◄
► **Team members** ► *Lotfi Berguiga, engineer CNRS; Audrey Fahys, postdoctoral fellow; Monique Marilley, research director; Pascale Milani, postdoctoral fellow; Thibault Roland, PhD student.* ◄

► **The 'Dynamics of biological molecules' team main research interest concentrates on physical properties of DNA-protein assemblies** (chromatin) in vitro and in vivo. Besides its structural functions: (i) packaging DNA into a very small nuclear volume and (ii) strengthening chromosomes during mitosis and meiosis, chromatin has also a dynamical role in the regulation of transcription and replication. The experimental study of this nonstationary system is a quite hard task since it paves several length and time scales: from nanometers (interbase distance 0.3 nm) to several micrometers (size of the nucleus) and from microseconds to hours. Very few physical tools offer the possibility to look at native chromatin inside the nucleus. Most of the previous physical studies on native chromatin have concluded to different pictures of these nucleo-proteic complexes. On the other side, in vitro characterization of chromatin on dyalisis reconstituted nucleosomes on isolated DNA strands led to concept of nucleosome positioning by DNA sequences with a very high affinity with the histone proteins making these nucleosomes. Artificial strongly positioning sequences were synthetized and used as a model of this positioning model.

(a) SSPM imaging of fibroblast cells. (b) zoom of (a) showing the nucleolus compartment in the middle. (c) AFM imaging in liquid of mono-nucleosomes and di-nucleosomes along the yeast (chr. 7) DNA fragment (L = 595 bp) containing the geneYRG105W. (d) Statistical analysis of mono-nucleosome positioning (N = 113 molecules); red bars: experimentally detected dyad locations, red curve: experimental nucleosome occupancy profile, black curve: theoretical predictions of our physical modeling after symmetrization. ▼



AFM visualization of nucleosome positioning by excluding genomic energy barriers

Combining theoretical models and experiments on short DNA strands, we found that rather than positioning, the DNA sequence codes for high energy barriers that inhibit nucleosome formation thus providing some understanding of the nucleosome free regions (NFRs) observed in vivo. Thanks to atomic force microscopy (AFM) visualization of nucleosomes reconstituted on short genomic DNA strands with well characterized sequences we have brought the first experimental demonstration that these excluding genomic energy barriers condition the collective positioning of neighboring nucleosomes consistenly with equilibrium statistical ordering principles. When further investigating how nucleosomes populate two gene promoter regions in Saccharomyces cerevisiae and the human genome, we showed also that the sequence specifies the intrinsic nucleosome occupancy at regulatory sites, thereby contributing to gene regulation.

Imaging nanoscale objects by a nonintrusive optical method.

A high resolution surface plasmon microscope (SSPM) was constructed in the LJC to image nanoscale particles (both metal and polymer) down to 5 nm in size. As compared to other methods, this microscopy is (i) non intrusive and non destructive since it does not require any fluorescent dye tagging, (ii) versatile because it can be oprated in liquid media and coupled to microfluidic systems. With this system we have also succeeded in imaging single nucleosomal particles and internal compartments (nucleolus) of fibroblast cells as illustrated in the figure.

Selected publications:

►L. Berguiga, S.J. Zhang, F. Argoul, J Elezgaray, High resolution surface-plasmon imaging in air and in water: V(z) curve and operating conditions. Optics Lett. 32 (2007) 509-511.

►P. Milani, G. Chevereau, C. Vaillant, B. Audit, Z. Haftek-Terreau, M. Marilley, P. Bouvet, F. Argoul, A. Arneodo Nucleosome positioning by excluding genomic energy barriers. Proc. Natl. Acad. Sci. U.S.A. (2009), under revision.

►T. Roland, A. Fahys, P. Milany, Z. Haftek-Terreau, P. Bouvet, A. Arneodo, F. Argoul, Single nucleosome particle imaging through the optics of a SSPM microscope. (2009), in preparation.

►JOLIOT-CURIE LABORATORY - LJC◄

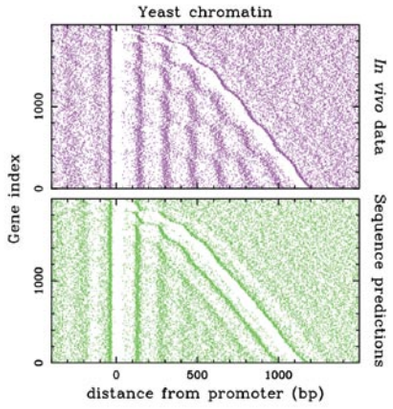
►Genome organization and chromatin structure◄

► **Team leader** ► ***Alain Arneodo,*** *research director first class, CNRS - Alain.Arneodo@ens-lyon.fr* ◄
► **Team members** ► *Benjamin Audit, research associate first class, CNRS; Antoine Baker, PhD student; Guillaume Chevereau, PhD student; Cédric Vaillant, research associate first class, CNRS; Lamia Zaghloul, PhD student.*◄

► **The «Genome organization and chromatin structure» group** is composed of theoretical physicists with expertise in the study of multi-scale phenomena (turbulence, crystal growth, financial time series, etc.) combining the use of concepts from dynamical systems theory and statistical physics with the development of multi-resolution signal and image processing techniques (wavelet transform).

For about a decade, our group has been extending its field of research to the study and modeling of the structure and dynamics of biological molecules (DNA and proteins). Using our wavelet-based methodology to analyze the scale-invariance properties of DNA walk profiles generated with structural tri-nucleotide codings of DNA sequences, we revealed the existence of long-range correlations (LRC), up to ~ 40kbp, in the fluctuations of the double helix local curvature. These LRC are the signature of the DNA-histone protein's interaction within the nucleosomes, the basic units for DNA compaction in eukaryotic cell nuclei that constitute a regulatory factor for accessibility to genetic material. By further modeling DNA as a semiflexible polymer explicitly taking into account the structural disorder induced by the sequence, we have provided some evidence that the observed LRC favor the spontaneous formation as well as the cooperative positioning of nucleosomes along the chromosomes including the nucleosome free regions experimentally observed at gene promoters (see figure below).

Recently, we have broadened our studies of genomic sequences to encompass scales on the order of chromosome lengths (Mbp) while considering alternative codings with a clear functional significance. During evolution, DNA transcription and replication induce some compositional asymmetry (skew) along the DNA sequences. By deploying a multi-scale strategy of sharp upward jump detection in noisy skew profiles, we have identified more than 1000 putative master origins of replication that are central to Human genome organization. Around these putative origins, genes are abundant and broadly expressed, and their transcription is co-oriented with replication fork progression. These features weaken progressively with the distance from putative replication origins. We have proposed that this specific organization could result from the constraints of accommodating the replication and transcription initiation processes at chromatin level, and reducing head-on collisions between the two machineries. Our findings have provided a new model of gene organization in the human genome which integrates transcription, replication, and chromatin structure as coordinated determinants of genome architecture.



▲ *Nucleosome positioning via excluding genomic energy barriers. Nucleosome occupancy (white corresponding to large occupancy values) for the 2000 shortest S.Cerevisiae genes ordered by increasing length from top to bottom and aligned on the promoter (when distance is null). (top) Tiled microarray experimental data (Lee et al., Nature Genetics 39, 1235 (2007)). (bottom) Predictions based on a physical modeling of a sequence-dependent nucleosome energy profile. Note that the organization of the nucleosomal assembly results from the confinement of nucleosomes between sequence induced high energy barriers corresponding to the nucleosome free regions observed at the promoters and gene ends.*

Selected publications:

►B. Audit, S. Nicolay, M. Huvet, M. Touchon, Y. D'aubenton-carafa, C. Thermes & A. Arneodo. DNA replication timing data corroborate in silico human replication origin predictions. Phys. Rev. Lett. 99, 248102 (2007).

►M. Huvet, S. Nicolay, M. Touchon, B. Audit, Y. D'aubenton-carafa, A. Arneodo & C. Thermes. Human gene organization driven by the coordination of replication and transcription. Genome Res. 17, 1278-85 (2007).

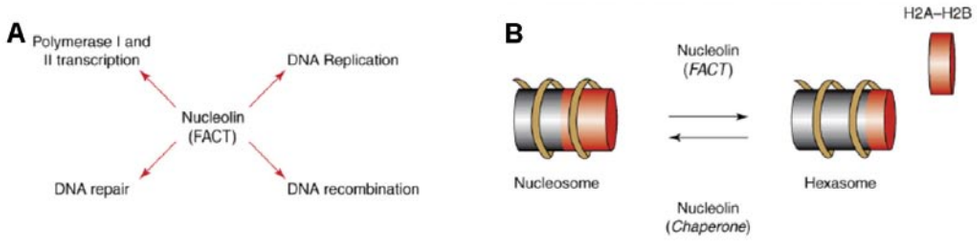
►C. Vaillant, B. Audit & A. Arneodo. Experiments confirm the influence of genome long-range correlations on nucleosome positioning. Phys. Rev. Lett. 99, 218103 (2007).

►JOLIOT-CURIE LABORATORY - LJC◄

►Chromatin assembly and ribosome biogenesis◄

► **Team leader** ► ***Philippe Bouvet,*** *professor - pbouvet@ens-lyon.fr* ◄
► **Team members** ► *Sadhan Das, PhD student; Hélène Delage, technician; Benoit Moindrot, PhD student; Fabien Mongelard, assistant professor; Karine Monnier, postdoctoral fellow; Rodrigo Pinto, postdoctoral fellow; Cong Rong, PhD student.* ◄

► **The alteration of chromatin structure is an important step in the process of gene activation or silencing.** Different factors may influence chromatin dynamics: the incorporation of histone variants on specific chromatin domains, the targeting of post-translational histone modification, and the activity of chromatin remodelers. We use in vitro biochemical approaches, in vivo assays and biophysical experiments in collaboration with the other teams at the Joliot-Curie Laboratory to study the different aspects of chromatin structure and dynamics. In particular, we are contributing to determining the role of the DNA sequences in nucleosome positioning and dynamics and the influence of histone variants on chromatin properties and in the regulation of gene expression. We have previously shown that one histone chaperone was able to assist nucleosome dynamics by the remodeling machineries SWI/SNF and ACF. We are pursuing this work studying the function of several histone chaperones in nucleosome dynamics in vitro and in vivo. The presence of chromatin domains within the cell nucleus also seems to be an important level of organization that may regulate basic processes such as DNA replication and transcription. A. Arneodo's bioinformatics team here at the LJC has identified numerous DNA replication origins. Using cell biology and the latest molecular biology techniques we are studying the organization of these origins within the cell nucleus. In summary, along with the other teams at the Joliot-Curie laboratory, we have adopted an interdisciplinary approach to the study of diverse aspects of chromatin regulation.



A- The histone chaperone nucleolin as a general chromatin modulating factor? FACT and nucleolin have been found to be involved either directly or through interaction with other factors in DNA replication, DNA repair and DNA recombination. These functions might be the consequences of their action on chromatin structure and dynamics. B- The histone chaperone and FACT-like activities of nucleolin. In vitro, nucleolin destabilizes nucleosomes to promote the formation of hexasomes (loss of one H2A–H2B dimer) helping the passage of Pol II through chromatin templates. The histone chaperone activity of nucleolin helps the reformation of nucleosomal structures after the passage of the polymerase. ►

Selected publications :

►MONGELARD F., BOUVET P. Nucleolin: a multifaceted protein. Trends in Cell Biology, 2007, 17,80-6.
►UGRINOVA I., MONIER K., IVALDI C., THIRY M., STORCK S., MONGELARD F., BOUVET P. Inactivation of nucleolin led to nucleolar disruption, cell cycle arrest and defects in centrosome duplication. BMC Mol Biol. 2007, 8: 66.
►CALLÉ A., UGRINOVA I., EPSTEIN A.L., BOUVET P., DIAZ JJ, GRECO A. Nucleolin is required for an efficient herpes simplex virus type 1 infection. J. Virol., 2008, 82: 4762-4773.

►JOLIOT-CURIE LABORATORY - LJC◄

►Polymers for bi-photon fluorescence imaging in infectiology◄

► **Team leader** ► ***Marie-Thérèse Charreyre,*** *research associate first class - marie-therese.charreyre@ens-lyon.fr* ◄
► **Team members** ► *Salim Adjili, PhD student; Cristina Cepraga, PhD student; Marie-Thérèse Charreyre, research associate first class; Arnaud Favier, research associate second class.* ◄

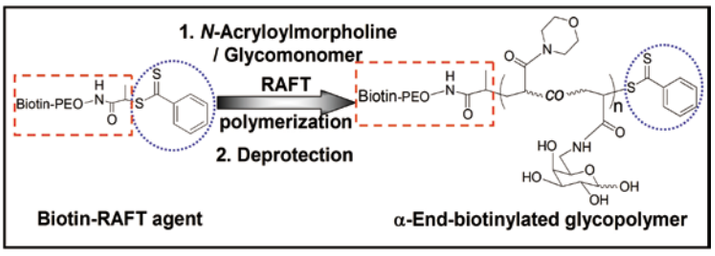
► **In the 13 years it has spent in the CNRS/ bioMérieux laboratory, our group** has acquired expertise in macromolecular engineering for biology especially in *in vitro* diagnostics applications. The originality of our approaches relies on several axes:

- kinetics and mechanistic studies of so-called "living" polymerization techniques (especially the RAFT process) providing very well-defined polymer chains,
- the synthesis of several kinds of macromolecular architectures, such as random copolymers, block copolymers, graft copolymers, end-functional copolymers (including reactive copolymers, glycopolymers and fluorescent polymers),
- the elaboration of polymer/biomolecule conjugates via the immobilization of biomolecules (oligonucleotides and DNA plasmids) onto the various polymer architectures; validation of the resulting conjugates in diagnostic tests or in cell transfection studies.

This new project at the Joliot-Curie laboratory is dedicated to fluorescence imaging, more precisely to the design of original bio-imaging probes combining multifunctional polymers and biphotonic fluorescent chromophores, and to their applications in regards to three specific biological problems:

- the assembly and spreading of viral particles from the host cell,
- the multi-labeling of various phagocyte sub-populations,
- the apoptosis pathway induced by photo-dynamic therapy.

The specific contribution of multifunctional polymers to the bio-imaging probes is based on the immobilization of recognition moieties, labeling moieties and possibly therapeutic or cytotoxic moieties along the chain.



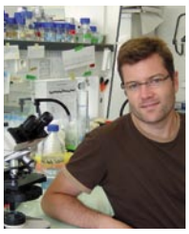
▲ *Synthesis of biotin end-functionalized glycopolymer by RAFT copolymerization*

The project's objective appears relevant for many applications including *ex vivo* cell imaging and *in vivo* diagnostics possibly combined with a local therapy (theranostics). It is based on a multidisciplinary approach that associates chemistry (molecular and macromolecular), spectrophysics and biology (virology and immuno-apoptosis).

Selected publications:

►FAVIER A., DE LAMBERT B., CHARREYRE M.-T. Toward new materials prepared via the RAFT process: From drug delivery to optoelectronics? In Handbook of RAFT Polymerization, Ed. Christopher Barner Kowollik, Wiley-VCH, 2008, pp 485-535..
►DE LAMBERT B., CHAIX C., CHARREYRE M.-T., MARTIN T., AIGUOUI A., PERRIN-RUBENS A., PICHOT C., MANDRAND B. Block copolymer–oligonucleotide conjugates for genotyping on microarrays. Analytical Biochemistry, 2008, 373, pp. 229-238.
►GODY G., BOULLANGER P., LADAVIERE C., CHARREYRE M.-T., DELAIR T. Biotin ·-end-Functionalized Gradient Glycopolymers Synthesized by RAFT Copolymerization. Macromolecular Rapid Communications, 2008, 29, pp. 511-519.

►JOLIOT-CURIE LABORATORY - LJC◄



►Single cell biophysics of epigenetic processes◄

► **Team leader** ► ***Gilles Charvin,*** *junior research investigator - gcharvin@ens-lyon.fr* ◄
► **Team members** ► *Lea Schroeder, Engineer* ◄

► **Over the recent years, single cells time-lapse microscopy has proven very powerful** to study regulatory networks in a quantitative manner. The development of live cell imaging has greatly benefited from the possibility to achieve precise control of cell environment using versatile microfluidics techniques, and from the engineering of numerous fluorescent protein variants.

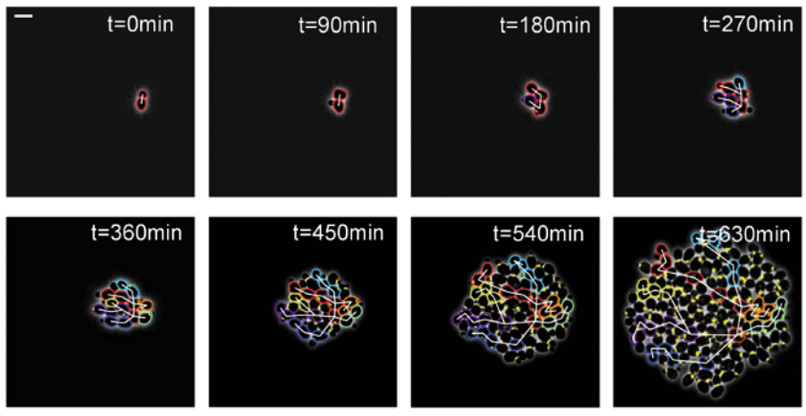
We have developed a microfluidic setup which allows one to induce controlled and reversible gene expression in single dividing cells, whose growth can be tracked over typically 8-10 generati ons. Using this system, we have studied the response of the cell cycle dynamics to periodic forcing of G1 cyclins. This assay, which revealed a powerful way to maintain the synchrony in a population of dividing cells, also shed new light on the mechanism by which the cell implements the control of its size during a division cycle

Further developments of our single cell biophysics approach leads us to the study of long-term biological processes. However, tracking cells over time is intrinsically limited to several generations, due to cell exponential growth (see Figure). As a result, a large class of biological issues spanning larger timescales (typically 10-100 cell generations), like epigenetic processes, can't be followed in real-time. Our goal is to develop novel biophysical techniques to expand the range of tools available in single cell biology, with a main focus on the study of replicative aging in yeast. Other applications include the monitoring of the regulation of chromatin silencing, the control of cell growth, and the adaptation of cell physiology in a changing environment.

Selected publications:

►A microfluidic device for temporally controlled gene expression and long-term fluorescent imaging in unperturbed dividing yeast cells.
Charvin G., Cross F.R., Siggia E.D.
PLoS One. 2008, 3(1):e1468.

►Forced periodic expression of G1 cyclins phase-locks the budding yeast cell cycle.
Charvin G., Cross F.R., Siggia E.D.
Proc Natl Acad Sci U S A. 106(16):6632-7.



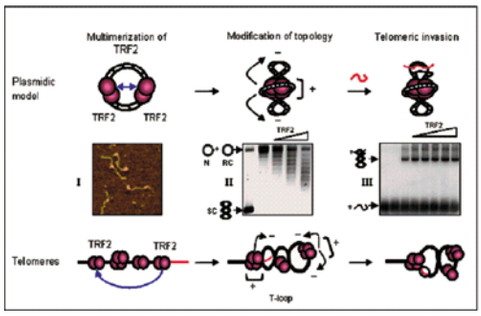
Yeast cells growing the microscope (phase contrast images snapped at indicated timings). We use a custom microlfuidic device to constrain cells in the same focal plane, so that cell contours can be retrieved over many generations. A bud neck marker (CDC10-YFP, see overlayed yellow fluoreccence signal) is used to mark the cell-bud interface and therefore helps with the determination of cell parentage (see colored contours, where each color represent a chain of successive daughters). ►

►JOLIOT-CURIE LABORATORY - LJC◄

►Telomeric complex assembly◄

► **Team leader** ► ***Marie-Josèphe Giraud-Panis,*** *research associate first class - mjgiraud@ens-lyon.fr* ◄
► **Team members** ► *Sabrina Pisano, postdoctoral fellow; Anaïs Poulet, PhD student; Delphine Benarroch-Popviker, postdoctoral fellow.* ◄

► **Telomeres are nucleoproteic structures that cap the end of eukaryotic chromosomes.** They are essential for the stability of the genome and are thought to constitute potential targets for cancer therapy. Telomeres are constructed around specialized proteins that bind the telomeric DNA such as the protein TRF2 which plays a vital role in telomere dynamics and protection against illicit recombination or repair. TRF2 also acts as an essential building block of the telomeric architecture through the folding of telomeric DNA into a lasso-like structure called the t-loop. In a recent publication we have uncovered striking new properties for this protein. We have observed that TRF2 forms multimeric complexes, where the DNA substrate is wrapped around the protein therefore changing the topological state of the surrounding DNA. We have hypothesized that this multimerization and the change in DNA topology are essential events for the formation of the t-loop structure on telomeres. The aim of our current work is to decipher the biological implications of these new findings in t-loop formation in vivo, telomere elongation in cancer cells and telomere biology as a whole. Mutants of the TRF2 protein impaired in various functions (multimerization, wrapping, DNA binding) are constructed and analyzed for their physical (NMR, X-ray crystallography, SAXS, AFM), biochemical (DNA-protein, protein-protein interactions, DNA topology) and biological (effect on telomere physiology) properties. We also investigate the possibility of affecting telomeric functions in cancer cells through the targeting of TRF2 by using functionalyzed peptides.



◄ *When TRF2 binds telomeric DNA, it forms multimeric complexes where DNA is wrapped around the protein core (I, atomic force microscopy image of TRF2-DNA complexes). This wrapping leads to the supercoiling of the neighbouring DNA (II, formation of supercoiled topoisomers on a relaxed closed plasmid). This supercoiling stimulates the invasion of a telomeric single stranded probe in the plasmidic target (III, invasion assay showing the increase in the amount of invaded plasmid with TRF2 concentration). In natural telomeres, TRF2 is thought to create a supercoiled DNA loop by forming multimeric complexes and wrapping DNA. This will stimulate the invasion of the telomeric single strand tail in the telomeric duplex. In our model, the t-loop is formed and stabilized by a process driven by protein-protein association and topological modification of DNA.*

Selected publications:

►Amiard S, Doudeau M, Pinte S, Poulet A, Lenain C, Faivre-Moskalenko C, Angelov D, Hug N, Vindigni A, Bouvet P, Paoletti J, Gilson E, Giraud-Panis MJ.
A topological mechanism for TRF2-enhanced strand invasion.
Nat Struct Mol Biol. 2007 Feb;14(2):147-54.

►Temime-Smaali N, Guittat L, Wenner T, Bayart E, Douarre C, Gomez D,
Giraud-Panis MJ, Londono-Vallejo A, Gilson E, Amor-Guéret M, Riou JF.
Topoisomerase IIIalpha is required for normal proliferation and telomere
stability in alternative lengthening of telomeres.
EMBO J. 2008 Apr 17

►JOLIOT-CURIE LABORATORY - LJC◄

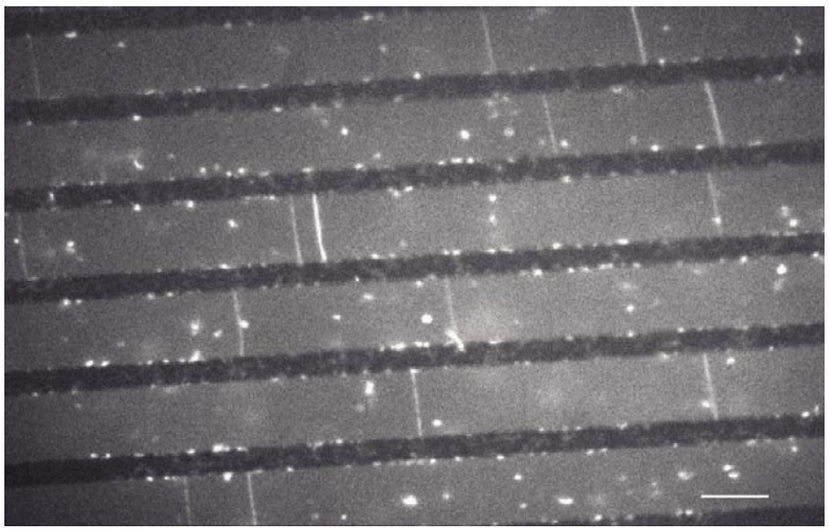
►Physics to study the living◄

► **Team leader** ► ***Christophe Place and Laurence Lemelle**, research associates first class - christophe.place@ens-lyon.fr and llemelle@ens-lyon.fr* ◄
► **Team members** ► *Elodie Chatre, engineer.* ◄

► **Our objective is to lead projects at the interface of physics and biology by developing original technological approaches.** Our main interest, covering different thematic areas, relates to (1) the analysis of single protein behaviour in interaction with immobilized DNA such as the T7 RNA transcription on combed DNA observed by fluorescence microscopy. (2) The characterisation of the whole dynamics of a living cell nucleus by the analysis of the dynamics of the scattered light from the nucleus and (3) the description and hydrodynamics modelling of the behaviour of motile bacteria in the vicinity of a surface using videomicroscopy and Total Internal Fluorescence Microscopy (TIRFM). The techniques developed are based on soft matter physics and optical microscopy, and rely on experiments in biochemistry, microbiology and cell biology.

Selected publications:

►M. Suissa, C. Place, E. Goillot, E. Freyssingeas (2008) ìInternal Dynamics of a Living Cell Nucleus Investigated by Dynamic Light Scatteringî Eur. Phys. J. E, 26, 435-448.
►R. Pomerantz, R. Rashid, Z. Gueroui, C. Place, J. Zlatanova, M. Anikin, W. T. McAllister (2005) ìA tightly regulated molecular motor based upon T7 RNA polymerase.î, Nano Letters, 5, 1698-1703.



Single T7 DNA are bridged over a micropatterned surface. The black lines are 250 nm above the surface floor (grey). The DNA are visualized by fluorescence microscopy using a fluorescent intercalant (bar = 8 µm)
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►PURE AND APPLIED MATHEMATICS UNIT - UMPA◄

► **Director** ► **Laurent Berger**, *professor - dirlab@umpa.ens-lyon.fr* ◄
► **Total personnel** ► *about 50* ◄
► **Partners** ◄ *CNRS* ◄
► **Web** ◄ *www.umpa.ens-lyon.fr* ◄

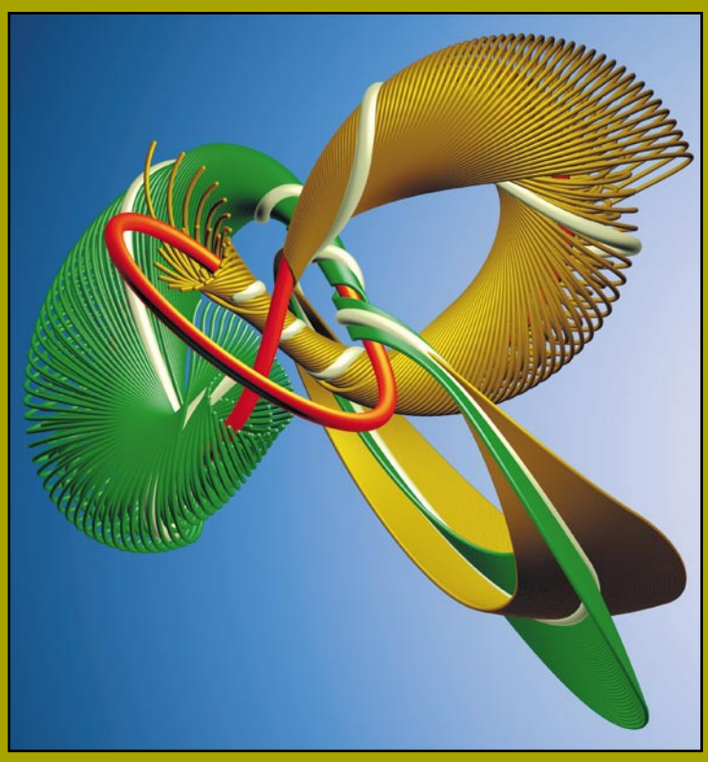
► The ENS Lyon mathematics department is an international-level research institution, in spite of its small size and the youth of its members (half of whom are under 36). Its strong points include:
- the wealth of exchanges between the various themes of research: many researchers participate in the activities of several teams, many seminars and scientific activities are held together;
- as in all Écoles normales supérieures, the rich interactions between research and training, which benefits students as well as researchers.

Scientific activities are lively and training is personalized. For instance, some courses are organized in small groups of 5-6 students around a researcher.

Mathematicians are not keen on splitting their laboratories into distinct "teams," so the UMPA lab only consists of four teams: partial differential equations and modeling; geometry; probability theory; and the most recent of all: algebra and number theory, which is still under development. For simplicity we shall list researchers only once, but it should be noted that many of them actually belong to several teams. This is still another illustration of the great unity of mathematics in general, and of our unit in particular!

Each team has its own seminar and its working seminars. There is also a generalist internal seminar which allows members of the laboratory to be up to date on the activity of their colleagues.

CURRENT RESEARCH TOPICS
Pure and applied mathematics (algebra, number theory, analysis, partial differential equations, geometry, dynamical systems, probability theory, statistical mechanics, modeling, etc.)



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This picture shows the trajectories of the stable and unstable curves at a point with respect to the flow due to the one-parameter subgroup of diagonal matrices of SL2(R) acting on SL2(R)/SL2(Z). The beautiful properties of dynamical systems of this kind have been the object of much study in the geometry group. Picture by Étienne Ghys and Jos Leys.

►PURE AND APPLIED MATHEMATICS UNIT - UMPA◄

►Number theory◄

► **Team leader** ► ***Laurent Berger,*** *professor - lberger@umpa.ens-lyon.fr* ◄
► **Team members** ► *Laurent Berger, full professor; François Brunault, associate professor; Agnès David, assistant professor; Sandra Rozensztajn, associate professor; Mathieu Vienney, PhD student.* ◄

► **The algebra and number theory team** is the most recent addition to the department. So far, it consists of three permanent members and one assistant professor, all of whom are working in arithmetic geometry.

Number theory has its origin in the study of so called Diophantine equations. One wants to find integer solutions of certain equations; a typical example is «find all the right triangles whose three sides have integer length». The «3-4-5» triangle is one such example (and we now know how to generate all the possible solutions). The equations which one studies can also be used to define geometric objects, the locus of their zeroes, and a most surprising discovery is the fact that the geometric properties of these objects have a direct bearing on the properties of the integer solutions of the equations. For example, if one considers an equation in two variables, it defines a Riemann surface which has a certain number of «holes». If that number of holes is two or more, then the equation only has a finite number of integer solutions. A typical example of this phenomenon is Fermat's equation for n equal to three or more.

The study of the interaction between arithmetic and geometry is naturally called arithmetic geometry. The topics studied by our team are at the heart of current research in that subject. They include elliptic curves and modular forms, L functions and their special values, moduli spaces and their compactifications, Galois representations and p-adic Hodge theory. In the future, we hope to expand our team in all domains of algebra and number theory.

Selected publications:

►Berger, Laurent.
Construction de (phi,Gamma)-modules : représentations p-adiques et B-paires.
Algebra & Number Theory, 2 (2008), no. 1, 91--120.
►Brunault, François.
Valeur en 2 de fonctions L de formes modulaires de poids 2 : théorème
de Beilinson explicite.
Bull Soc Math France 135 (2007), no. 2, 215--246.
►Rozensztajn, Sandra.
Compactification de schémas abéliens dégénérant au-dessus d'un diviseur régulier. Doc. Math. 11 (2006), 57--71 (electronic).

►PURE AND APPLIED MATHEMATICS UNIT - UMPA◄

►Probability◄

► **Team leader** ► ***Alice Guionnet,*** *research director - aguionne@umpa.ens-lyon.fr* ◄
► **Team members** ► *Vincent Beffara, research associate; Cédric Bernardin, research associate; Alice Guionnet, research director; Edouard Maurel-Segala, PhD student; Julien Michel, associate professor; Yann Ollivier, research associate; Sylvain Porret-Blanc, PhD student; Nick Sonigo, PhD student.* ◄

► **The probability team flourished quickly after its creation in 2001.** It is remarkable for its dynamism and the variety of the themes it works on. Following the principle that nothing is ever completely knowable, probability theory reached into various domains during the last century. The team's activity is a reflection of this diversity. To highlight this diversity, we will present, in a few lines, the main domains of our research.

Among the classical problems of probability theory, at the interface with statistical mechanics, we are interested in random walks in a complex medium. Another axis is the study of the critical behavior of models from condensed matter physics, such as percolation and the Ising model.

In symbiosis with the Partial Differential Equations team (PDE), we study questions of particular approximations of some of the equations of physics, and the dual question of how to obtain these equations from a microscopic modeling (hydrodynamic limits). We are also preoccupied with the derivation of coercivity inequalities (of the Sobolev type) and the study of the long time behavior of Markov processes.

Last but not least, a strong component of our team studies problems with a geometric taste to them, such as random geometries (the study of random shapes), random groups as introduced by Gromov, large random matrices and free probability, introduced by Voiculescu at the interface of probability theory and quantum mechanics.

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►Geometry◄

► **Team leader** ► ***Étienne Ghys,*** *research director - ghys@umpa.ens-lyon.fr* ◄
► **Team members** ► *Aurélien Alvarez, PhD student; Thierry Barbot, research associate; Maxime Bourrigan, PhD student; Claude Danthony, associate professor; Pierre Dehornoy, PhD student; Bruno Duchesne, PhD student; Albert Fathi, full professor; Hélène Eynard-Bontemps, PhD student; Damien Gaboriau, research director; Étienne Ghys, research director; Emmanuel Giroux, research director; Alexey Glutsyuk, research associate; Antonin Guilloux, assistant professor; Jean Lacroix, PhD student; Patrick Massot, PhD student; Yann Ollivier, research associate; Pierre Py, PhD student; Ana Rechtman, PhD student; Bruno Sévennec, research associate; Jean-Claude Sikorav, full professor; Alexey Tsygvintsev, associate professor; Jean-Yves Welschinger, research associate; Maxime Zavidovique, PhD student; Abdelghani Zeghib, research director.* ◄

► **Since the discovery of non-Euclidean and Riemannian geometries two centuries ago,** the concept of geometry has undergone tremendous evolution, if only through the recent, revolutionary works of Gromov and Thurston. Some UMPA members have greatly contributed to this evolution and still work on as yet unfinished programs. Other types of non-Riemannian geometries, e.g. symplectic, affine, projective, conformal, Lorentzian, holomorphic, etc., are still fascinating to mathematicians, including UMPA members, through their beauty and problems.

Topology is strongly linked with geometry. It deals with the study of properties of spaces which are invariant under deformations. This domain of mathematics is especially healthy and was deeply transformed in recent decades due, in particular, to new tools coming directly from a seemingly distant area: mathematical analysis.
The classical theory of dynamical systems emerged from a failure: it is not possible to solve all differential equations explicitly. Hence the interest, following Poincaré, of a qualitative study. At UMPA we work on hyperbolic (chaotic), holomorphic, Lagrangian, ergodic, etc. systems and also on extending the classical theory to arbitrary group actions.

This team has experts in these three fields, but it would be futile to try to split it into three sub-teams. The interactions between team members are numerous. There are plenty of working seminars, and collaborations arise in a natural way. Although it is impossible here to do justice to the results obtained, to illustrate the work done by the team we will present a few examples giving a general idea of their activity.

In 2005, Jean-Yves Welschingher solved an old problem dealing with "classical algebraic geometry." In 1856, Chasles established that given 5 conics in the plane (ellipses, parabolas, or hyperbolas) there exist in general 3264 conics which are tangent to them, but he was dealing with the complex plane and many of these 3264 conics may be "imaginary." Welschinger developed a "real enumerative geometry" which implies, in particular, the following: Given 5 ellipses in the real plane whose interiors are disjoint, there exist at least 32 conics which are tangent to them (see figure)! It is remarkable that the proof of such a classical statement would not have been possible a few years ago, before the definition of Gromov-Witten's invariants, themselves strongly motivated by theoretical physics!

The mathematical study of relativistic cosmology is a good example of the "mixture" of geometry and physics. From a geometrical point of view, it deals with Lorentzian manifolds for which the metric tensor is not positive. The light cone defines a kind of dynamical system whose global structure yields fascinating questions from the mathematical point of view as well as from the physical point of view. One could ask, for instance,

if it is possible to define global "time functions" on the whole space, and one studies global causality conditions. Two members of our team, Thierry Barbot and Abdelghani Zeghib have contributed greatly to the investigation of these questions. As a matter of fact, Thierry Barbot ran an "ACI-research project" on the subject.

One of the most abstract branches of dynamical systems is called "ergodic theory." It consists in the study of properties of dynamical systems which are independent of the topology of the ambient space and which only depend on the "measurable" properties. This theory originates from classical Hamiltonian mechanics, according to which Hamiltonian evolutions preserve measures (the so-called Liouville measures.) Much more recently, this theory even became time independent and concentrated on the study of measurable orbital equivalence, where the crucial role is played by orbits. Damien Gaboriau is one of the best experts on these questions. In particular, he introduced a powerful invariant that he called "cost" and which deeply transformed the theory.
Finally, at the intersection of topology and dynamics, there is contact topology. This theory also originates from classical mechanics through the concept of non-holonomic constraint. These contact structures progressively took a more and more important place in modern topology and dynamics. Emmanuel Giroux introduced new approaches to the theory of contact topology in dimension 3. In particular, his idea of using topological structures called open book decompositions enabled a completely new understanding of contact manifolds and generated a wealth of new classification theorems.
At the end of this rapid look at but a few of the topics covered by this team, it becomes apparent that the richness of the interactions inside the team and also with the other teams is a very pleasant aspect of UMPA research.

►PURE AND APPLIED MATHEMATICS UNIT - UMPA◄

►Partial differential equations and modeling◄

► **Team leader** ► ***Denis Serre,*** *full professor - serre@umpa.ens-lyon.fr* ◄
► **Team members** ► *Marc Bernot, assistant professor; Léa Blanc-Centi, graduate teaching assistant; Pierre Bousquet, assistant professor; Jérôme Demange, assistant professor; Olivier Druet, research associate; Emmanuel Grenier, full professor; Paul Laurain, PhD student; Valérie Le Blanc, PhD student; Rémi Peyre, PhD student; Denis Serre, full professor, Cédric Villani, full professor* ◄

► **The most structured topic concerns the PDEs of non-equilibrium statistical mechanics,** in particular the Boltzmann equation and its variants (Landau equation in plasma physics.) We address regularity questions and convergence rate towards equilibrium. That leads to the study of logarithmic Sobolev inequalities, measure concentration (functional viewpoint), optimal transport and information theory. A key tool is given by the Wasserstein distances between probability measures. Interactions with probability and geometry (within singular spaces) are important. At the level of functional analysis, we have uncovered the notion of hypo-coerciveness, which unifies the notions of hypo-ellipticity and controllability. It provides regularity results as well as decay estimates towards the equilibrium.

Optimal transport is considered also from the point of view of color image processing: forming a single image (panoramic view) from two pictures having a zone in common, for instance.
The optimality of classical Sobolev inequalities is linked with so-called “critical” non-linear elliptic PDEs. These display a defect of compactness that leaves room for concentration phenomena. One shows that they arise in a quantized way. These PDEs have a strongly geometric contents and have had a prominent place since G. Perelman proved the Poincaré conjecture by following Hamilton’s program through the heat flow for the Ricci curvature. The team is especially concerned with problems coming from conformal geometry.
We also study the influence of the geometry of a Riemannian manifold on the spectrum of its Laplacian, and more generally the way the waves propagate on such a surface.

The analysis of systems on conservation laws and hyperbolic PDEs is one of the most developed topic in our team. We examine the symmetrization and the hyperbolicity, with application to well-posedness of the Cauchy problem. This remains a fruitful domain for realistic models in elastodynamics and magnetohydrodynamics. We continue our analysis of initial-boundary value problems. The case of a homogeneous boundary condition when the problem is given by a variational principle is promising. It ensures, in particular, that surface waves resembling Fayleigh waves propagate in every direction of the boundary. An immediate application is to nonlinear elastodynamics.

Boundary layers arise, for instance, in oceanography, meteorology and magnetohydrodynamics. We determine their scales and characterize their linear or non-linear stability properties. We also study the existence of layer profiles for conservation laws, where the shock front plays the role of a free boundary. Such profiles appear when one quits the hyperbolic context. This may happen in presence of diffusion or dispersion. Viscous or viscous-capillary profiles are well known, though still the object of active research. The analysis of

discrete profiles, which is crucial in numerical analysis, involves deep notions of the theory of dynamical systems. Their properties (existence, localization and regularity) dramatically depend on the arithmetic properties of the ratio between the shock speed and the grid velocity.

Such profiles are particular cases of traveling waves. Other patterns of this family appear as well in our most applied research activity, the one that develops the fastest, with many exterior collaborations and new doctoral students. A lot of models in medicine involve PDEs (Krebs cycle, brain strokes, regulation of insulinemy, cell death, tumor development.) In many cases, where the PDEs are parabolic and non-linear, it is the inhomogeneity (white vs. gray matter) and the complexity of the geometry (convolutions) that are responsible for the complex behavior of wave propagation. The goal is to identify the waves, then act upon the system (through medical or chemical means) in order to control them. Obviously, this is a major target for public health.

In complement to these modeling and theoretical approaches, we work on the numerical analysis of diffusive or dispersive evolutionary PDEs. On the one hand, we study the approximation of semi-groups by splitting methods, where the order of the scheme with respect to the time variable may be high. Special attention is devoted to the stability with respect to stiff terms. On the other hand, we consider the implementation of artificial boundary conditions, for instance transparent ones. This requires the understanding of the coupling between finite volumes (for interior cells) and integral methods (for boundary meshes.)

In the more specific area of fluid mechanics, we collaborate, on the one hand, on a research program about multidimensional phase transitions in van der Waals fluids. We study, on the other hand, the motion of rigid solids in a Newtonian fluid. In particular, we examine the (im)possibility of collision between two bodies or a body and the boundary. This leads naturally to the analysis of fluids where particles deposit. Another topic of ours is the propagation of density waves in a viscous compressible fluid.

►PHYSICS LABORATORY◄

► **Director** ► **Jean-François Pinton** - *pinton@ens-lyon.fr* ◄
► **Total personnel** ► *111* ◄
► **Partners** ◄ *CNRS, ENS-Lyon* ◄
► **Web** ◄ *http://www.ens-lyon.fr/PHYSIQUE* ◄

► The research conducted at the laboratory includes theoretical, numerical and experimental physics as well as applications, with extensive collaboration between theoreticians and experimentalists. Many research projects share a common interest for complex and out-of-equilibrium systems. The experiments performed in the laboratory are small in scale and flexible with an emphasis on ultra-sensitive techniques with high space and time resolution.
All our groups have long-standing collaborations with other laboratories in France and abroad.

The following are areas of particular interest for our laboratory:

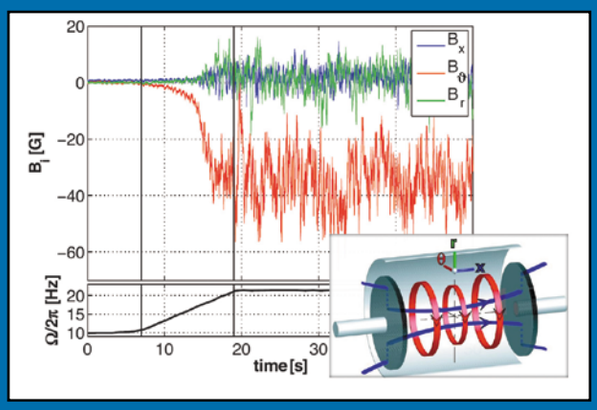
- Complex fluids: flows of shear-banding wormlike micelles, Van der Waals interactions in water/hydrocarbon-based mixtures, the viscoelasticity of entangled polymer liquids, the rheology of fractal gels, the rheology of foams, foam drainage, and liquid crystals (defect dynamics, backflow, growth instabilities, phase transitions, thermomechanical coupling, flexoelectricity, anchoring, and free-standing films),
- Granular systems: electrical conduction; transport, friction and dissipation in immersed granular materials; and washboard instabilities (ripples formed by rolling wheels),
- Biosciences: the dynamics of chromatin, long-range correlations of nucleosome positioning in the genome, the modeling of DNA beacons at mesoscopic scales, AFM analysis of DNA, the dynamics of a cell nucleus from dynamic light scattering experiments, cell mechanics, and air decontamination levels for high-risk hospital areas,
- Fluid turbulence: Lagrangian measurements in Rayleigh-Benard convection, the dynamics of inertial particles in fully developed turbulence, the simulation of wall-bounded flows, mixing by inertial waves, magnetohydrodynamics and dynamo instability,
- Statistical signal processing: time-frequency, empirical mode decomposition, wavelet analysis and scaling, multiscale processes, non-Gaussianity and long-memory, applications to turbulence, bio-medical signal and Internet traffic,
- Statistical physics: the aging of amorphous media, scaling, fluctuation theorems for harmonic oscillators, the dynamics of slow cracks, entropy production in out-of-equilibrium systems, systems with long-range interactions, and correlated systems,
- Quantum physics: decoherence and dissipative systems, disordered systems, nanotubes and quantum nanoconductors, geometrical frustration and quantum fluctuations, and strongly correlated phases in ultra-cold atoms,
- Mathematical physics: integrable systems, quantum gravity, quantum field theory, exact solutions in turbulence and disordered systems.

CURRENT RESEARCH TOPICS
statistical physics of complex systems, soft matter, non-linear physics, biophysics, fluid mechanics, signal analysis, condensed matter, mathematical physics

AREAS OF APPLICATION
crack growth, aging, rheology, granular media, ocean dynamics

INDUSTRIAL PARTNERS
CEA, Rhodia, Mathworks, Saint-Gobain, Boiron, L'Oreal, AirInSpace, EDF, Bluestar, Biotray

EQUIPMENT
atomic force microscopes, rheometers, optical tweezers, high-speed imaging, wind tunnel, lasers and dynamic light scattering apparatus, thin film evaporator



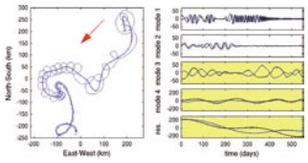
► *Self-excitation of a dynamo in a turbulent flow of liquid sodium (VKS collaboration, with ENS-Paris and CEA-Saclay). When the (mechanical) stirring of the flow exceeds a threshold, a magnetic field is spontaneously generated and self-sustained. In the presence of global rotation, this dynamo exhibits time-dynamics similar to the observations made in natural objects (irregular reversals of the dipole like in the case of the Earth, oscillatory regimes in the case of the Sun and other stars).*

►PHYSICS LABORATORY◄

►SiSyPh: Signals, Systems and Physics◄

► **Team leader** ► ***Patrice Abry,*** *CNRS research director - patrice.abry@ens-lyon.fr* ◄
► **Team members** ► *Patrice Abry, research director CNRS; Pierre Borgnat, research associate CNRS; Bernard Castaing, full professor; Laurent Chevillard, research associate CNRS; Patrick Flandrin, research director CNRS; Hannes Helgason, postdoctoral fellow; Pablo Jensen, research director CNRS; Nicolas Mallick, PhD student; Azadeh Moghtaderi, postdoctoral fellow; Edmundo Pereira de Souza Neto, professor in hospital; Stéphane Roux, associate professor; Antoine Scherrer, postdoctoral fellow* ◄
www.ens-lyon.fr/PHYSIQUE/Signal

Left: Sample path of a buoy used as a passive tracer for a measurement during an oceanographic experiment. Right: Empirical Mode Decomposition enabling to show the existence of «rotation coherent structures» at different time scales (Collaboration with ESR, Seattle, USA). ▼



► **The SiSyPh (Signals, SYstems and PHysics) group** is a statistical signal processing group within the physics department at the ENS Lyon. The spirit of the research conducted in the SiSyPh group lies in the interaction between the analysis of the data collected from actual experiments and the development of solutions for theoretical signal processing issues, resulting from the need t- process real life data.

The collaboration of the signal processing group with other research teams from the physics lab, such as the non-linear and hydrodynamic group, provides a perfect illustration of the way our research is conducted. The study of the advantages of using wavelet transforms for the analysis of the energy cascade in hydrodynamic turbulence, has led t- general research themes on «Scale Invariance, Multiresolution and Wavelets». Within this theoretical framework, the signal processing tools elaborated for the study of scaling have been applied t- the analysis of computer network traffic scaling properties, hence inducing a renewed use in the context of turbulence.

SiSyPh organizes its research activities in tw- major theoretical directions:

- Non-stationarity and time frequency analysis
  - Empirical Modal Decomposition (with P. Gonçalvès, LIP, ENS Lyon)
  - Tests of (non-)stationarity (with C. Richard, UTT, ANR support)
  - Signal processing with deformation operators (with P.O. Amblard, INPG, ANR support)
- Scale Invariance and Wavelets
  - Multifractal Analysis (with S. Jaffard, Département de mathématiques, Université Paris XII, and V. Pipiras, Department of mathematics, North Carolina University, USA)
  - Synthesis of Multifractal Processes (with P. Chainais, ISIMA, Université de Clermont-Ferrand, and R. Riedi, Department of Statistics, Rice University, Houston, Texas, USA)

SiSyPh is involved in the analyses of various types of applications:

- Hydrodynamic Turbulence (in collaboration with the lab's non-linear & hydrodynamic group)
- Computer Network traffic (with D. Veitch, Melbourne University, Australia, the French METROSEC project: Metrology for Security, OSCAR ANR RNRT and CNRS-WIDE France-Japan project)
- Mobility network analysis (with ARES/INRIA and LIP Lyon, and LIP6 Paris)
- Social networks modeling (with the LET, Université Lyon 2)
- Baro-reflex regulation (with the Hospices Civils de Lyon, French public hospital)
- Neuron Dynamics (with the Laboratoire des Neurosciences et Systèmes sensoriel, UCB Lyon 1)
- Analysis of waves in the Ionosphera (with the Department of Physics of Atmosphere, Prague, Czech Republic)

SiSyPh develops various Physics experiments, implying the use of advanced Signal processing analysis:

- Granular medium (Branly effect),
- Non-linear surface waves, Super-solid study,
- Turbulent thermal convection (with the non-linear & hydrodynamic group).

Selected publications:

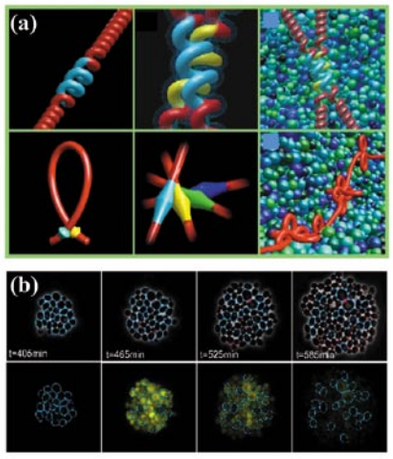
►H. Wendt, P. Abry et S. Jaffard, Bootstrap for Empirical Multifractal Analysis with Application t- Hydrodynamic Turbulence, IEEE Signal Processing Mag., 24(4): 38-48, 2007. A. Scherrer, N. Larrieu, Ph. Owezarski, P. Borgnat, P. Abry,
►Non Gaussian and Long Memory Statistical Characterisations for Internet Traffic with Anomalies. IEEE Trans. on Dependable and Secure Computing, 1(4):57:70, 2007. G. Rilling, P. Flandrin,
►One or Two Frequencies? The Empirical Mode Decomposition Answers. IEEE Trans. on Signal Proc., 56(1):85:95, 2008.

►PHYSICS LABORATORY◄

►Genome and chromatin◄

► **Team leader** ► ***Françoise Argoul,*** *research director - francoise.argoul@ens-lyon.fr* ◄
► **Team members** ► *Françoise Argoul, research director second class; Alain Arneodo, research director first class; Antoine Baker, PhD student; Benjamin Audit, research associate first class; Lotfi Berguiga, research engineer; Gilles Charvin, research associate second class; Guillaume Chevereau, PhD student; Audrey Fahys, postdoctoral fellow; Pascale Milani, postdoctoral fellow; Thibault Roland, PhD student; Cedric Vaillant, research associate first class; Lamia Zaghloul, PhD student* ◄ ***www.ens-lyon.fr/PHYSIQUE***

► **In cells, DNA is in permanent interaction** with a great number of structural or enzymatic proteins. Over the past few years, the study of structures resulting from DNA interaction with structural proteins (chromatin) has significantly improved our vision of the molecular mechanisms underlying the processes of replication, gene expression and control of the cell cycle. Knowledge of the architecture and dynamics of chromatin is crucial to further improve our understanding of cellular processes. Since the intrinsic structural and mechanical properties (bending and torsion) of the DNA polymer strongly depend on the sequence, it is also likely to influence DNA interaction with structural proteins including remodeling factors, consequently playing a role in the condensation-decondensation of chromatin. The central activity of our team concerns the characterization and the modeling of the importance of the sequence on the structure and the dynamics of DNA in eukaryotic cell nuclei in relation to replication and transcription processes. The originality of the approach developed by our team relies on the fact that we are hosted by a transdisciplinary platform: the LJC Joliot Curie Laboratory at the École Normale Supérieure de Lyon, where theoretical and experimental physicists together with cellular and molecular biologists share a common interest in the study of the structure and dynamics of chromatin in relation to the regulation of DNA replication and gene expression. Our studies pave the way from molecular to cellular aspects, for instance: (i) modeling and experimental characterization of sequence effects on DNA elastic properties and DNA-histone interactions, (ii) evidencing a remarkable gene organization around putative replication origins in mammalian genomes [1], (iii) characterization of chromosomal organization inside cells and their influence on cell growth and mitosis [2].



◄ *(a) Illustrating multi-scale mechanisms involved in the spontaneous emergence of rosette-like folding of the chromatin fiber in the crowded environment of the cell nucleus. (b) Transient controlled pulse of YFP expression from the MET3 promoter in yeast cells. Top panel series displays overlayed phase contrast and MYO1- mCherry, bottom panel shows transient YFP fluorescence appearance following a 20 min pulse of media lacking methionine [2].*

Experimental approaches involve fluorescence microscopy, atomic force microscopy (AFM), scanning surface plasmon microscopy (SSPM) [3] and magnetic tweezers. The theoretical approaches rely on genomic sequence multi-scale (wavelet) analysis, bioinformatics, statistical physics of polymers, dynamical system theory and molecular dynamic simulations.

Selected publications:

►B. Audit, C. Vaillant, L. Zaghloul, G. Chevereau, F. Argoul, Y. D'Aubenton-Carafa, C. Thermes, A. Arneodo, Open chromatin encoded in DNA sequence is the signature of "master" replication origins in human cells. Nucleic Acid Research (2009) doi: 10.1093/nar/gkp631.

►G. Charvin, F. Cross, E. Siggia, Forced expression of G1 cyclins phase-locks the budding yeast cell cycle. Proc. Natl. Acad. Sci. USA 106 (2009) 6632-6637.

►L. Berguiga, S.J. Zhang, F. Argoul, J Elezgaray, High resolution surface-plasmon imaging in air and in water: V(z) curve and operating conditions. Optics Lett. 32 (2007) 509-511.

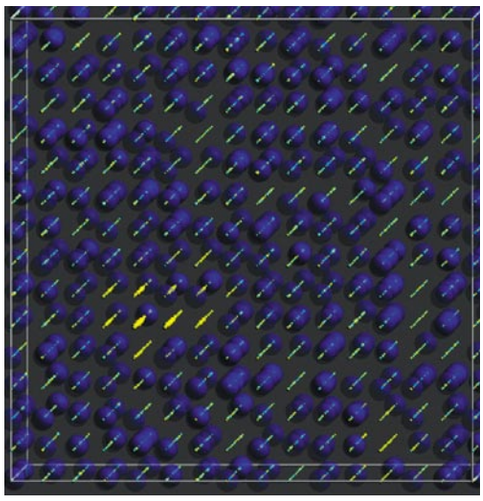
►PHYSICS LABORATORY◄

►Theoretical Physics◄

► **Team leader** ► ***Jean Michel Maillet,*** *research director CNRS - maillet@ens-lyon.fr* ◄
► **Team members** ► *Angel Alastuey, research director CNRS; Eric Bertin, research associate CNRS; David Carpentier, research associate CNRS; Pascal Degiovanni, research associate CNRS; François Delduc, research director CNRS; Andrei Fedorenko, postdoctoral researcher; Laurent Freidel, research associate CNRS (on leave at the Perimeter Institute, Canada); Krzysztof Gawedzki, research director CNRS; Peter Holdsworth, professor ENS Lyon; Etera Livine, research associate CNRS; Marc Magro associate professor ENS Lyon (on leave at the Albert Einstein Institute in Potsdam); Edmond Orignac, research associate CNRS; Tommaso Roscilde, associate professor ENS Lyon; Henning Samtleben, professor ENS Lyon; Véronique Terras, research associate CNRS; Fabio Toninelli, research associate CNRS; Robert Wimmer, postdoctoral researcher; Pierre Adroguer, PhD student; Quentin Berger, PhD student; Maïté Dupuis, PhD student; Arnaud Le Diffon, PhD student; Charles Grenier, PhD student ; Nicolas Grosjean, PhD student; Guillaume Paulin, PhD student.* ◄ *www.ens-lyon.fr/PHYSIQUE/*

► **The theoretical physics team has a broad spectrum** of activity leading in several directions in modern theoretical physics. Beyond their diversity, these research activities enable the team to offer ENS Lyon students broad perspectives covering the most recent developments in theoretical physics including field theory and fundamental interactions (string theory, quantum gravity, super-gravity and super-symmetry), mathematical physics, theoretical condensed matter physics, statistical mechanics and complex systems. Members of the theoretical physics team collaborate with other, more experimental, teams from the ENS Lyon Physics Laboratory and with other laboratories and institutes in France and around the world.

The team's research activities branch out in three main directions: mathematical physics, theoretical condensed matter and statistical mechanics, and complex systems. These include research on various topics (the following list is certainly not complete, and subject to change with time):



Imaging of the local magnetization across a phase transition from a «magnetic Bose glass» to a «magnetic super-fluid» of bosonic triplet quasi-particles induced by a magnetic field. The system under investigation is made of weakly coupled S=1 chains with strong single-ion anisotropy, mimicking the behavior of NiCl2-4SC(NH2)2. In this compound the application of a magnetic field drives the system from a singlet ground state to a condensate of triplet magnetic quasi-particles. Doping the lattice with non-magnetic impurities, e.g. Cd (represented here as blue balls) turns the condensate phase into a Bose glass of localized bosons (left panel), whose density is proportional to the local magnetization shown in the figure. Increasing the density of localized particles by increasing the field drives the system through a quantum percolation transition, corresponding to condensation of the quasi-particles over a disordered network (right panel). [see also F. R. Yu, T. Roscilde, and S. Haas New J. Phys. 10, 013034 (2008).] ►

Mathematical Physics:

- Integrable models and applications (correlation functions, quantum groups, etc.)
- Quantum gravity (loop quantum gravity, spin foams, etc.)
- Quantum field theories and fundamental interactions (string theory, super-gravity, super-symmetric gauge theories, branes and boundary CFT, etc.)
- Exact methods in turbulence and disordered systems (spin glasses, polymers in random environment, stochastic dynamics of interfaces)
- Quantum plasmas

Theoretical Condensed Matter Physics:

- Quantum phase transitions: disorder, frustration and slow dynamics
- Novel quantum phases in low-dimensional systems
- Dissipative dynamics of mesoscopic quantum systems
- Quantum transport
- Decoherence

Statistical Mechanics and Complex Systems:

- Stationary states for dissipative systems
- Global measurable quantities
- Out of equilibrium systems

Selected publications :

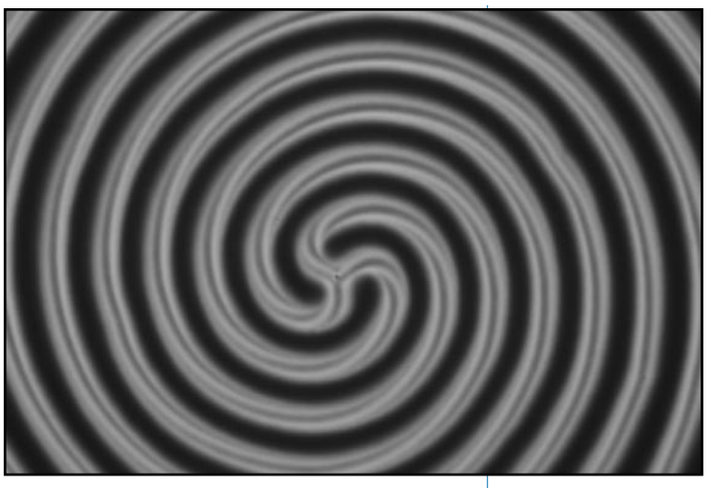
►G. Giacomin and F. L. Toninelli, Comm. Math. Phys. 266 (2006) 1.
►L. Freidel and E.R. Livine, Phys. Rev. Lett. 96 (2006) 221301.
►D. Carpentier and E. Orignac, Phys. Rev. Lett. 100 (2008) 057207.

►PHYSICS LABORATORY◄

►Soft condensed matter and physics of biological systems◄

► **Team leader** ► ***Patrick Oswald,*** *research director first class - patrick.oswald@ens-lyon.fr* ◄
► **Team members** ► *Nils Becker, postdoctoral fellow; Vance Bergeron, research director second class; Martin Castelnovo, research associate first class; Thibaut Divoux, PhD student; Ralf Everaers, full professor; Eric Freyssingeas, associate professor; Daniel Jost, PhD student; Hervé Gayvallet, associate professor; Jean-Christophe Géminard, research associate first class; Johannes-Geert Hagmann, PhD student; Shiqiong Hu, PhD student; Sébastien Manneville, full professor; Amine Methani, PhD student; Cendrine Moskalenko, associate professor; Patrick Oswald research director first class; Jean-François Palierne, research associate first class; Michel Peyrard, full professor; Christophe Place, research associate first class; Patrick Rigord, assistant professor; Stéphane Santucci, research associate second class; Nicolas Taberlet, associate professor; David Tamarii, research engineer; German Varas, PhD student; Valérie Vidal, research associate second class;* ◄ ***www.ens-lyon.fr/PHYSIQUE/***

► **This group studies a wide range of aspects of the field of soft condensed matter physics and biological systems,** combining experimental work with theory and numerical simulations. Research interests are focused on the physics of soft materials, such as liquid crystals, melted polymers, elastomers, emulsions, gels, foams, sand, and biological materials including proteins, DNA, cells and certain bacteria and biological tissues. Emphasis is placed on understanding their transport properties (diffusivities and thermo-mechanical coupling coefficient) in addition to their rheology (linear and non-linear), phase transitions, mechanical instabilities, interfacial properties, defects, and aging. Both microscopic and macroscopic approaches are used to understand the structure-property relationships in these different systems. Continuum mechanics along with statistical physics, optics, and non-linear analysis are some of the primary tools used by the group. A great effort is made to bridge the gap between fundamental studies and real-world applications. This is supported by the work done concerning washboard effects on roads, or viruses and air purification using non-thermal plasma, with collaborations in the public health sector being well established. Recent work has also addressed cell adhesion, the motion of bacteria near a substrate, the biomechanical aspects of the brain, and the effects of trauma on biological tissue. Finally, efforts are made to understand naturally occurring phenomena such as the formation of crack patterns in soils and the dynamics of degassing processes in volcanoes in studies conducted in international collaboration with geophysicists.



▲
Triple spiral in a cholesteric liquid crystal subjected to a temperature gradient. It rotates at a constant angular velocity under the action of a thermomechanical effect discovered by O. Lehmann in 1900 and which we re-observed for the first time in 2007.

Selected publications:

►P. Oswald, A. Dequidt, « Measurement of the continuous Lehmann rotation of cholesteric droplets subjected to a temperature gradient », Phys. Rev. Lett. 100 (2008) 217802-5.

►Thibaut Divoux, Hervé Gayvallet, and Jean-Christophe Géminard, Creep Motion of a Granular Pile Induced by Thermal Cycling , Phys. Rev. Lett. 101, 148303 (2008)

►Peyrard M, Cuesta-Lopez S, Angelov Experimental and theoretical studies of sequence effects on the fluctuation and melting of short DNA molecules, J. Phys. Condensed Matter, 21 034103-1-13 (2009)

►PHYSICS LABORATORY◄

►Non linear physics, hydrodynamics and turbulence◄

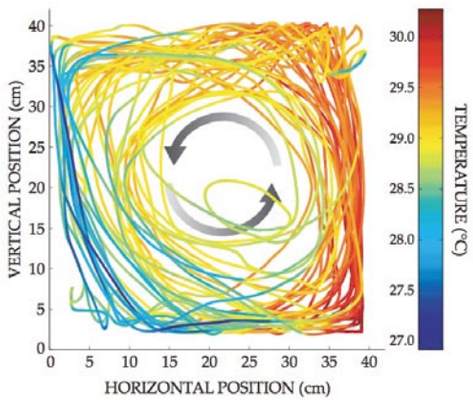
► **Team leader** ► ***Jean-François Pinton,*** *research director - pinton@ens-lyon.fr* ◄
► **Team members** ► *Ludovic Bellon, research associate; Enrico Calzavarini, postdoctoral fellow; Francesca Chilla, associate professor; Sergio Cilberto, research director; Thierry Dauxois, research director; Nicolas Garnier, research associate; Yoann Gasteuil, PhD student; Sylvain Joubaud, PhD student; Emmanuel Lévêque, research associate; Matthieu Mercier, PhD student; Vincent Morin, graduate teaching assistant; Antoine Naert, associate professor; Philippe Odier, associate professor; Pierdomenico Paolino, PhD student, Artyom Petrosyan, research associate; Jean-François Pinton, research director; Nicolas Plihon, research associate; Osvanny Ramos, postdoctoral fellow; Loic Vanel, associate professor; Gautier Verhille, PhD student; Romain Volk, associate professor*◄ ***www.ens-lyon.fr/PHYSIQUE/***

► **The team studies experimentally, theoretically and numerically** the role of non-linear effects on the dynamics of several out-of-equilibrium systems. Recent studies have been done in the following areas:

• Fluctuations in stochastic systems: thermal fluctuations of energy input and dissipation in a harmonic oscillator driven out of equilibrium; time-reversal symmetry of nonequilibrium fluctuations. The properties of systems with long-range interactions, such as negative specific heat or ensemble inequivalence, have also been studied.

• Fracture: characteristics of slow crack growth in brittle materials have been analyzed both theoretically and experimentally, and a model proposed, based on a thermally activated rupture process. Another case is the slow growth of a single crack in polycarbonate films submitted to C and constant imposed stress.

• Turbulence: large eddy simulations have been developed for wall-bounded flows, Lagrangian and inertial particles are studied in numerical simulations and are tracked experimentally using optical and acoustical techniques.



Reflection of internal wave on an inclined plane. L. Gostiaux & T. Dauxois, Phys. Fluids, 19, 028102 (2007). Motion of lagrangian temperature sensor in Rayleigh-Bénard convection. Y. Gasteuil et al., PRL 99, 234302 (2007). ►

• Geophysical fluid dynamics: turbulent convection in narrow vertical channels has been studied and the role of thermal plumes clarified by using instrumented particles. Internal gravity waves, which play an essential role for mixing in the oceans, are studied in a 2D stratified fluid. Another geophysical process concerns the self-generation of magnetic fields in flows of electrically conducting fluids: a fully turbulent dynamo has been observed in a von Karman flow of liquid sodium (VKS collaboration).

Selected publications:

►ANDRIEUX D, GASPARD P, CILIBERTO S, GARNIER N., JOUBAUD S., PETROSYAN A., Entropy production and time asymmetry in nonequilibrium fluctuations,. Physical Review Letters, 98 (2007), 150601.

►BERHANU, R. MONCHAUX, M. BOURGOIN, M. MOULIN, PH. ODIER, J.-F. PINTON, R. VOLK, S. FAUVE, N. MORDANT, F. PETRELIS, A. CHIFFAUDEL, F. DAVIAUD, B. DUBRULLE, C. GASQUET, L. MARIE, F. RAVELET, Magnetic field reversals in an experimental turbulent dynamo, Europhysics Letters, 77 (2007), 59007

►LEVEQUE E., TOSCHI F., SHAO L., BERTOGLIO JP, Shear-improved Smagorinsky model for large-eddy simulation of wall-bounded turbulent flows, Journal of Fluid Mechanics 570, 491 (2007)

►PLANT REPRODUCTION AND DEVELOPMENT LABORATORY - RDP◄

► **Director** ► **Jan Traas,** *research director first class - jan.traas@ens-lyon.fr* ◄
► **Total personnel** ► *62* ◄
► **Partners** ◄ *CNRS, UCB Lyon 1, INRA* ◄
► **Web** ◄ *www.ens-lyon.fr/RDP/* ◄

► Our laboratory is currently composed of six research teams supported by a group of technicians. The research unit benefits from excellent facilities for molecular biology, biochemistry and cell biology. It is equipped with environmentally controlled plant growth chambers and a dedicated greenhouse. In addition, we have access to the local technology platforms, including state-of the art imaging equipment, proteomic facilities, etc. In addition to research, a large number of our researchers are involved in teaching activities at the university and the ENS Lyon.

We study the mechanisms which govern sexual reproduction in plants, with a particular focus on the developmental aspects. Our scientific program covers all stages of reproductive development in plants, from the initiation of the flower at the shoot apex to early embryo development. Although most of our projects use the model plant Arabidopsis, we also work on species of agronomic interest such a Rosa and maize. In addition, since we are studying the evolution of flower development, a set of primitive angiosperms such as Cabomba is used. Within the large theme of flower development, the teams are mainly working on transcriptional regulation and intercellular signaling. In this context our approaches involve molecular genetics, genomics, transcriptomics, and in vivo imaging. More recently, several teams have taken a systems biology approach involving collaboration with mathematicians and computer scientists. In this context, the ENS Lyon, with its highly multidisciplinary character, offers an optimal environment.

CURRENT RESEARCH TOPICS
Flower development, plant reproduction, embryo development, signal transduction, membrane traffic

RELATED FIELDS
Developmental biology, cell biology, plant biotechnology

AREAS OF APPLICATION
Agronomy, plant biotechnology

INDUSTRIAL PARTNERS
Biogemma, Pioneer

EQUIPMENT
Growth chambers, greenhouse, in vitro culture facilities, confocal microscopes

► *Pictures representative of ongoing research at the laboratory.*

►PLANT REPRODUCTION AND DEVELOPMENT LAB - RDP◄

►Flower Morphogenesis◄

► **Team leader** ► ***Mohammed Bendahmane, Research director*** *- mbendahm@ens-lyon.fr* ◄
► **Team members** ► *Philippe Vergne, engineer, INRA; Olivier Raymond, assistant professor, UCB-Lyon 1; Annick Dubois, research associate second class, INRA; Sylvie Baudino, assistant professor, Université St. Etienne visiting scientist; Anne Marie Thierry, technician, UCB-Lyon 1; Florian Brioudes, PhD student; Emilie Varaud, PhD student; Marion Maene, PhD student.* ◄

► **Our group's work is aimed at understanding the factors that influence three floral important traits:** flower shape, longevity and scent. We use a combination of Arabidopsis thaliana, as a genetic tool, and the rose as a more applied model species. The petal is the major organ determining flower quality. The role of floral homeotic genes in the determination of petal identity is relatively well understood. However, very little is known about three important aspects that influence flower quality:

(i) Flower shape: Flower shape is determined by petal characters such as shape, size and number. The final shape and size can be influenced by cell number or cell expansion or both. We focus our work on a novel petal-expressed transcription factor that we recently identified and showed to limit petal size by interfering with post-mitotic cell expansion (Szecsi et al., 2006 EMBO J 25, 3912-3920). A number of genes have been shown to control petal number mostly in Arabidopsis. We are studying the molecular interactions between these genes in order to control petal number in the rose.

(ii) Flower longevity: The final stage of petal developmental (petal senescence) is particularly important as it has a major influence on the vase life and the quality of ornamental plants. Using a genetic screen, we identified an Arabidopsis mutant that is affected in flower senescence (early flower senescence). The functional characterization of the gene associated with this phenotype is one of our aims.

(iii) Rose Scent: Flower scent is determined by a complex mixture of volatile molecules produced by the petals. Using the rose as a model plant, we are investigating the molecular, cellular and evolutionary aspects of scent production. Several genes involved in scent biosynthesis have been characterized and used to investigate scent evolution in the genus Rosa (Scalliet et al., 2008 PNAS 105 5651-5946).

(a) Petal final size is remarkably constant within a given species, indicating the existence of checkpoints that control/terminate organ growth. We identified an Arabidopsis thaliana mutant that is affected by a gene that controls final petal size (right) compared to the wild-type (left).

(b, c) Model roses used in our studies aimed at understanding the double flower phenomenon. Two Rosa chinensis varieties that exhibit simple flower (5 petals) and double flower (25 petals) phenotypes. ▼

Selected publications:

►Scalliet G, Piola F, Douady CJ, Réty S, Raymond O, Baudino S, Bordji K, Bendahmane M, Dumas C, Cock JM, Hugueney P (2008) Scent evolution in Chinese roses. Proc Natl Acad Sci USA 105: 5927 -5932

►Asurmendi S, Berg RH Smith TJ, Bendahmane M, Beachy RN (2007) Aggregation of TMV CP plays a role in CP functions and in coat-protein-mediated resistance. Virology 366: 98-106

►Szécsi J, Joly C, Bordji K, Varaud E, Cock JM, Dumas C, Bendahmane M. (2006). BIGPETALp, a bHLH transcription factor is involved in the control of Arabidopsis petal size. EMBO J. 25: 3912-3920.

►PLANT REPRODUCTION AND DEVELOPMENT LAB - RDP◄

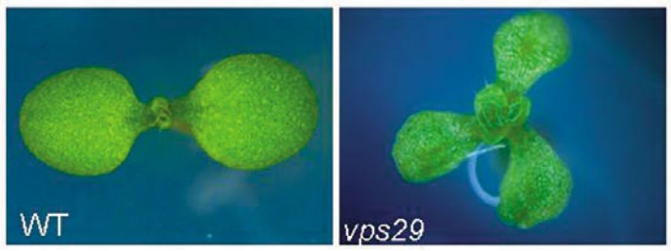
►SiCE - CELL SIGNALING AND ENDOCYTOSIS◄

► **TEAM LEADER** ► ***Thierry Gaude,*** *research director first class, CNRS - thierry.gaude@ens-lyon.fr* ◄
► **TEAM MEMBERS** ► *Vincent Bayle, postdoctoral fellow CNRS; Isabelle Fobis-Loisy, research associate first class CNRS; Thierry Gaude, research director CNRS; Christine Miège, associate professor ENS Lyon; Sara Pietrozotto, PhD student MRT; Martina Santambrogio, PhD student MRT; Nelcy Thazar, PhD student Cluster 9; Anne-Marie Thierry, Technician UCB Lyon I.* ◄ ***www.ens-lyon.fr/RDP/SiCE***

► **THE GROUP HAS TWO MAIN SUBJECTS OF INTEREST IN THE FIELD OF PLANT CELL SIGNALING AND DEVELOPMENT**, which are: (i) to decipher the molecular bases of self-pollen rejection that occurs during the self-incompatibility (SI) response in the Brassicaceae family, and (ii), to better our understanding of the regulatory functions played by endocytosis in plant development. SI in the Brassicaceae is controlled by a receptor-ligand interaction, which involves the S-locus receptor kinase (SRK) on the female side and the S locus Cysteine-Rich peptide (SCR) on the male side. We identified a Sorting Nexin-like protein (SNX1) as a novel interactor of the SRK kinase domain (Vanoosthuyse et al., 2003). In yeast and mammalian cells, SNX proteins are components of a multiprotein complex, known as the retromer complex, which plays a role in intracellular trafficking of membrane receptors. We are developing diverse genetic and cellular approaches to investigate the functions of plant SNXs and retromer components in self-pollen rejection and plant development.

We recently showed that: (i) SNX1 is involved in trafficking of the phytohormone auxin carriers of the PIN family (Jaillais et al., Nature 2006), (ii) the retromer complex mediates cell polarity, organogenesis and plant development (Jaillais et al., Cell 2007), and (iii) SNX1-containing endosomes function as sorting endosomes (Jaillais et al., Plant J 2008). Our work reveals unanticipated functions for retromer components in mediating developmental processes.

We use tools of molecular genetics, cell imaging and proteomics, which all are available at the ENS Lyon and IFR 128 BioSciences Gerland-Lyon Sud.



▲ *Retromer mutant seedlings (vps29) exhibit severe developmental defects illustrated here by the presence of three embryonic leaves (cotyledons) instead of the normally two cotyledons found in the wild type plant (WT).*

SELECTED PUBLICATIONS:

►Ivanov, R., and Gaude, T. (2009). Endocytosis and endosomal regulation of the S-receptor kinase during self-incompatibility response in Brassica oleracea. Plant Cell 21, 2107-2117. (IF = 10.45)

►Jaillais, Y. and Gaude, T. (2008). Plant Cell Polarity: Sterols Enter into Action after Cytokinesis. Dev Cell 140, 318-320 (IF = 12.882)

►Jaillais, Y., Santambrogio, M., Rozier, F., Fobis-Loisy, I., Miège, C. and Gaude, T. (2007). The retromer protein VPS29 links cell polarity and organ initiation in plants. Cell 130, 1057-1070 (IF = 31.253)

►Jaillais, Y., Fobis-Loisy, I., Miege, C., Rollin, C., and Gaude, T. (2006). AtSNX1 defines an endosome for auxin-carrier trafficking in Arabidopsis. Nature 443, 106-109. (IF = 31.43)

►PLANT REPRODUCTION AND DEVELOPMENT LAB - RDP◄

►DetFlor – floral determination◄

► **Team leader** ► ***Ioan Negrutiu*** *- ioan.negrutiu@ens-lyon.fr* ◄
► **Team members** ► *Aurélie Chauvet, technician; Patrice Morel, research associate first class; Nathanaël Prunet, graduate teaching assistant; Steve de Ribou de Bosseoreille, PhD student; Christophe Tréhin, associate professor.* ◄

► **We are studying mechanisms at the origin of evolutionary innovations in flowering plants** and which have generated developmental diversity and plasticity. One such process is floral determination (production of defined numbers of floral organs). The question here is to understand in genetic and molecular terms the links between stem cell arrest, female program initiation (carpel organogenesis) and bisexuality in the flower. These are processes that take place at the summit of the flower meristem. They have been instrumental in flower evolution, but also have been main targets in domestication and plant breeding. To study these processes, genetic, genomic and biochemical approaches are being undertaken.

► *This is an indeterminate flower resulting from a double mutation in genes controlling flower termination (such as ag-4 ult1). The result is a flower continuously producing petals.*

Selected publications :

►Zluvova J, Georgiev S, Janousek B, Charlesworth D, Vyskot B, Negrutiu I. (2007) Early events in the evolution of the Silene latifolia Y chromosome: male specialization and recombination arrest. Genetics 177:375-86

►Prunet N, Morel P, Thierry AM, Eshed Y, Bowman J, Negrutiu I and Trehin C (2008) The REBELOTE, SQUINT and ULTRAPETALA1 genes function redundantly in the temporal regulation of floral meristem termination in Arabidopsis thaliana Plant Cell 20 : 901-919

►Mrackova M, Nicolas M, Hobza R, Negrutiu I, Moneïger F, Widmer A, Vyskot B and Janousek B (2008) Independent origin of sex chromosomes in two species of the genus Silene, Genetics (in press)

►Prunet N., Morel P., Negrutiu I. and Trehin C. (2009) Time to stop: flower meristem termination. Plant Physiology. DOI:10.1104/pp.109.141812.

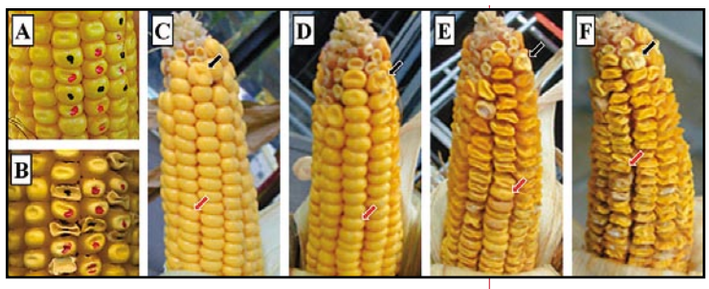
►PLANT REPRODUCTION AND DEVELOPMENT LAB - RDP◄

►Maize kernel Development◄

► **Team leader** ► ***Peter Rogowsky,*** *research director - peter.rogowsky@ens-lyon.fr* ◄
► **Team members** ► *Annick Berne-Dedieu, engineer; Nathalie Depège, associate professor; Marie Gauthier, PhD student; Ghislaine Gendrot, engineer; Catherine Klein, PhD student; Benjamin Pouvreau, engineer; Davide Sosso, PhD student; Vanessa Vernoud, research associate.* ◄
www.ens-lyon.fr/RDP/

► **The aim of the Maize Kernel Development team is to understand the molecular mechanisms** that govern early embryo and endosperm development in maize. Both the embryo and the endosperm undergo a very precise and tightly regulated development from a single cell into a multi-cellular, highly differentiated organism. An estimated 1000 genes are involved in this process but less than a quarter are known today. To identify novel genes involved in maize kernel development, to determine their function and to understand their regulation, the team uses both «forward» and «reverse» genetics. In the first strategy mutants in kernel development (*emb, emp, miniature*) are isolated; their phenotype is characterized and the underlying genes are cloned and characterized at a molecular level. In the second strategy differential methods are used to isolate genes expressed only in certain parts of the kernel or only at certain developmental stages (*OCL, Vpp1, CC, EBE*). Mutants or transgenic plants mis-expressing the respective genes are isolated and their phenotype characterized.

Maize was chosen for this research because of its long-standing record as a model plant in genetics and because of its agronomic and industrial importance. This species represents a turnover of 2.3 billion euros for the French economy and with 600 Mt it is the most highly produced cereal in France. Since maize grain development is quite different from that of the model plant Arabidopsis, specific research efforts are justified and necessary and may serve as a basis for the improvement of maize and other cereals.



▲ *Macroscopic phenotype of the bt2-H2328 mutant A, B: On a segregating ear of maize, wildtype kernels were marked with a black dot and mutant kernels with a red dot. Mutant kernels were plumper than wildtype kernels at 30 DAP (A) but collapsed at 60 DAP (B). C-F: The same ear of a self-pollinated bt2-h2328 homozygous mutant plant was photographed at 31 (C), 35 (D), 40 (E) and 45 DAP (F). Black arrows indicate mutant kernel already collapsed at 31 DAP. Red arrows indicates mutant kernel still plump at 40 DAP.*

Selected publications:

►Cosségal M, Chambrier P, Mbelo S, Balzergue S, Martin-Magniette M-L, Moing A, Deborde C, Guyon V, Perez P and Rogowsky PM (2008) Transcriptional and metabolic adjustments in AGPase deficient bt2 maize kernels. Plant Physiol 146: 1553-1570.

►Muller B, Bourdais G, Reidy B, Bencivenni C, Massonneau A, Condamine P, Rolland G, Conéjéro G, Rogowsky P, Tardieu F (2007) Association of specific expansins with growth in maize leaves is maintained under environmental, genetic, and developmental sources of variation. Plant Physiol 143: 278-290.

►Vernoud V, Laigle G, Rozier F, Meeley RB, Perez P, Rogowsky PM (2009) The HD-ZIP IV transcription factor OCL4 is necessary for trichome patterning and anther development in maize. Plant J, in press.

►PLANT REPRODUCTION AND DEVELOPMENT LAB - RDP◄

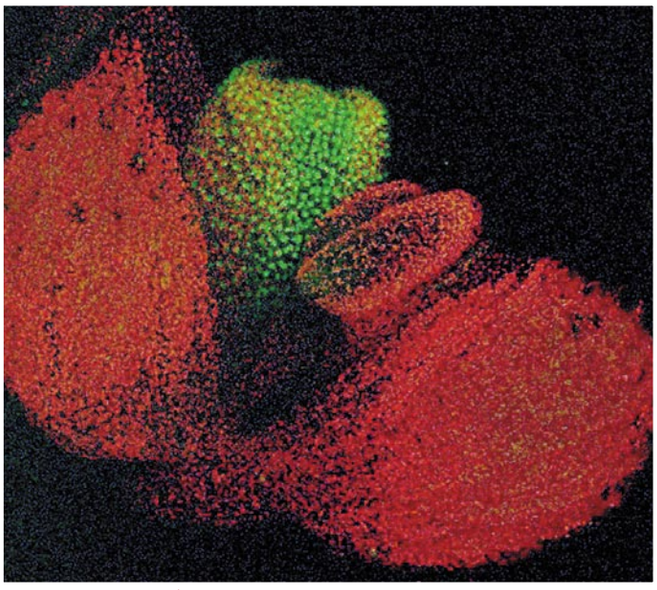
►Evolution and development of the flower◄

► **Team leader** ► ***Charlie Scutt,*** *researcher, CNRS - charlie.scutt@ens-lyon.fr* ◄
► **Team members** ► *Amélie Andrès-Robin, PhD student; Françoise Monéger, research director; Edwige Moyroud, PhD student; Sandrine Paindavoine, engineer; Mathieu Reymond, PhD student; Anne-Marie Thierry, technician; Aurélie Vialette-Guiraud, PhD student.* ◄

► **We are studying the evolution and development of the flower,** the reproductive structure that characterizes the flowering plants. In particular, we are interested in the mechanisms controlling the development of the flower's female reproductive organ, the carpel, and of the molecular events that shaped the anatomical evolution of this structure. We are following two main approaches:

1. We are comparing the structure, expression and function of genes that control carpel development in species whose lineages diverged early in the evolution of the flowering plants. This work takes us as far afield as the South Pacific in search of representatives of early-diverging plant groups, and involves the adaptation of laboratory methods for the investigation of these non-model species. Through this approach, we aim to identify the molecular changes that led to the closure of the carpel around the ovules in an ancestor of the flowering plants, over 150 million years ago, and thus to the evolution of the 300 000 species of flowering plants alive today.

A young flower of the model plant Arabidopsis thaliana, transformed with a reporter gene construction to show the expression domain (green fluorescence) of the carpel development gene CRABS CLAW. ▼



2. We are studying the transcriptional control network that regulates carpel development in the model flowering plant, Arabidopsis thaliana. To achieve this, we are using micro-array analyses to identify genes whose expression is regulated downstream of numerous transcription factors with known phenotypic effects on carpel development. We are collaborating with other groups of biologists and mathematicians to combine the results of our analyses into a predictive model of carpel development: "The Virtual Carpel."

Selected publications:

►Moyroud E, Reymond M, Parcy F, Scutt CP (2009, in press). The analysis of entire gene promoters by Surface Plasmon Resonance. The Plant Journal. doi: 10.1111/j.1365-313X.2009.03903.x
►Fourquin C., Vinauger-Douard M., Chambrier P., Berne-Dedieu A Scutt CP (2007) Functional conservation between CRABS CLAW orthologues from widely diverged angiosperms. Annals of Botany 100: 651-657
►Scutt CP, Vinauger-Douard M, Fourquin C, Finet C, Dumas C (2006). An evolutionary perspective on the control of carpel development. †Journal of Experimental Botany 57: 2143-2152
►Fourquin C, Vinauger-Douard M, Fogliani B, Dumas C, Scutt CP (2005) Evidence that CRABS CLAW and TOUSLED have conserved their roles in carpel development since the ancestor of the extant angiosperms. Proceedings of the National Academy of Sciences of the United States of America 102: 4649-4654

►PLANT REPRODUCTION AND DEVELOPMENT LAB - RDP◄

►INITIATION AND FUNCTION OF THE FLORAL MERISTEM◄

► **TEAM LEADER** ► ***Jan Traas,*** *research director - jan.traas@ens-lyon.fr* ◄

► **TEAM MEMBERS** ► *Fabrice Besnard, PhD student; Géraldine Brunoud, engineer CNRS; Pradeep Das, associate professor; Annick Dedieu, assistant engineer CNRS; Soazig Guyomarc'h, postdoctoral fellow; Olivier Hamant, research associate second class INRA; Vincent Mirabet, AGPR ENS; Valérie Morin, engineer; Jan Traas, research director INRA; Magalie Uyttewaal, postdoctoral fellow; Teva Vernoux, research associate first class CNRS.* ◄

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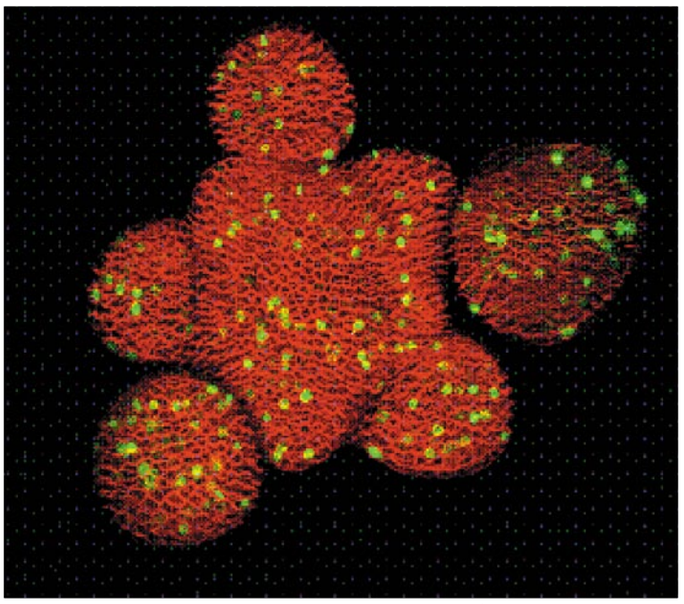
► **PLANT ARCHITECTURE DEPENDS ON GROUPS OF RAPIDLY DIVIDING NON-DIFFERENTIATED CELLS CALLED SHOOT APICAL MERISTEMS,** which constantly initiate new organs and tissues. Since they define essential agronomic traits such as organ number and position, meristem function is an important topic of research. The goal of our project is to understand the mechanisms that regulate the function of the shoot apical meristem, which generates all the aerial parts of the plant. In particular, we are interested in the initiation of flowers by this meristem in the model plant Arabidopsis. For this purpose we are using molecular genetics and genomics combined with in vivo imaging methods. In parallel we are developing modeling tools. The goal here is to create a virtual floral meristem that integrates our results and use this model to generate new hypotheses concerning the initiation and function of floral meristems. At present, research in the group is focused on two aspects. First we investigate the hormone signal transduction cascades that coordinate development at the meristem. Second, we are trying to understand how the signals are translated into specific morphogenetic responses. In this context, we are collaborating with physicists and mathematicians to elaborate a multidisciplinary view of plant development.

SELECTED PUBLICATIONS:

►CBarbier de Reuille P. Bohn-Courseau I., Ljung K., Morin H., Carraro N., Godin, C. and Traas J. (2006) Computer simulations reveal properties of the cell-cell signaling network at the shoot apex in Arabidopsis. P.N.A.S. USA.103(5):1627-1632

►Hamant O., Heisler MG., Jonsson H., Krupinski P., Uyttewaal M., Bokov P., Corson F., Sahlin P., Boudaoud A., Meyerowitz EM., Couder Y., Traas J. (2008) Developmental patterning by mechanical signals in Arabidopsis. SCIENCE, 322 (5908), 1650-1655.

A shoot meristem producing flower buds, visualized in a confocal scanning laser microscope. The cell membranes are colored in red. Cells that are about to divide express a fluorescent protein and appear as green spots.
▼



►HUMAN VIROLOGY DEPARTMENT - VIRO◄

► **Director** ► **François-Loïc Cosset,** *CNRS research director - directeur.virologieHu@ens-lyon.fr* ◄
► **Total personnel** ► *110* ◄
► **Partners** ◄ *Inserm, UCB Lyon 1* ◄
► **Web** ◄ *http://hvd.ens-lyon.fr* ◄

► The human virology laboratory pursues basic research on the molecular and cellular biology of pathogenic human viruses, their interactions with the cellular factors that govern most aspects of their viral cycle, and the characterization of pathologies associated with infection, such as chronic infections (e.g. HIV and HCV). These projects are particularly rich both in scientific approaches (biochemistry, biophysics, molecular cellular biology, and physio-pathology) and pathogens investigated: retroviruses, flaviviruses, hepaciviruses, gamma-herpesviruses, filoviruses, paramyxoviruses, avian influenza viruses, adeno-associated viruses, and prions. They should strongly contribute to the clarification of the physio-pathological mechanisms of the viruses studied as well as to the discovery of novel therapeutic targets or strategies.

The scientific projects fall into four types of fundamental studies related to different aspects of virus/cell interactions: 1) cell entry (interaction with cell surface receptors, cell entry processes and cell activation, membrane fusion and post-entry mechanisms and restriction), 2) replication and gene expression (transcription, RNA export, and translation controls), 3) virus assembly (intracellular trafficking of virus components, nucleocapsid assembly, envelope assembly, and viral egress), and 4) viral pathogenesis and oncogenesis. It is also important to highlight the primary role of animal models in several of these projects and, particularly, the major role of the animal facilities on the campus (A2/A3) and of the P4 laboratory for studying these viruses.

Several of these basic studies are followed up by several translational research projects in association with clinical teams, aimed at a better understanding at the patient level of the immune responses or physio-pathological mechanisms which should provide insight for further therapeutic approaches. Other projects derived from the knowledge gained through these basic projects aim to develop biotechnology applications using the viruses that are studied as tools (e.g., transgenesis using vector derived from lentiviruses or genetic vaccines derived from alternative viral vectors) and to define antiviral strategies against some major human pathogens such as HIV, HCV, Ebola, and Nipah via, for example, gene therapy, screening of antiviral compounds and vaccinology.

CURRENT RESEARCH TOPICS
Virology, biotherapy

RELATED FIELDS
Molecular biology, cellular biology, biochemistry, vectorology, vaccinology

AREAS OF APPLICATION
Antiviral strategy, gene therapy, gene transfer, vaccines

INDUSTRIAL PARTNERS
Epixis, Transgene

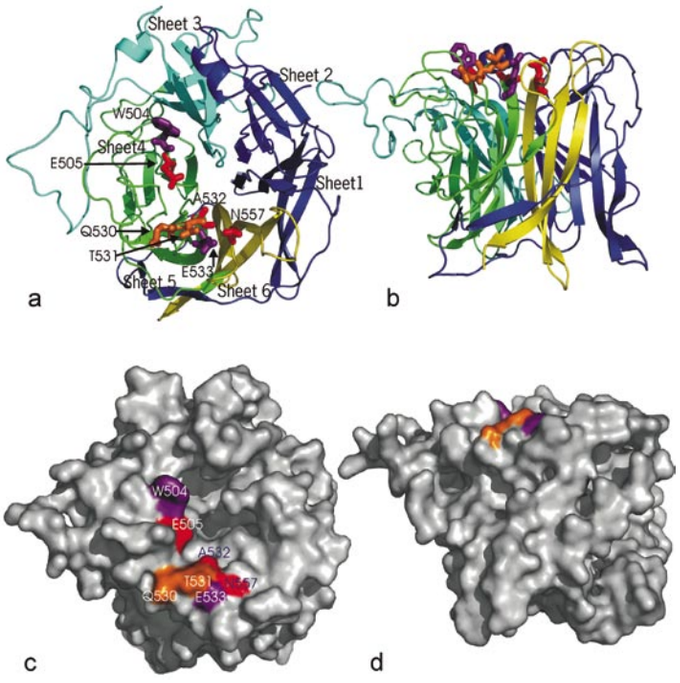
EQUIPMENT
Flow cytometer, etc.

▲ *Members of the Human Virology Department on break*

►HUMAN VIROLOGY DEPARTMENT - VIRO◄

►Molecular basis of paramyxovirus entry◄

► **Team leader** ► ***Robin Buckland,*** *research director second class, CNRS - robin.buckland@inserm.fr* ◄
► **Team members** ► *Michelle Ainouze, technician Inserm; Christine Pohl, post-doctoral researcher; Hasan Kweder, PhD student; Olivier Pernet, PhD student* ◄ ***http://hvd.ens-lyon.fr/human_virology_dpt***



▲ *Binding site for ephrinB2 on the globular head of the Nipah virus attachment protein*

► **Our group is studying the molecular basis of paramyxovirus entry into the host cell.** The paramyxoviruses we study are the Morbillivirus measles virus (MV) and the Henipaviruses Nipah virus (NiV) and Hendra virus (HeV). Due to their zoonotic nature, their capacity to cause high mortality in man, and a present lack of effective antivirals, NiV and HeV are classified as BSL-4 pathogens. The availability of the Jean MÈrieux P4 laboratory on campus allows us to make in vitro and in vivo studies on these dangerous pathogens but we also carry out P2 level mutagenesis studies in expressing the viral glycoproteins and receptors from eukaryotic expression vectors.

Up to now it has been assumed that the Henipaviruses enter the host cell by fusion at the plasma membrane but we have recently discovered that both NiV and HeV entry occurs by receptor-mediated macropinocytosis. This finding is important because it should result in the development of an effective low-cost antiviral strategy against these dangerous pathogens. We are also investigating whether MV enters by the same endocytic mechanism, as well as the molecular basis of escape from the anti-MV humoral response.

Selected publications :

►O. Pernet, C. Pohl, M. Ainouze, H. Kweder, and R. Buckland. Nipah virus can enter by macropinocytosis. Virology (In press).
►V. Guillaume, K.T. Wong, G. Looi, M.C. Georges-Courbot, L. Thevenet-Barrot, R. Buckland, T.F. Wild, and B. Horvat. 2009. Hamster model of acute Hendra virus infection and passive antibody protection. Virology 387 : 459-465.

►HUMAN VIROLOGY DEPARTMENT - VIRO◄

►Viral envelopes and retrovirus engineering◄

► **Team leader** ► ***Dr. François-Loïc Cosset,*** *research director first class - flcosset@ens-lyon.fr* ◄
► **Team members** ► *Bertrand Boson, technician; François-Loïc Cosset, research director; Caroline Costa, engineer; Viet Laon Dao Thi, PhD student; Cécilia Frécha postdoctoral fellow; Judith Fresquet, engineer; Floriane Fusil, postdoctoral fellow; Emmanuel Gauthier, postdoctoral fellow; Christelle Granier, engineer; Camille Levy, PhD student; Jean-Christophe Meunier, postdoctoral fellow; Ophélie Granio, postdoctoral fellow; Dimitri Lavillette, research associate first class; Guillemette Maurin, PhD student; Didier Nègre, research associate first class; Karine Ruel, engineer ; Judit Szecsi postdoctoral fellow; Els Verhoeyen, research associate first class ; Géraldine Verney, engineer.* ◄ *http://hvd.ens-lyon.fr*

► **The manipulation of viral genomes and the engineering of viral particles** lead to fascinating and powerful perspectives in several areas of biomedical research, pending a precise understanding of the molecular mechanisms of viral replication. Thanks to their capacity to be integrated in host cell DNA, retroviruses allow the production of attractive tools for gene delivery. Furthermore, the flexibility with which different viral or cellular components can be assembled on/in viral particles allows us to derive macromolecular platforms that display miscellaneous polypeptides of interest, an approach useful in the domains of vaccinology, gene therapy and compound screening.

Our projects focus on (i) the investigation of the properties of the viral surface glycoproteins derived from retroviruses, flaviviruses, hepaciviruses and influenza viruses, and (ii) the development of novel gene transfer vectors and viral engineering techniques.

On the fundamental side, an important objective of a large part of our work is to understand the function and the regulation of these proteins at the level of (i) the assembly of enveloped viral particles, (ii) their interaction with the external environment, notably the innate and adaptive immune systems, and (iii) the molecular processes governing the cellular entry of enveloped viruses and subsequent membrane fusion.

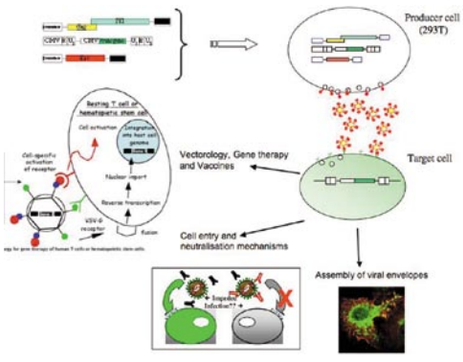
We are also pursuing studies aimed at optimizing methods allowing efficient gene delivery in vivo, by direct inoculation of defective viral vectors. The specific objectives are (i) the development of gene transfer vectors derived from onco-retroviruses and lentiviruses, (ii) the investigation of strategies allowing a targeted gene transfer, restricted to cells expressing a specific cell surface receptor, through modifications of the viral surface glycoproteins. These studies will ultimately lead to the development of new tools suitable for in vivo transgenesis and human gene therapy._ Finally, our studies on viral engineering and more particularly on the viral surface glycoproteins allow several therapeutic applications, particularly in (i) diagnostics, (ii) antiviral compounds screening and (iii) vaccine development. Some of these applications are being investigated, particularly in the field of hepatitis C and influenza.

Selected publications :

►Frecha, C., C. Costa, D. Negre, E. Gauthier, S. J. Russell, F. L. Cosset, and E. Verhoeyen. 2008. Stable transduction of quiescent T cells without induction of cycle progression by a novel lentiviral vector pseudotyped with measles virus glycoproteins. Blood 112:4843-52.

►Dreux, M., V. L. Dao Thi, J. Fresquet, M. Guerin, Z. Julia, G. Verney, D. Durantel, F. Zoulim, D. Lavillette, F. L. Cosset, and B. Bartosch. 2009. Receptor complementation and mutagenesis reveal SR-BI as an essential HCV entry factor and functionally imply its intra- and extra-cellular domains. PLoS Pathog 5: e1000310.

►Szecsi, J., G. Gabriel, G. Edfeldt, M. Michelet, H. D. Klenk, and F. L. Cosset. 2009. DNA Vaccination with a Single-Plasmid Construct Coding for Viruslike Particles Protects Mice against Infection with a Highly Pathogenic Avian Influenza A Virus. J Infect Dis. 200(2): 181-90.



EVIR team research. Retroviral vector particles are a common tool and are used in most of our areas of research to study: 1) Envelope assembly processes. The incorporation of envelope glycoproteins onto viral cores is a complex process that relies on interactions with different intracellular adaptor proteins. Understanding this process will help the development of pseudoparticles that are useful in vector development and might help to identify new antiviral targets; 2) Cell entry and neutralization studies. Pseudoparticles can incorporate envelope glycoproteins from many different viruses. They are used to study the cell entry processes of highly pathogenic viruses in level 1 or 2 laboratories. More particularly, some of our projects focus on the study of HCV cell entry processes. Moreover, as such pseudoparticles closely mimic the antigenic properties of the wild type viruses from which they are derived, they can be used to screen, determine or characterize the inhibitory effects induced by several molecules at the cell entry steps, e.g. neutralizing antibodies or sera from infected/immunized patients or animals; 3) Vectorology, gene therapy and vaccine developments. Vectors derived from lentiviruses can be easily engineered by surface display of T cell- or hematopoietic stem cell-specific ligands that, via activation of their cellular receptors, allows targeted gene delivery to these cells. Retroviral-based pseudotyped particles are also attractive immunogens that induce efficient humoral response and form promising vaccines, as currently evaluated for HCV or avian flu infection. ◄

►HUMAN VIROLOGY DEPARTMENT - VIRO◄

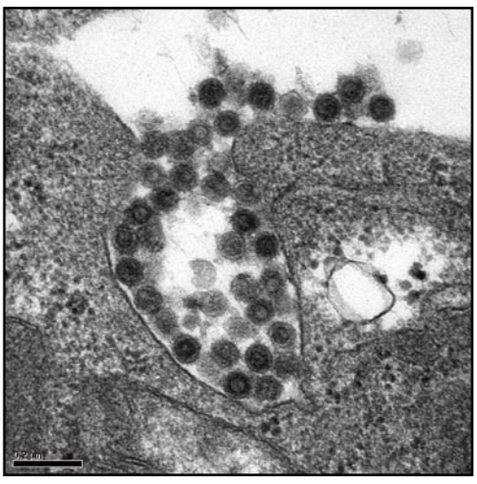
►LaboRetro◄

► **Team leader** ► ***Jean-Luc Darlix,*** *professor, DRE Inserm - jldarlix@ens-lyon.fr* ◄
► **Team members** ► *Sandrine Alais, engineer, Inserm; Greg Berger; PhD student; Anne Bocquin, engineer INSERM; Andrea Cimarelli, research associate first class, CNRS; Antoine Corbin, associate professor, ENS Lyon; Stéphanie Cordeil, Phd student; Gael Cristofari, research associate first class, Inserm; Stéphanie Durand, postdoctoral fellow; Boyan Grigorov, postdoctoral researcher; Elise Hamard-Perron, PhD student; Monika Kuciak, PhD student; Pascal Leblanc, research associate first class, CNRS; Julia Leinard, engineer; Delphine Muriaux, research associate first class, CNRS; Lise Rivière, PhD student: Xuan-Nhi Nguyen, engineer* ◄ *http://hvd.ens-lyon.fr/human_virology_dpt/teams/gs_lr*

► HIV and AIDS, HCV and hepatitis, and Endogenous Retroviruses in all of us

Viruses are widespread in the living world and, in some instances such as for HIV-1 and HCV, can be a serious threat to human health. The research done by LaboRetro is aimed at investigating the replication of HIV-1 and HCV in human cell lines and primary cells targeted by these pathogenic viruses. Since a major avenue of research in virology is to characterize the complex relationships between the infecting virus and host cells, we at LaboRetro are studying HIV-cell interactions at the physiological and molecular levels in an attempt to understand the mechanisms of virus formation, release and dissemination in cell populations. In that respect we are making a long standing efforts to dissect the role of cellular cofactors such as ribosomal proteins and tetraspanins, and of restriction factors such as proteasomal components and the prion. In a long lasting search for new lead compounds against HIV-1 and HCV, we have recently discovered, within a European Community collaborative network, new compounds inhibiting HIV-1 and HCV genome replication with an IC50 in the range of 1 nM.

One of the most striking discoveries made in genomics is the fact that almost half of our genome encodes endogenous retroviruses and retrovirus-like elements called retrotransposons. We at LaboRetro are combining complementary fundamental approaches to study the interactions between these mobile retro-elements and their host and how they replicate. Such investigations should help understand the origin of ancient retroviruses and of anti-viral defenses.



Picture by Electron Microscopy of HIV-1 infected human T-CD4 cell. Newly made HIV-1 particles accumulating in a cytoplasmic vesicle known as MVB are shown here to be released in the extra-cellular medium. A total of 30 virions – 110 nm in diameter each- can be seen with a dense internal core (Grigorov, Roingeard, Muriaux & Darlix). JMB 2006.
►

Selected publications:

►Ivanyi-Nagy R, Lavergne JP, Gabus C, Ficheux D, Darlix JL. RNA chaperoning and intrinsic disorder in the core proteins of Flaviviridae. Nucleic Acids Res. 2008;36(3):712-25.

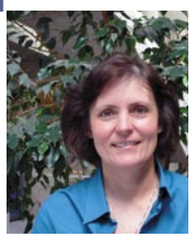
►Darlix JL, Garrido JL, Morellet N, Mély Y, de Rocquigny H. Properties, functions, and drug targeting of the multifunctional nucleocapsid protein of the human immunodeficiency virus. Adv Pharmacology 2007;55:299-346.

►Grigorov B, Décimo D, Smagulova F, Péchoux C, Mougel M, Muriaux D, Darlix JL. Intracellular HIV-1 Gag localization is impaired by mutations in the nucleocapsid zinc fingers. Retrovirology. 2007, 3;4:54.

►Goujon C, Rivière L, Jarrosson-Wuilleme L, Bernaud J, Rigal D, Darlix JL, Cimarelli A. SIVSM/HIV-2 Vpx proteins promote retroviral escape from a proteasomedependent restriction pathway present in human dendritic cells. Retrovirology. 2007 9;4:2.

►HUMAN VIROLOGY DEPARTMENT - VIRO◄

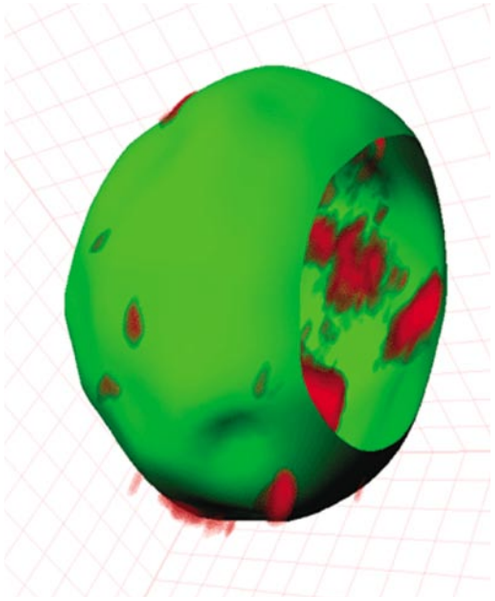
►IMMUNOBIOLOGY OF VIRAL INFECTION◄



►**TEAM LEADER** ► ***Branka Horvat*** *- branka.horvat@inserm.fr* ◄
► **TEAM MEMBERS** ► *Fahran Cyprian, PhD student; Céline Garcia, Engineer; Géraldine Gourru-Lesimple, Technician; Patrick Havener-Dughton Colin, Postdoctoral fellow; Jean-François Jegou, postdoctoral fellow; Julien Marie, Research associate second class; Cyrille Mathieu, PhD student; Joséphine Reynaud, PhD student Olga Romanets, PhD student; Anne Rouiz, Technician; Thomas Thevenet, Pharmacist resident; Fabian Wild, Professor emeritus.* ◄ ***http://hvd.ens-lyon.fr/human_virology_dpt/teams/gs_immunoviro***

►**VIRUSES AND THE IMMUNE SYSTEM ARE IN CONSTANT INTERACTION**, resulting with either elimination of a virus or infectious disease. Our group is studying several aspects of this dynamic relation, trying to understand the immunopathogenesis of viral infection and evasion from the immune control as well as to characterize major players in the regulation of immune reaction. We are particularly interested in:

1. Study of immunopathogenesis of measles virus infection, implication of interferon type 1 and analysis of the role of measles virus receptors, CD46 and CD150 (SLAM) in the induction of T cell mediated immunosuppression.
2. Analysis of the role of cytokine TGF beta in the regulation of lymphocytes T, by studing the effects of TGF-beta on the biology of T regulatory lymphocytes and NKT cells.
3. Immunopathology of recently discovered emerging viruses Nipah and Hendra by studying the susceptibility of different cell types to infection and role of non-structural virus genes in pathogenesis, using BSL4 laboratory.



3D representation of the localisation of measles virus nucleoprotein (in red) both inside and outside of a transfected cell (labelled in green). ◄

SELECTED PUBLICATIONS:

►Sellin C.I., Jégou J.F., Renneson J., Druelle J., Wild T.F., Marie C.J., Horvat B. Interplay between virus-specific effector response and Foxp3+ regulatory T cells in measles virus immunopathogenesis. PloS ONE, 4(3):e4948, 2009.

►Doisne J.M., Bartholin L., Yan, K., Garcia C.N., Duarte N., Martel, S., Horvat B., Vincent, D., Cyprian F., Rimokh R., Losson R., Benlagha K. and Marie J.C.: iNKT cell-development is orchestrated by different branches of TGF-ß1 signaling. J. Exp. Med., 206: 1365-1378, 2009.

►Guillaume V., Thong W., Looi R.Y., Georges-Courbot M.C., Barrot L., Buckland R., Wild F.T., Horvat B., Acute Hendra virus infection: Analysis of the pathogenesis and passive antibody protection in the hamster model. Virology, 387: 459-465, 2009.

►HUMAN VIROLOGY DEPARTMENT - VIRO◄

► Retroviral oncogenesis◄

► **Team leader** ► ***Renaud Mahieux,*** *Professor - renaud.mahieux@ens-lyon.fr* ◄
► **Team members** ► *Madeleine Duc Dodon, Research director; Estelle Douceron, PhD student; Louis Gazzolo, Research director; Chloé Journo, PhD student; Anne-Sophie Kuhlmann, PhD student; Renaud Mahieux, full professor; Mélanie Wencker, Graduate teaching assistant; Malgorzata Borowiak, PhD student; Julien Villaudy, PhD student* ◄
http://hvd.ens-lyon.fr/human_virology_dpt/teams

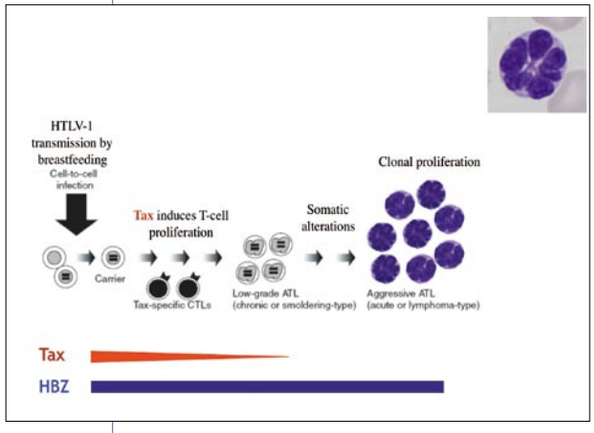
► **HTLV-1 was the first oncogenic human retrovirus to be discovered, followed by HTLV-2 and HTLV-3.** HTLV-1 is etiologically linked to two main diseases: Adult T Leukemia/Lymphoma and Tropical Spastic Paraparesis/HTLV-1 Associated Myelopathy.

I. Modulation of the expression of cellular genes by Tax.
We are determining the effect of Tax expression on the proliferation and differentiation of human immature thymocytes.
Tax represses hTERT transcription resulting in telomerase inactivation. We are investigating how this contributes to chromosomal instability during early leukemogenesis.
We are also investigating how Tax post-translational modifications play a role in NF-κB activation.

II. Functional analyses of the antisense proteins: HBZ HTLV-1 in the transformation process, and APH-2 HTLV-2 protein in chronic lymphocytosis.
HBZ interacts with Jun D to enhance transcription of hTERT gene and thus may contribute to the development and maintenance of the leukemic process. We are looking at the specific effect of HBZ on cell proliferation and/or transformation.
We have recently uncovered the existence of an antisense transcript in HTLV-2 infected cells encoding a protein that we named APH-2 (Antisense Protein of HTLV-2). We are investigating the function(s) of this protein.

III. Characterization of HTLV-3 regulatory proteins.
Our group has obtained the first infectious HTLV-3 molecular clone. We have recently uncovered the existence of different accessory proteins that are encoded by this virus. We are characterizing these proteins.

IV. Elaboration of new antiviral strategies
Using STLV-1 naturally infected animals, we try to determine how new compounds might decrease the proviral load in vivo and therefore prevent disease occurrence.



ATLL pathogenesis. Natural course from HTLV-1 primary infection by prolonged breast-feeding to the onset of the malignant proliferation of ATLL cells. Top panel: ATLL cell with multilobulated nuclei (May-Grunwald-Giemsa staining).

Selected publications:

►Wencker M, Sausse C, Derse D, Gazzolo L, Duc Dodon M. HTLV-1 Tax protein down-regulates the pre-TCRα gene transcription in human immature thymocytes. J. Virology. 2007. 81:301-308.
►Chevalier SA, Ko T, Calattini S, Mallet A, Prévost MC, Kehn K, Kashanchi F, Gessain A, Mahieux R. Construction and characterization of a Human T-cell Lymphotropic Virus Type-3 molecular clone. J. Virology. 2008. 82: 6747-6752.
►Journo C, Filipe J, About F, Chevalier SA, Brady JN, Afonso PV, Flynn D, Tangy F, Israël A, Vidalain PO, Mahieux and Robert Weil. NRP/Optineurin Cooperates with TAX1BP1 to Potentiate the Activation of NF-κB by Human T-Lymphotropic Virus Type 1 Tax Protein. Plos Pathogens. 2009. 5(7): e1000521.

►HUMAN VIROLOGY DEPARTMENT - VIRO◄

►Molecular biology of the G-herpesvirus◄

► **Team leader** ► ***Evelyne Manet*** *- emanet@ens-lyon.fr* ◄
► **Team members** ► *Quentin Bazot, PhD student; Henri Gruffat, research assistant first class; Franceline Juillard, PhD student; Evelyne Manet, research director second class; Fabrice Mure, engineer; Alain Sergeant, research director first class* ◄
http://hvd.ens-lyon.fr/human_virology_dpt

► **The Epstein-Barr virus (EBV) is a ubiquitous human γ-herpesvirus which is associated with several human malignancies** in immuno-competent individuals (the undifferentiated nasopharyngeal carcinoma (NPC), Burkitt's lymphoma (BL), Hodgkin's disease (HD)....as well as lymphoproliferations and lymphomas in immuno-compromised individuals. Furthermore, EBV has the unique capacity to induce the indefinite proliferation (or immortalization) of quiescent human B-lymphocytes, upon their infection in vitro. In these cells, there is no viral replication, but nine viral proteins are expressed which collaborate to induce and maintain the continuous proliferation of the cells.

One of our research objectives is to investigate the interactions between these nine EBV proteins and human proteins by using a stringent high-throughput yeast two hybrid screen. Such a systematic approach will help both to understand how the viral proteins cooperate to immortalize B-lymphocytes (integrative approach) and to generate new hypotheses on the molecular mechanisms involved in the function of each individual protein.

Our team's second objective is to understand the mechanisms of viral reactivation. After primoinfection, the virus persists during the life-time of individuals who are subjected to phases of viral production. These phases are thought to be a risk factor for the emergence of certain cancers. We are interested in the study of the regulation of expression (or function) of EB1, a viral transcriptional activator responsible for induction of the viral productive cycle. We are also interested in understanding the function of EB2, an essential early viral protein which is involved in the efficient export of viral mRNAs.

▲ *The Epstein-Barr virus EB2 protein colocalizes with the cellular protein, TAP, a major mRNA export factor, in the nucleus of the cells.*

Selected publications:

►CS. Aho., J. Lupo, P.-A. Coly, A. Sabine, M. Castellazzi, P. Morand, A. Sergeant, E. Manet, V Boyer,H. Gruffat (2009). Characterization of the Ubinuclein protein as a new member of the Nuclear and Adhesion Complex components (NaCos). Biol. Cell, 101(6), 319-334.

►E. P. Ricci,F. Mure, H. Gruffat, D. Decimo,C. Medina-Palazon, T. Ohlmann and E. Manet (2009). Translation of intronless RNAs is strongly stimulated by the Epstein-Barr virus mRNA export factor EB2. [Epub ahead of print]. Nucleic Acids Res. 2009 Jun 15.

►HUMAN VIROLOGY DEPARTMENT - VIRO◄

►Translational control of eukaryotic and viral mRNAs◄

► **Team leader** ► ***Théophile Ohlmann,*** *research associate, Inserm - théophile.ohlmann@ens-lyon.fr* ◄
► **Team members** ► *Laurent Balvay, Lecturer ENS-Lyon; Didier Decimo, Engineer INSERM; Coralie Cellier, Engineer, Sidaction; Sylvain De Breyne, Post-doc; Emiliano Ricci, PhD student; Ricardo Soto Rifo, PhD student; Taran Limousin, Master Student; Christelle Daude, Technician INSERM.* ◄
http://hvd.ens-lyon.fr/human_virology_dpt

► **We are interested in host-virus interactions** that are established in the course of viral translation with a particular emphasis on the molecular mechanisms which control the binding of the ribosomes to the 5' region of the genomic RNA. The structure of the genomic RNA is of particular importance in determining translational activity with the presence of Internal Ribosome Entry Sites (IRES) that have the unique ability to promote ribosome attachement in a 5' and cap-independent manner.

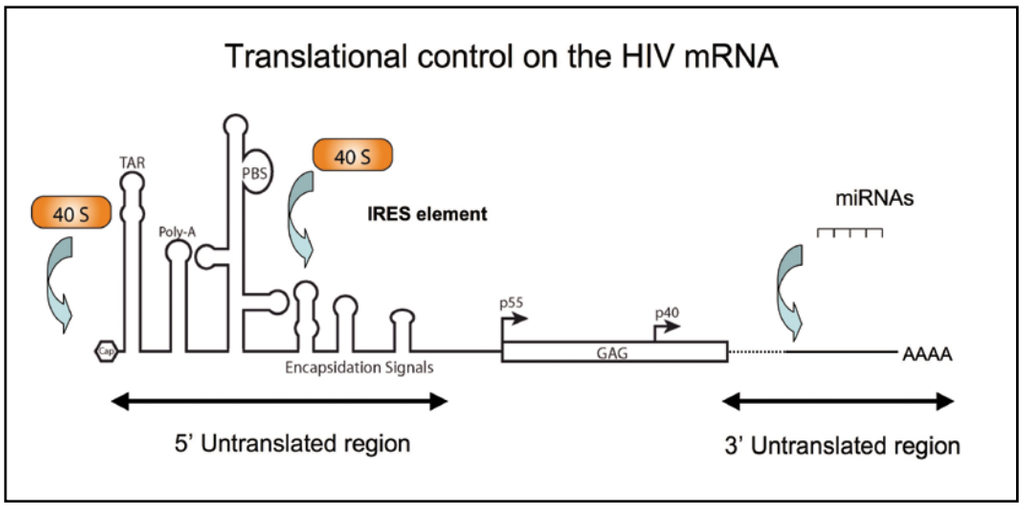
More recently, it has also been shown that gene expression can also be regulated at the translational level by 22-nt small non coding RNAs that can hybridize on the 3' untranslated region of the mRNA. These RNAs are called micro RNAs (miRNAs) and have the ability to hybridize to the 3' UTR of target genes. This results in the specific inhibition of these mRNAs at the level of translation given that they possess a 5' cap and a 3' end poly(A) tail. Therefore, we are currently investigating the molecular mechanism that triggers translational repression upon binding of these miRNAs to target mRNAs.

Selected publications:

►C.H.Herbreteau, E.P Ricci, D.Decimo , A.Schaupp, S.A.K.Datta, A.Rein, JL.Darlix and T.Ohlmann (2008). In vitro expression of the HIV-2 genomic RNA is controlled by 3 independent IRESes which are regulated by the HIV protease and the Gag polyprotein. RNA 2008 Jul;14(7):1443-55

►K.Dieterich, R.Soto Rifo, S.Hennebicq, B.Ben Amar, M.Zahi, J.Perrin, D.Martinez, A.Karen Faure, B.Sèle, PS.Jouk, T.Ohlmann, S.Rousseaux, J.Lunardi and P.F Ray (2007). A founding mutation of Aurora Kinase C yields large-headed polyploid spermatozoa causing infertility in man. Nat Genet. 39(5):661-5.

►L.Balvay, M.Lopez-Lastra, B.Sargueil, JL.Darlix and T.Ohlmann (2007), Translational Control of Retroviruses. Nat Rev Microbiol. 5(2):128-40.



Translation control on the HIV mRNA
Gene expression is controlled at the translational level on HIV mRNA. As such the mechanism of ribosome binding to the 5'UTR can occur in a cap-dependent manner or via an IRES element. Protein synthesis is also regulated by 22-nucleotide micro RNAs that bind to the 3' UTR of the target mRNA, resulting in translation inhibition. Our lab is primarily interested in understanding how viral protein synthesis is regulated by these mechanisms. ►

►HUMAN VIROLOGY DEPARTMENT - VIRO◄

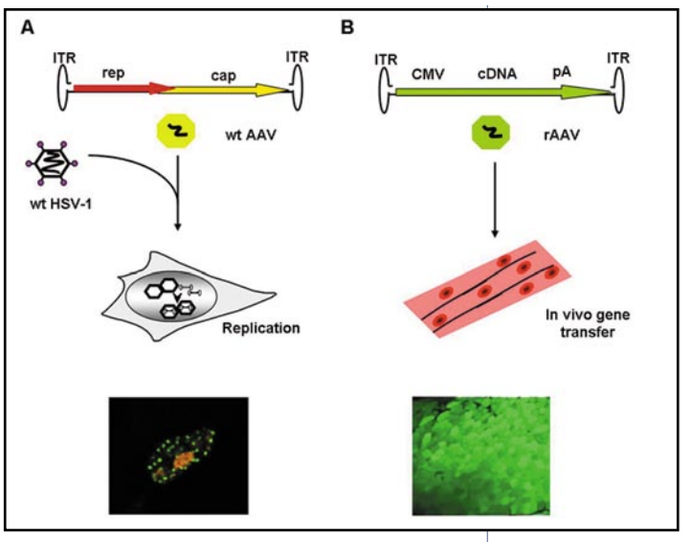
►Adeno-Associated Viruses and recombinant AAV vectors◄

► **Team leader** ► ***Anna Salvetti,*** *research director second class - anna.salvetti@ens-lyon.fr* ◄
► **Team members** ► *Nathalie Alazard-Dany, assistant professor; Emmanuel Gauthier, postdoctoral fellow; Armel Nicola, PhD student; Aurelie Ploquin, PhD student; Nelly Jolinon, technician* ◄
http://hvd.ens-lyon.fr/human_virology_dpt

► **The research activities of the team are oriented in two directions:**

1. The study of AAV replication. The objective of this research program is to identify the helper factors encoded by the Herpes Virus type 1 and the cellular proteins that are essential to induce AAV replication. This project is situated at the interface between fundamental research on AAV replication and biotechnological applications. It aims at improving our understanding of the biology of AAV vectors through the study of the wild type virus.
Collaborators: A. Epstein and A. Greco (CGMC UM5534, Lyon, France), C. Fraefel (U of Zurich, CH), S. Weller (U of Connecticut, USA), H. Büning (U of Cologne, Germany).

2. The use of rAAV vectors for vaccination against viral infections. The high efficiency of rAAV-mediated gene transfer is exploited to express in vivo various viral glycoproteins derived either from Hepatitis C or Nipah virus. These studies involve the characterization of humoral and cellular responses induced by rAAV vectors in comparison with other viral vectors. The objective of this research program is to define, in two different models, the potential of rAAV vectors for vaccination.
Collaborators: FL Cosset, B Horvat (Inserm U758).



▲ *A. Co-infection of cells with wt AAV in the presence of HSV-1 leads to the formation of nuclear replication centers where AAV Rep proteins (red) and HSV-1 DBP (green) co-localize.*

B. Recombinant AAV vectors mediate high efficiency gene transfer and expression of transgenes in vivo (here GFP expression in muscular cells).

Selected publications:

►Alazard-Dany N, Nicolas A, Ploquin A, Strasser R, Greco A, Epstein AL, Fraefel C. Salvetti A. 2009. Definition of Herpes Simplex Virus Type 1 Helper Activities for Adeno-Associated Virus Early Replication Events. PLoS Pathog 5(3): e1000340.
►Guilbaud M, Chadeuf G, Avolio F, François A, Moullier P, Recchia A, Salvetti A. Relative influence of the AAV-2 p5 element for rAAV vector site-specific integration. 2008. J. Virol. 82:2590-2593.

►HUMAN VIROLOGY DEPARTMENT - VIRO◄

►Biology of filoviruses◄

► **Team leader** ► ***Viktor Volchkov,*** *professor, UCBL - Viktor.volchkov@inserm.fr* ◄
► **Team members** ► *Sebastien Delpeut, PhD student; Mathieu Mateo, PhD student; Audrey Page, PhD student; St Patrick Reid, postdoctoral fellow; Olivier Reynard, engineer Inserm; Valentina Volchkova, engineer UCBL* ◄

http://hvd.ens-lyon.fr/human_virology_dpt

► **The filovirus laboratory seeks to identify the molecular bases of the high pathogenicity of filoviruses,** with a particular emphasis on Ebolavirus. In Volchkov's laboratory, experimental systems and approaches were developed for dissecting the events in a virus's replication cycle and the analysis of a variety of processes involved in viral genome replication, expression of viral proteins and virus-host interactions as independent phenomena. The systems include infectious cDNA copies of the genomes and mini-replicons. These reverse genetics systems are used to study the role of viral proteins in virus replication and pathogenicity.

Dr. Volchkov's Lab is also involved in a study of the molecular biology of the Nipah virus, which is another human pathogen requiring BSL P4 laboratory conditions. In this study, the investigators developed a reverse genetics system allowing live virus manipulations. The goal is to identify the molecular mechanisms that determine the ability of the virus to replicate in human cells, so as to advance our understanding of the pathogenesis of this virus and to target potential therapies.

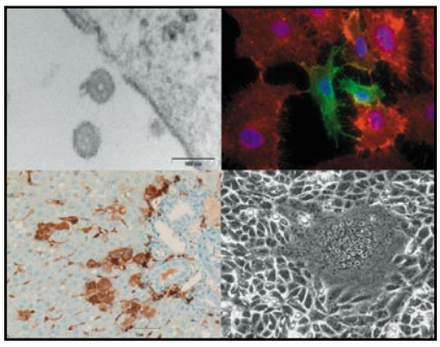
Selected publications :

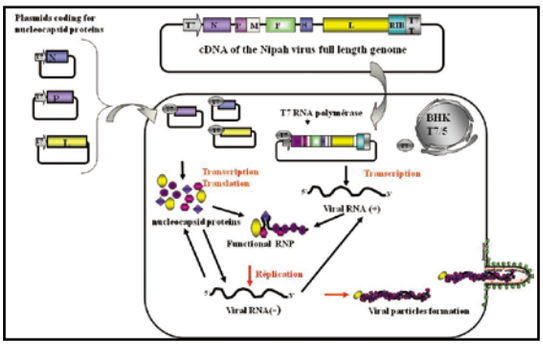
►Reynard O, Borowiak M, Volchkova VA, Delpeut S, Mateo M, Volchkov VE. Ebola virus glycoprotein GP masks both its own epitopes and the presence of cellular surface proteins. J Virol. 2009 Jul 8. [Epub ahead of print] PubMed PMID: 19587051.

►Ciancanelli MJ, Volchkova VA, Shaw ML, Volchkov VE, Basler CF. Nipah virus sequesters inactive STAT1 in the nucleus via a P gene-encoded mechanism. J. Virol. 2009 Jun 10. [Epub ahead of print] PubMed PMID: 19515782.

►Martínez MJ, Biedenkopf N, Volchkova V, Hartlieb B, Alazard-Dany N, Reynard O, Becker S, Volchkov V. Role of Ebola virus VP30 in transcription reinitiation. J Virol. 2008 Dec;82(24):12569-73. Epub 2008 Oct 1. PubMed PMID: 18829754; PubMed Central PMCID: PMC2593317.

►Volchkov VE, Volchkova VA, Muhlberger E, Kolesnikova LV, Weik M, Dolnik O, Klenk HD. Recovery of infectious Ebola virus from complementary DNA: NA editing of the GP gene and viral cytotoxicity. Science. 2001 Mar 9;291(5510):1965-9. Epub 2001 Feb 1. PubMed PMID: 11239157.





►RESEARCH AND TECHNICAL FACILITIES◄

► SHARED SERVICE:

PSMN (Pôle Scientifique de Modélisation Numérique)

This center maintains and operates computing facilities acquired within the framework of the Fédération Lyonnaise de Calcul Haute Performance (FLCHP) with additional financial support from the ENS Lyon, the Rhône-Alpes region, and the Ministère de l'éducation nationale, de l'enseignement supérieur et de la recherche (MENESR).

The center's principal mission is to make flexible, high-performance computing resources - including software and assistance staff - available to research laboratories at the ENS and, more widely, the University of Lyon. The PSMN also provides training in high-performance computing for the personnel of these laboratories, including doctoral and postdoctoral students.

Equipment: about 1000 cores (AMD and Intel)

► TECHNICAL AND RESEARCH FACILITIES:

The ENS Lyon, as a partner in the *Institut Fédératif de Recherche (IFR 128) BioSciences Gerland-Lyon Sud,* has access to the IFR's different technical facilities.

The IFR128 is composed of nine departments, 77 groups, and a research staff of nearly 700 members on the Gerland and Lyon Sud sites. (http://www.ifr128.prd.fr). The work carried out by the IFR covers the major fields of research in modem biology including cell biology, plant biology, protein biochemistry, bioinformatics, structural biology, molecular evolution, genomics, immunology and virology.

► IFR BIOSCIENCES GERLAND-LYON SUD TECHNICAL FACILITIES:

• **Genetic analysis:** Three services are associated with this facility: a sequencing service, a real-time PCR service and a vectorology service.

• **Fishery:** This facility raises and keeps different strains of the zebrafish, a species whose embryo is used as a model in experiments principally involving microinjection, and in situ and hybridization. Since March 2007, facility also raises medakas, southern platyfish, green swordtails, and guppies.

• **Protein microanalysis center:** This facility comprises three services: peptide, synthesis, sequencing proteins (Edman degradation), and mass spectrometry (instruments: API 165, MALDI-TOF Voyager DE-PRO, and Q-STAR XL).

• **Flow cytometry:** This facility is specialized in the multiparametric study of single cells suspended in a stream of fluid passing before lasers for analysis and high speed sorting along 4 paths (DiVa digital electronics).

• **Imagery/microscopy:** This center offers 9 systems of microscopy: confocal laser scanning microscopy, conventional fluorescence microscopy, video microscopy, stereo microscopy, and image analysis.

• **P3/IFR128 laboratory Facility:** This high security laboratory permits the manipulation of level 3 pathogens. It is equipped to permit cell culture and the extraction of lipids (incubators, fume hood, ultracentrifuges, etc.)

• **Production and analysis of proteins:** This facility is composed of three services: the production of recombinant proteins (prokaryotic and eukaryotic expression systems), structural and functional analysis of proteins (apparatus: circular dichroism, florescence spectropllotometer, Biacore T100) and the IFR128 cell bank.

► RESEARCH FACILITIES
LOCATED ON THE ENS LYON SITE:

• **Greenhouse type 2** (approved for the culture of transgenic plants)
This transgenic greenhouse has 8 growth rooms/chambers for a combined usable area of 240 square meters and is equipped with an automated climate control system which controls the environmental parameters thanks to equipment including: an evaporative cooling unit, heating (circulating warm air), shading mechanisms, under bench heating, supplemental lighting (sodium), fertiirrigation, wastewater treatment, etc.

• **PBES**
(Plateau de Biologie Expérimentale de la Souris)
This facility is specialized in the breeding, housing, and characterization of murine strains whether genetically modified or not. The facility currently houses approximately 200 specific pathogen free (SPF) strains, which translates into about 14,000 mice. Experiments can currently be carried out by researchers or as a service provided by the PBES under confinement conditions satisfying biosafety levels 1, 2 and 3.
Other activities at the PBES include the rederivation of mouse lines produced in other laboratories, the creation of new lines of genetically modified mice, and genotypic and phenotypic characterization (bone, fatty tissue, and immunological markers).
The PBES also offers new services in collaboration with laboratories belonging to IFR128. Projects currently under development include the cryopreservation of embryos, transgenesis using a lentivirus, and genotyping using QPCR, as well as perfecting new methods of phenotyping. The structural organization of the PBES makes it a high performance facility, allowing the introduction and rapid characterization of genetically modified murine strains.

• **PALGENE**
The French national paleogenetic platform PALGENE (CNRS/ENS Lyon) is dedicated to the ancient DNA analyses with 130 square meters of clean rooms with filtered air, positive pressure and UV light irradiation, equipped with the required molecular biology equipment. With the support of the "Paleogenetics and Molecular Evolution" team, PALGENE offers facilities to the entire scientific community to perform analyses and projects related to ancient DNA on all types of ancient biological materials.

• **Inductively coupled plasma mass spectrometer (ICP-MS)**
After many years of work and waiting, the Nu1700, third true high resolution and multicollection ICP-MS in the world, has been introduced/inaugurated at the Earth Science laboratory in May 2008.
This instrument will enable high precision isotopic measurements of elements previously only estimated/deduced with this type of machine (i.e. Fe, S, Si, Mg, Cu...)
The increase in precision may reach one order or magnitude for iron isotopes compared to a pseudo high resolution and multicollection instrument. A building has been specially commissioned to receive the instrument with draconian standards for vibrations, temperature and humidity.

• **NMR**
The European Center for High Field NMR in Lyon is the home to multidisciplinary research groups actively involved in developing NMR spectroscopy in chemistry, physics and biology including medicine. The center is an European large scale NMR facility offering access to European users to spectrometers (solid/liquid) from 500 MHz to 1GHz, hosting the first 1GHz spectrometer in the world.

►HIGHLIGHTING RESEARCH◄

► 11 new businesses have been created benefiting trom knowledge and know-how developed in ENS Lyon labs or benefiting trom an incubation period at the time of their creation.

► EXAMPLES:

- Varioptic: liquid lenses with electronically controlled focal length thanks to electrowetting technology. www.varioptic.com

- Genoway: development of animal models for therapeutic purposes. www.Genoway.com

- Altrabio: comprehensive solutions in exploration, mining and integrative analysis of life science data. www.altrabio.com

- Edelris: Conception, production and sales of innovative, therapeutically relevant, natural product-mimetic screening compounds. www.edelris.com

ln four years, over **20** co-owned patents have been filed, half of whichhave been licensed.

►AWARDS AND DISTINCTIONS◄

- Francis ALBAREDE, Professor, Earth Science Laboratory, Goldschmidt Award of the Geochemical Society, 2008.

- Nalini ANANTHARAM, Pure and Applied Mathematics Unit, Prix Gabrielle Sand et Marie Guido Triossi from the French Académie des Sciences, 2007.

- Philippe BOUVET, Director of research at the CNRS, Joliot-Curie Laboratory, CNRS Silver Medal, 2008.

- Martin CASTELNOVO, CNRS Research Associate, Physics/Joliot-Curie Laboratory, Prix Simone et Cino Del Duca from the Institut de France, 2009.

- François-Loïc COSSET, Director of research at the CNRS, Human Virology Department, ERC Advanced Grant, 2008.

- Marie DELATTRE, CNRS Research Associate, Molecular Biology of the Cell Laboratory, CNRS Bronze Medal, 2009.

- Thierry GAUDE, Director of research at the CNRS, Plant Reproduction and Development Laboratory, European Molecular Biology Organization Member (EMBO), 2008.

- **Etera LIVINE,** CNRS Research Associate, Physics Laboratory, CNRS Bronze Medal, 2008.

- Jean-François PINTON, Director of research at the CNRS, Physics Laboratory, Prix des Ingénieurs, 2007 and Prix CEA from the French Académie des Sciences, 2009.

- Cendrine MOSKALENKO, CNRS Associate Professor, Physics/Joliot-Curie Laboratory, Prix Simone et Cino Del Duca from the Institut de France, 2009.

- Delphine MURIAUX, CNRS Research Associate, Human Virology Department, Prix Simone et Cino Del Duca from the Institut de France, 2009.

- Philippe SAUTET, Director of research at the CNRS, Chemistry Laboratory, CNRS Silver Medal, 2007.

- Fabio Lucio TONINELLI, Physics Laboratory, CNRS Bronze Medal, 2007.

- Jan TRAAS, Director of research at the INRA, Plant Reproduction and Development Laboratory, Prix Jaffé from the Institut de France 2007.

- Cédric VILLANI, professor, Pure and Applied Mathematics Unit, Prix Jacques Herbrand from the French Académie des Sciences, 2007. Prix Henri Poincaré from the International Association of Mathematical Physics, 2009.

- Jean-Yves WELSCHINGER, CNRS Research Associate, Pure and Applied Mathematics Unit, Prix Ernest Déchelle from the French Académie des Sciences, 2008 and CNRS Bronze Medal, 2009.

- Gaël YVERT, CNRS Research Associate, Molecular Biology of the Cell Laboratory, CNRS Bronze Medal, 2009.

14 professors from the ENS Lyon belong to the Institut Universitaire de France.

►EUROPEAN CONTRACTS FP6 (2002-2006)◄

Project acronym	Scientist's name	Project title	Lab	Theme	Instrument
BIMAMOSI	B. SMIT	Materials Molecular Simulations	CECAM	Marie Curie actions	Excellence grants
CASCADE	V. LAUDET F. FLAMANT	Chemical as contaminants in the food chain	LBMC/ IGFL	LSH	NoE
CHROMOSOMAL CONTEXT	B. AUDIT	From the structural and dynamical chromosomal context to the functionnal organisation of genomes	LJC	Marie Curie actions	European Re-integration Grants
COMPUVAC	F.L. COSSET	Relation design and standardized evaluation of novel genetic vaccines	VIRO	LSH	IP
CONCORDE	P. SAUTET	Coordination of Nanostructured Catalytic Oxides Research and Development in Europe	CHIMIE	NMP	CA
CONSERT	F.L. COSSET	Concerted Safety & Efficiency Evaluation of Retroviral Transgenesis in Gene Therapy of Inherited Diseases	VIRO	LSH	IP
CONSTELLATION	I. BARAFFE	The origin of stellar masses	CRAL	Marie Curie actions	Research Training Networks
COREGRID	F. VIVIEN	European research network on foundations, software infrastructures and applications for large scale distributed, grid and peer-to-peer technologies	LIP	IST	NoE
CRESCENDO	J. SAMARUT V.LAUDET	Consortium fo Research into Nuclear Receptors in Development and Aging	LBMC	LSH	IP
EC-GIN	P. VICAT-BLANC	Europe-China Grid Internetworking	LIP	IST	STREP
EU-NMR	L. EMSLEY	European Network of Research Infrastructures for Providing Access and Technological Advancements in bio-NMR	CRMN	INFRASTR	Integrating activities
EUMODIC	J. MARVEL	european mouse disease clinic	PBES	LSH	IP
EUROSIM	B. SMIT	European Molecular Sumulations Training Program	CECAM	Marie Curie actions	Early-stage Training
GEOBIOCHRONOS	F. ALBAREDE	Uranium-lead dating of phosphate minerals	LST	Marie Curie actions	International Incomong fellowships
IDECAT	P. SAUTET	Integrated Design of Catalytic Nanomaterials for a Sustainable Production	CHIMIE	NMP	NoE
MAGMANET	P. SAUTET	Molecular approach to nanomagnets and multifunctional materials	CHIMIE	NMP	NoE
MATHLOGAPS	P. KOIRAN	Mathematical logic and applications	LIP	Marie Curie actions	Early-stage Training
MODELLING FLOWERS	J.TRAAS	Examining Arabidopsis floral organ number patterning using a dynamic computer model	RDP	Marie Curie actions	International Incoming Fellowships
MOLSIMU	B. SMIT	Molecular Simulations	CECAM	Marie Curie actions	Conferences and training courses
MONET	M. L.BOCQUET	Molecular Networks at Phase Boundaries	CHIMIE	Marie Curie actions	Early stage Training
MORPHEX	M. MORVAN	Morphogenesis and gene regulatory networks in plants and animals	LIP	IST	STREP
NL-LOC-SOLID	M. PEYRARD	Nonlinear Vibrational Localization on Solid Surfaces : Application to Catalysis	PHYS	Marie Curie actions	Intra European Fellowships
NONREGWKAM	A. FATHI	Non regular Weak Theory	UMPA	Marie Curie actions	Intra European Fellowships
ODEON	C. ANDRAUD	Design and Fabrication of Optoelectronic Devices Based on Innovative Second-order Non linear Organic Nanomaterials	CHIMIE	NMP	STREP
ONCE-CS	M. MORVAN	Open Network for Conneeting Excellence in Complex Systems	LIP	IST	CA
PSI-K TRAINING	B. SMIT	Training in Computationnal Nanoscience	CECAM	Marie Curie actions	Conferences and training courses
RISC RAD	E. GILSON	DNA damage responses, Genomic instability and radiation induced Cancer : the problem of risk at low and protracted doses	LBMC	LSH	IP
SY-STEM	J. TRAAS	Systems biology of stem cell function in Arabidopsis Thaliana	RDP	Marie Curie actions	Research Training Networks
TRIOH	JL. DARLIX	Targeting replication and integration of HIV	VIRO	LSH	IP
X-OMICS	V. LAUDET	Xenopus Comparative Genomics :coordinating integrated and comparative functional genomics for understanding normal and pathologic development	LBMC	LSH	CA

►EUROPEAN CONTRACTS FP7 (2007-2013)◄

Project acronym	Scientist's name	Project title	Lab	Theme	Instrument
AUTOI	L. LEFEVRE	Autonomic Internet	LIP	ICT	Collaborative project
DYNANETS	E. BOIX	Computing Real World with Dynamically Changing complex	LIP	ICT	Small or medium-scale focused research project
EURO-NF	P. VICAT-BLANC	Anticipating the Network of the future - from theory to design (EURO-NF)	LIP	ICT	Networks of Excellence
HEPCENT	FL. COSSET	Molecular analysis of hepatitis C virus neutralization and entry for the development of novel antiviral immunopreventive strategies	VIRO	ERC Advanced Grants	Advanced Grant
LUPAS	C. ANDRAUD	Luminescent polymers for in vivo imaging of Amyloid Signatures	CHIMIE	HEALTH	Collaborative project
METAGENOGRIDS	F. VIVIEN	Algorithmics for metagenomics on grids	LIP	PEOPLE	MC Action International Outgoing Fellowships
MODEL-IN	D. ANGELOV	Genomic determinants of inflammation: from physical measurements to system perturbation and mathematical modelling	LBMC	HEALTH	Small or medium-scale focused research project
OGF Europe	L. LEFEVRE	Mobilising and integrating communities on grid standards and best practices globally	LIP	INFRA	Coordination and support actions
P53ADHESION	B. MOLLEREAU	The role of Drosophila suppressor gene p53 in apoptosis and adhesion	LBMC	PEOPLE	MC Action European Reintegration Grants
PACCAP	N. PORTIER	Problems in Algebraic Complexity ans complexity of Algebraic problems	LIP	PEOPLE	MC Action International Outgoing Fellowships
PERSIST	F.L. COSSET	Persisting Transgenesis	VIRO	HEALTH	Large-scale integrating project
PROTEIN DYNAMICS	L. EMSLEY	Conformational Dynamics of Proteins in the Solid-State	CRMN	PEOPLE	MC Action European Intra-European Fellowships MC Action International Reintegration Grants
SME RECEPTOR	V. LAUDET	SME-Academia Nuclear Receptor Knowledge Transfer	IGFL	PEOPLE	Industry-Academia Partnerships and Pathways (IAPP)
T3NET	P. JURDIC	Tissue Transmigration Training Network	IGFL	PEOPLE	Initial Training Networks
TELOMARKER	E. GILSON	Identification and characterization of novel human telomere-related biomarkers	LBMC	HEALTH	Small or medium-scale focused research project

Whole funding from FP7 (Framework Programme - European Commission) for the contracts signed in 2008: 1 100 000 €

▸GRANTS FROM THE FRENCH NATIONAL AGENCY FOR RESEARCH (ANR)◂

Project acronym	Scientist's name	Call	Labo	Theme	ANR Programme
RetroMyriads	Gaël CRISTOFARI	2008	VIRO	Non thématique	JC (Jeunes chercheurs)
EXO PRION	Pascal LEBLANC	2008	VIRO	Biologie Santé	MIE (Maladies infectieuses et leur environnement)
KISMET	Vincent LAUDET	2008	IGFL	Biologie Santé	CES (Contaminants, Écosystème, Santé)
seXYphophorus	Jean-Nicolas VOLFF	2008	IGFL	Non thématique	Blanc (Biologie agronomiques et écologiques)
AtHeRoma	Jacques SAMARUT	2008	IGFL	Biologie Santé	GENOPAT (Gène physiopathologie maladies rares aux maladies communes)
SEXYTROUT	Jean-Nicolas VOLFF	2008	IGFL	GENOMIQUE ANIMALE	Écosystème et Développement Durable
ERROS	Jean-Marc VANACKER	2008	IGFL	Biologie Santé	GENOPAT (Gène physiopathologie maladies rares aux maladies communes)
RETROMER	Thierry GAUDE	2008	RDP	Non thématique	Blanc (Biologie agronomiques et écologiques)
Hipcal	Pascale PRIMET VICAT-BLANC	2008	LIP	Sciences et Technologies de l'information	CIS (Calcul Intensif et Simulation)
Dmasc	Paulo GONCALVES	2008	LIP	Sciences et Technologies de l'information	SYSCOMM (Systèmes complexes et modélisation mathématique)
Geneshape	Éric BOIX	2008	LIP	Sciences et Technologies de l'information	SYSCOMM (Systèmes complexes et modélisation mathématique)
Spades	Eddy CARON	2008	LIP	Sciences et Technologies de l'information	ARPEGE (Programme Systèmes Embarqués)
Complice	Daniel HIRSCHKOFF	2008	LIP	Non thématique	Blanc (Sciences et Technologies de l'information et Communication)
PIWO	Tierry DAUXOIS	2008	PHY	Non thématique	Blanc (Physique)
VKS	Jean François PINTON	2008	PHY	Non thématique	Blanc (Physique)
MUSE	Paul FLEURAT-LESSARD	2008	CHIMIE	Ingénierie, Procédés et Sécurité	Chimie et Procédés pour le Développement Durable
GuiChiHeli	Laure GUY	2008	CHIMIE	Non thématique	Blanc (Chimie)
MAFALDA	David LOFFREDA	2008	CHIMIE	Énergie durable & environnement	«PANH (Plan d'action national sur l'hydrogène et les piles à combustible)»
Dyn-BMO	Stéphane LABROSSE	2008	LST	Non thématique	JC (Jeunes chercheurs)
SUBDEF	Bruno REYNARD	2008	LST	Non thématique	Blanc (Sciences de l'univers et géo-environnement)
PARA-NMR	Guido PINTACUDA	2008	CRMN	Non thématique	Blanc (Chimie)
mQTL	Marc-Emmanuel DUMAS	2008	CRMN	Biologie Santé	GENOPAT (Gène physiopathologie maladies rares aux maladies communes)
GranMA	Alice GUIONNET	2008	UMPA	Non thématique	Blanc (Interdisciplinaire)
BIMBO	Emmanuel GRENIER	2008	UMPA	Biologie Santé	SYSCOMM (Systèmes complexes et modélisation mathématique)
Floer Power	Jean-Yves WELSCHINGER	2008	UMPA	Non thématique	Blanc (Mathématique et interactions)
17myclmPact	Christine DELPRAT	2008	LBMC	Biologie Santé	MIE (Maladies infectieuses et leur environnement)
agingstat	Hugo AGUILANIU	2008	LBMC	Biologie Santé	PCV (Physique et chimie du vivant)
CMS	Laurent SCHAEFFER	2008	LBMC	Biologie Santé	MIE (Maladies infectieuses et leur environnement)
USS SimGrid	Frédéric VIVIEN	2008	LIP	Sciences et Technologies de l'information	ARPEGE (Programme Systèmes Embarqués)
ModPol	Chantal ANDRAUD	2007	CHIMIE	Matière et Information	TLCOM (Télécommunications)
DSPET	Jean François PINTON	2007	PHY	Non thématique	Blanc (Physique)
fdp magnets	Robert VINCENT	2007	CHIMIE	Non thématique	JC (Jeunes chercheurs)
DUSTY DISKS	Jean-François GONZALEZ	2007	CRAL	Non thématique	Blanc (Science de l'univers et géo-environnement)
MAPP	Gilles CHABRIER	2007	CRAL	Non thématique	Blanc (Science de l'univers et géo-environnement)

Project acronym	Scientist's name	Call	Labo	Theme	ANR Programme
PROTEIN MOTION	Lyndon EMSLEY	2007	CRMN	Biologie et Santé	PCV (Physique et chimie du vivant)
ChemoNMRBiomed	Marc-Emmanuel DUMAS	2007	CRMN	Non thématique	JC (Jeunes chercheurs)
SPECICUIR	Catherine HANNI	2007	IGFL	Biologie et Santé	RIB (Recherche et innovation en biotechnologie)
PERHAMO	Catherine HANNI	2007	IGFL	Non thématique	Blanc (Sciences humaines et sociales)
EpiDev	Francesca PALLADINO	2007	LBMC	Non thématique	Blanc (Biologie santé)
SYSBIOX	Marc-Emmanuel DUMAS	2007	CRMN	Ingénierie, Procédés et Sécurité	CP2D (Chimie et Procédés pour le Développement Durable)
TF-CODE	Charlie SCUTT	2007	RDP	Non thématique	Blanc (Sciences agronomiques et écologiques)
SWITCH	Frédéric FLAMANT	2007	IGFL	Biologie et Santé	NEURO (Neurosciences, Neurologie et Psychiatrie)
YEASTDROPLETS	Gaël YVERT	2007	LBMC	Non thématique	Blanc (Projet interdisciplinaires)
GIMIC	Francesca CHILLA	2007	PHY	Non thématique	Blanc (Sciences et technologies de l'information et la communication)
CATHECLOSM	Véronique DUFAUD	2007	CHIMIE	Non thématique	Blanc (Chimie)
TCHATER	Florent DUPONT DE DINECHIN	2007	LIP	Matière et Information	TLCOM (Télécommunications)
RAnteriorHox	Michael SCHUBERT	2007	IGFL	Non thématique	Blanc (Biologie santé)
NUCLEOLIN	Philippe BOUVET	2007	LJC	Non thématique	Blanc (Biologie santé)
stochaGrid	Yves ROBERT	2007	LIP	Non thématique	Blanc (Sciences et technologies de l'information et de la communication)
STaRAC	Patrick FLANDRIN	2007	PHY	Non thématique	Blanc (Physique)
DualSugraSring	Henning SAMTLEBEN	2007	PHY	Non thématique	Chaire d'excellence
KAMFAIBLE	Marc-Emmanuel DUMAS	2007	UMPA	Non thématique	Blanc (Mathématique et interactions)
OPT-HIP	Pierre JURDIC	2007	IGFL	Biologie et Santé	PMP (Programme Matériaux et Procédés)
AUXFATE	Samuel Teva VERNOUX	2007	RDP	Non thématique	JC (Jeunes chercheurs)
CHOCO	Daniel HIRSCHKOFF	2007	LIP	Non thématique	Blanc (Sciences et technologies de l'information et de la communication)
BIOCAPT	Vance BERGERON	2007	PHY	Biologie et Santé	Santé Environnement et santé- travail
SCLAP	Philippe AUDEBAUD	2007	LIP	Matière et Information	SERUR (Sécurité et Sûreté Informatique)
GEODYCOS	Thierry BARBOT	2007	UMPA	Non thématique	Blanc (Mathématique et interactions)
EBORESISTANCE	Victor VOLCHKOV	2007	VIRO	Biologie et Santé	MIME (Microbiologie Maladie Émergentes)
SOLSTICE	Jean Yves L'EXCELLENT	2007	LIP	Sciences et Technologies de l'information	CIS (Calcul Intensif et Simulation)
H-INTER	Berend SMIT	2006	Cecam	Non thématique	Blanc (Sciences de l'ingénieur)
BULPOXI	Jean Pierre DUTASTA	2006	CHIMIE	Non thématique	PCV (Physique et chimie du vivant)
METHANO-METHANOL	Galina MATOUZENKO	2006	CHIMIE	Non thématique	Blanc (Chimie)
SIRE	Philippe SAUTET	2006	CHIMIE	Sciences et Technologies de l'information	CIS (Calcul Intensif et Simulation)
INESS	Marie Laure BOQUET	2006	CHIMIE	Non thématique	JC (Jeunes chercheurs)
PSD-NMR	Marc-Emmanuel DUMAS	2006	CRMN	Non thématique	Blanc (Chimie)
ECLAT	Philippe SAUTET	2006	CHIMIE	Sciences et Technologies de l'information	PNANO (Programme National en Nanosciences et Nanotechnologies)
NANOMOL	Galina MATOUZENKO	2006	CHIMIE	Sciences et Technologies de l'information	PNANO (Programme National en Nanosciences et Nanotechnologies)
Croissance	Yann Gael GANGLOFF	2006	LBMC	Non thématique	Blanc (Biologie santé)
TELOREG	Eric GILSON	2006	LBMC	Non thématique	Blanc (Biologie santé)
SIGNATOR	Jacques SAMARUT	2006	IGFL	Non thématique	Blanc (Biologie santé)
QUENOTTES	Vincent LAUDET	2006	IGFL	Non thématique	Blanc (Sciences agronomiques et écologiques)
PODOSOMES	Pierre JURDIC	2006	IGFL	Non thématique	Blanc (Biologie santé)
GENOSTEM	Catherine HANNI	2006	IGFL	Écosystèmes & Développement Durable	GENANIMAL (Réseau de génomique animale)
GWENDIA	Frédéric DESPREZ	2006	LIP	Sciences et Technologies de l'information	Masse de Données - Connaissances Ambiantes

Project acronym	Scientist's name	Call	Labo	Theme	ANR Programme
BEGDy	Janne BLICHERT	2006	LST	Non thématique	Blanc (Science de l'univers et géo-environnement)
ETHER	Yanick RICARD	2006	LST	Non thématique	Blanc (Science de l'univers et géo-environnement)
DNAnucl	Philippe BOUVET	2006	LJC	Biologie et Santé	PCV (Physique et chimie du vivant)
MESOGLASS	David CARPENTIER	2006	PHY	Non thématique	Blanc (Physique)
LQG-2006	Etera LIVINE	2006	PHY	Non thématique	Blanc (Physique)
PROTEUS	Yves Henri SANEJOUAND	2006	PHY	Sciences et Technologies de l'information	CIS (Calcul Intensif et Simulation)
SYMPLEXE	Etienne GHYS	2006	UMPA	Non thématique	Blanc (Mathématique et interactions)
AVC in silico	Emmanuel GRENIER	2006	UMPA	Biologie et Santé	BIOSYS (Biologie systémique)
INGEMOL	Stéphane DECOMBE	2006	UMPA	Non thématique	Blanc (Mathématique et interactions)
IRES Function	Jean Luc DARLIX	2006	VIRO	Non thématique	Blanc (Biologie santé)
EBV-INTER	Evelyne MANET	2006	VIRO	Microbiologie, Immunologie et Maladies Emergentes	MIME (Microbiologie Maladies Émergentes)
pseudoFlu	François-Loïc COSSET	2006	VIRO	Microbiologie, Immunologie et Maladies Emergentes	MIME (Microbiologie Maladies Émergentes)
ALPAGE	Yves ROBERT	2005	LIP	Sciences et Technologies de l'information	ARA MDMSA (Mod., Simu. Applications)
EVA-Flo	Nathalie REVOL	2006	LIP	Non thématique	Blanc (Sciences et Technologies de l'information et Communication)
VIRNET	Michel MORVAN	2006	LIP	Sciences et Technologies de l'information	CIS (Calcul Intensif et Simulation)
Mecamerge	Jacques MAZOYER	2006	LIP	Non thématique	Blanc (Sciences et Technologies de l'information et Communication)

►WHOLE FUNDING FOR ANR 2005-2008◄

Request for proposal	2005	2006	2007	2008	TOTAL
Number of submitted projects	87	84	85	82	338
Number of accepted projects	39	31	31	29	130
Success rate	45,00%	36,00%	36,00%	35,00%	38,00%
Amount granted to ENS teams (in million of €)	4,64	4,98	4,97	4,8	19,39

►INDEX◄

►**In bold** : Laboratory Directors

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