

SCIENTIFIC REPORT 2017



### THE PRESIDENT EDITORIAL

In 2017, LE STUDIUM operated on the very sustained rhythm set in the previous years and was honored to hear the recognition of the European Commission. The cumulative achievement of its two framework programmes – the original General SMART LOIRE VALLEY FELLOWSHIPS PROGAMME integrated in the Marie Sklodowska-Curie Actions of the European Union and the Ambition Research and the Development 2020 Programmes – have fully mobilized the LE STUDIUM team and its governance. LE STUDIUM, via several calls for projects targeted or open to all scientific disciplines, collects and submits to independent evaluators and then to its Scientific Council projects and senior profiles that once selected come to enrich the research teams of the Centre-Val de Loire region. Each year, an average of twenty international experienced researchers come for several monthsto live there, and more than two hundred researchers for several days or weeks to take part to scientific events organized by LE STUDIUM (Workshops, Conferences, Summer Schools, Experts Days, Consortia). So many ambassadors of the Loire Valley Intelligence who after their passage light a series of bright spots pointing to

It is important to highlight the actors who create and maintain, over time, at a high level, the quality value offered by LE STUDIUM. Quality of its evaluation processes, of its standards and the so essential quality of the care and environment offered to those who come from very far away to experiment in our region the science developed here and discover its patrimonial wealth.

In a circumstantial way in October 2017, the European Commissioner for Research, Science and Innovation, Carlos Moedas, has expressed an encouraging mark of gratitude for LE STUDIUM: « I have seen and visited many research institutes, I have not seen an organization of this nature elsewhere. It's a model for Europe ». Recognition that belongs right to its founder, Professor Paul Vigny, and to all those who have worked in its aftermath, recognition as well to elected representatives of the Centre-Val de Loire region, the Loiret council, the city of Orleans, and academic partners who support the creative intelligence and the openness to the world supported by LE STUDIUM programmes.

Reading this scientific report is a real cultural journey to discover LE STUDIUM researchers and the projects that drive them; it allows the reader to walk in the knowledge park of our region: the University of Orléans, the University of Tours, INSA Centre-Val de Loire, ESAD Orléans, the CNRS laboratories, the Centre Inra Val de Loire, BRGM, IRSTEA, CEA Le Ripault and INSERM. Through the plurality of themes and host laboratories, LE STUDIUM thus offers a reading of the varied intelligence landscape of the region, enriched by high-level international contributions. Combined with a rich heritage history of the Loire Valley, this knowledge park stands as a link between the elegance of the past inherited from our elders and the work of networked researchers who deepen the fundamentals for tomorrow. It is key to underline that the long-term efforts of all regional partners, with the Centre-Val de Loire Region at their head, are able to produce an attractive and harmonious signal of Quality, perceptible from distant territories. Europe has already identified it.

Following President Ary Bruand, it is now up to me to maintain it and enrich it with new colors and new flavors. I express to our partner members, to the elected officials who support us, to our dedicated LE STUDIUM team, my respect and thanks for their commitment to our side and my conviction of a singular radiance to shine on the Loire Valley.

Mr Yves-Michel Ginot.

President

our region.



### **IDENTITY & MISSION**

LE STUDIUM Loire Valley Institute for Advanced Studies: a unique support to research and innovation in the Centre-Val de Loire region and intellectual space for interdisciplinary exchanges

Established in 1996 and inspired by the historical, geographical and human cultures of the Loire Valley, LE STUDIUM Loire Valley Institute for Advanced Studies is an internationally recognised regional agency, whose mission is to create in the region Centre- Val de Loire an outward looking dynamic for the scientific community that includes public and private research stakeholders, to contribute to the strengthening of human capital for research, development and innovation and to participate in the valorisation of research and regional scientific and economic influence.

To achieve its objectives LESTUDIUM supports international collaborative research projects and the mobility of experienced international researchers across all scientific disciplines, selects, recruits and hosts experienced international researchers through calls for applications and develops a rich scientific animation programme with the organisation of international conferences, workshops, transdisciplinary seminars, and events for the promotion of the scientific culture and knowledge. Each selected researcher benefits from a dedicated assistance to facilitate his/her smooth and prompt integration in the region.

The SMART LOIRE VALLEY general programme, for the period 2015-2020, operates with a co-financing from the European Union in the framework of the Marie Skłodowska-Curie Actions - COFUND for the mobility of experienced researchers. Parallelly LE STUDIUM is the official partner for the international dynamic, recruitments and scientific events of the ARD 2020 smart specialisation programmes initiated by the Region Centre-Val de Loire.

Based in city center of Orléans at the Hôtel Dupanloup, the International University Centre for Research, LE STUDIUM maintains deep interactions with many regional cities, structures and agencies. It enjoys prestigious premises and exceptional facilities accessible to visiting and regional researchers. Its enhanced international presence in the city of Orléans strengthens its attractiveness to welcome high-level talents in the region Central-Val de Loire.

In order to achieve its mission at the interconnection between fundamental research and innovation, LE STUDIUM benefits from a strong regional network of scientific partners and works in close collaboration with regional research stakeholders:

- Higher education and research institutions:
  University of Orléans, University of Tours, INSA
  Centre-Val de Loire, ESAD Orléans
- National research institutes: BRGM, CNRS Centre Limousin Poitou-Charente, CEA Le Ripault, Centre Inra Val de Loire, Inserm, IRSTEA
- Poles of Competitiveness: Cosmetic Valley, Elastopole, Dream, S2E2
- Other clusters and organisations: Euclide, Dev'Up, Vegepolys, POLEPHARMA, Centre-Sciences, CCI, etc...

LE STUDIUM Loire Valley Institute for Advanced Studies awards are attributed thanks to the support and expertise of LE STUDIUM Scientific Council composed of more than twenty renowned scientists who regularly dedicate some of their precious time to evaluate research projects and candidacies.

LE STUDIUM Loire Valley Institute for Advanced Studies provides its researchers in residence an intellectual and human space, which favours interdisciplinary exchanges and debates, guided by the three necessary conditions required for creative activity, namely Curiosity, Imagination and Intuition.



# **SCIENTIFIC VISION**& SURROUNDINGS

# From fundamental research to innovation and socio-economic development

LE STUDIUM Loire Valley Institute for Advanced Studies is strongly imbedded in the Centre-Val de Loire region's research landscape. With more than 20 years of existence and holding a prestigious portfolio of regional and international research programmes, LE STUDIUM activities continue to grow and spread light on its partners. The focus of its mission remains to build the human capacity for research and scientific knowledge to foster socioeconomic development and innovation. As a matter of fact, LE STUDIUM's expertise displays from attracting, managing a growing flow of global research exchanges, creating new scientific value chains, and contributing to the emergence of innovative, collaborative research and enterprise activities. The impact of new knowledge on the economy is incremental, but the cumulative effect is substantial.

In November 2015, LE STUDIUM was awarded by the European Union Horizon 2020 COFUND in the category of the Marie Skłodowska-Curie Actions. As planned, the Smart Loire Valley Fellowship Programme (SLV) now enables LE STUDIUM to select and attract more than twenty experienced research fellows who come

to spend a one-year full time residency in the region Centre-Val de Loire. This award brought a five-year co-financing to the initial support provided by the Regional Council of Centre-Val de Loire and brings substantial benefits to all the laboratories of LE STUDIUM members.

In June 2017, LE STUDIUM Scientific Council reviewed sixty-five applications and recommended a total of seventeen awards, including two Research Professorships, thirteen Fellowships and two Consortia. Other recruitments and awards were conducted in the framework of the ARD 2020 smart specialization programmes initiated by the Regional Council Centre-Val de Loire in which LE STUDIUM is a key partner for the international dynamics and scientific events.

This past year, LE STUDIUM has attracted and welcomed a total of thirty-three international researchers from thirteen countries. These awards were across diverse disciplines from the social sciences, natural sciences and engineering at laboratories located in Orléans, Tours, Bourges and Blois.

The monthly transdisciplinary seminars, LE STUDIUM Thursdays, are praised by all participants, LE STUDIUM Thursdays enable Research Fellows to advance their presentation skills, to gain a deeper understanding of all regional research activities, to experiment concrete transdisciplinary exchanges and to enhance visibility of host laboratories. PhD students are invited to attend, an opportunity that allows them to validate transversal credits and increase their scientific culture and knowledge. The eleven events organised in 2017 have again demonstrated the diversity of research projects represented in the faculty of fellows and the creative interactions that emerged in all discussions.

As part of the awards given to selected candidates, LE STUDIUM finances the organisation of Conferences and Workshops; these multidisciplinary events continue to attract a large number of leading international researchers to the Centre-Val de Loire region each year. Their rather small size and peculiar specificity offer the ideal scenery for the creation of dynamic discussions, which often result in new ideas for research and international collaborations. This past year we have also been pleased to partner with regional laboratories to hold a number of affiliated scientific fora. These partnership events are a significant evidence of the collaborative dynamic existing between LE STUDIUM and the laboratories of our regional members.

Evening public conferences, LE STUDIUM Lectures and Rencontres Leonardo, contribute to the general public's awareness of research and stimulates the transfer of scientific knowledge to a wider audience; these events keep the local community informed about regional research activities and have become increasingly popular following the implementation of a new community linked promotion strategy. The partnership with the universities and other local actors is essential to increase visibility and participation to these events.

LE STUDIUM is an international outward looking regional partner offering opportunities to access and develop fundamental research projects. These are essential to lead to new knowledge and create the fund from which the practical application of knowledge must be drawn. LE STUDIUM's mission nurtures this process closely linked to innovation, together with the laboratories of our members, to achieve quality socio-economic outcomes for the region Centre-Val de Loire.

# THE SMART LOIRE VALLEY PROGRAMMES

# The Smart Loire Valley General Programme

The Smart Loire Valley Programme call for applications, open from November each year to February next year, for the period 2015-2020, operates with a co-financing from the European Union in the framework of the Marie Skłodowska-Curie Actions - COFUND (Co-Funding of regional, national and international programmes) for the mobility of experienced researchers. The Smart Loire Valley Programme is designed to foster international scientific exchanges and collaborations and to build human capacity and scientific knowledge for research, development and innovation in the region Centre-Val de Loire. It is open to all scientific disciplines and is a precious tool to access funding to develop fundamental research projects.

Events and the networking actions organised by LE STUDIUM aim at creating synergies between academic disciplines and links with the industrial world in order to increase interdisciplinary research and translational research to stimulate socioeconomic development. Scientific projects are evaluated and selected by independent external peer reviewers and an independent Scientific Council to award the best candidates and high added-value research projects. To be eligible, applicant researchers must be nationals or long-term residents of a country other than France and comply with the European mobility rules.

# LE STUDIUM RESEARCH FELLOWSHIP \*

This award enables experienced international researchers to work in a host laboratory for one-year. The award is designed to offer internationally competitive researchers the opportunity to discover and work in nationally accredited laboratories with international renown in the region Centre-Val de Loire. A salary and a fully furnished housing are associated to the award.

# PROFESSORSHIP

This award enables an experienced international Professor to participate in research, research team building and postgraduate teaching. The Professorship residency is a period of three months in the region Centre-Val de Loire for 4 consecutive years (12 months in total). For this award two laboratories in the region Centre-Val de Loire or three teams from the same laboratory need to be involved. A salary and a fully furnished housing are associated to the award.

# LE STUDIUM RESEARCH CONSORTIUM

This award enables the creation of a team of five researchers (including one researcher or research team from the region Centre-Val de Loire) and funds its regular gatherings for a full week twice a year over 2 years (4 meetings in total). The consortium projects have well-defined research objectives, a work plan to implement and milestone goals to achieve between meetings.

# The Ambition Research Development 2020 Programmes (ARD 2020)

The long-term Socio-economic development of the region Centre-Val de Loire, in a period of economic fragility, depends on the strength and growth of quality research, development and innovation.

The ARD 2020 programmes, the Centre-Val de Loire Region's initiative to implement the EU Smart Specialisation Strategy, have been designed to generate Socio-economic impacts by providing support to create strong regional research and develop centres of international scale, stimulate innovation and job creation and, socioeconomic dynamism in the territory.

Through these large research programmes, the Centre-Val de Loire Region supports the strengthening of quality research in five targeted domains to foster the development of world-class poles to enhance research and innovation activity in the region:

- ARD 2020 Biomédicaments (biopharmaceuticals),
- ARD 2020 Cosmetosciences (cosmetics),
- ARD 2020 LAVOISIER (renewable energies),
- ARD 2020 PIVOTS (environmental engineering),
- ARD 2020 Intelligence des Patrimoines (Cultural and Natural).

LE STUDIUM stands as the official partner of these five regional ARD 2020 programmes, holding a leading role on the recruitment of international experienced researchers, international actions and promotion of international exchanges.



# **ARD 2020**

### **BIOPHARMACEUTICALS**



A drug is any substance or composition presented as having properties for treating, preventing or diagnosing disease in humans or animals. Whereas BIOPHARMACEUTICALS in the strict sense of the term, are molecules that have the characteristic of being produced from living organisms or their cellular components. These molecules are intermediate between chemical drugs and organisms' intrinsic biologics. The proportion of biopharmaceuticals in the drug market should increase from 20% in 2014 to more than 40% by 2020. The region Centre-Val de Loire is at the cutting edge of research in the pharmaceutical sector and has included the development of biopharmaceuticals in its smart specialisation strategy for the period 2013-2020 injecting a strong financial support to research and to facilitate innovative inter-sectorial industrial development and partnerships for socioeconomic development beyond 2020. The ARD 2020 Biopharmaceuticals programme aims to further develop and strengthen the region Centre-Val de Loire biopharmaceuticals industry by capitalising on the recognised capabilities of the multidisciplinarity research teams from the regional research institutions in the view to:

- Develop a flagship research and development pole on biopharmaceuticals in the region Centre-Val de Loire.
- and innovation in the pharmacy/health sectors through start-ups, SMEs (Small and Medium Enterprises) including established local and regional based multinational companies.
- Promote the transfer of technologies/competences to existing and new

The Biopharmaceuticals Programme focuses on the design and biosynthesis of biomolecules for preclinical and clinical development by including the search for synergies with conventional chemically synthesised drugs. The programme involves working with a wide spectrum of biological molecules (vaccines, therapeutic antibodies, nucleic acids, lipoproteins...) with the need for a diverse range of competences and the involvement of teams with complementary expertise.

The researchers present in the region Centre-Val de Loire, working in the disciplines of life sciences, are invited to participate and work in synergy, for inter-sectorial development and innovation, in the pharmacy/health sectors to deliver socioeconomic outcomes.

















## **ARD 2020** COSMETOSCIENCES



In an international environment characterised by changing regulatory regimes and increasing harsh competition, research and innovation are key factors to ensure smart specialisation and sustainable economic development of territories and stakeholders. In the very well-established perfume and cosmetic industry of the region Centre-Val de Loire, the COSMETOSCIENCES programme aims at giving a significant impetus to research projects with a strong character of innovation to unlock industrial development blockages by opening the door to new concepts and enabling the creation of new startups. It fosters French leadership in the sector and the leadership of the region Centre-Val de Loire, particularly with regard to sustainable cosmetics.

Anchored in the region Centre-Val de Loire, this project articulates around the structuring of research at the national level on this cosmetic theme, including the research group (GDR) Cosmactifs, created by CNRS in January 2015. It brings together forty-eight laboratories and is driven by the University of Orléans. Focused on economic development, this project shares in the international influence of the French cosmetics industry across the region Centre-Val de Loire.

Together with the Cosmetic Valley competitiveness cluster and in conjunction with the cosmetic industry the programme creates the Centre of Expertise for the Cosmetics Industry. Located at the very heart of the territory covered by Cosmetic Valley, the centre's mission is to support business growth in the perfume and cosmetics sector with research, training and development activities and services specifically targeting very small and medium sized enterprises (VSEs and SMEs).

The centre focuses on three complementary developmental axes:

- Cosmétopée and Sustainable Cosmetic
- Glycochemistry and Glycobiology
- Innovation in Formulation, Cellular Tools and Technologies

The programme is funded by the Region Centre-Val de Loire for the period 2015-2020.



















### **ARD 2020 LAVOISIER**

### LAVOISIER Laboratory with a VOcation for Innovation of the Safety and Industrialisation of Renewable Energy.

The central subject of the LAVOISIER Programme revolves around promoting a process of design, research, development and industrialisation of materials and systems oriented towards new energies, including all considerations of reliability and safety of use for the devices studied during all stages of their deployment. This programme supports the development of the AlHyance platform.

The CEA Le Ripault Al Hyance platform is dedicated to joint research efforts (Universities, CNRS, industrials) in the field of non-emitting greenhouse gases energies, particularly in the hydrogen field (fuels and hydrogen storage cells). The thematics of research are the following: design and materials expertise, safety and effectiveness of the systems, synthesis and characterisation, and methods and implementations.

The LAVOISIER programme led by CEA Le Ripault covers activities through research to transfer of technologies and is supported by the Centre-Val de Loire Regional Government over 6 years till end of 2019 in the view to:

- Gather the conditions to support the energies of tomorrow and develop promising innovations of growth by strengthening academic and industrial collaborations.
- Accelerate the industrialisation and the dissemination of innovative new products for low-carbon energy, focusing on the storage of electrical energy and hydrogen.
- Stimulate research on storage of clean and renewable energies (hydrogen, wind and photovoltaic), in order to facilitate their delivery from the place of production to the place of consumption.
- Promote the transfer of technologies/competences to existing businesses at the regional level and beyond.

The research focuses on the storage of hydrogen, storage of electrical energy, energy conversion, fuel cells and the production of hydrogen, development of a new and emerging topic on materials related to solar thermodynamic systems and the mechanical storage of energy. The programme develops a new approach for the design and development of low carbon materials, supported by the analysis of the environmental safety and impact of systems throughout their development stages and life cycles.















### ARD 2020 PIVOTS



### PIVOTS - Environmental Technology Innovation, Development and Optimisation Platforms project

The PIVOTS project is a coordinated set of seven experimental and analytical platforms focused on environmental quality monitoring and sustainable management of natural resources (soil, subsurface, surface water, groundwater, sediment and air) within a context of global change (increased anthropogenic pressure and climate change).

The innovation through PIVOTS will be founded on an integrated approach based on excellent research by academic and industrial experts together at all stages of the value chain, from fundamental research to validation of products and services.

The platforms are identified as:

- DECAP: Development of Environmental Sensors and Pollutants Removal
- PRIME: Remediation and Innovation in the Service of Environmental
- O-ZNS: Observatory of transport in the Unsaturated Zone
- PERMECA: Testing and Research Platform in Collaborative and Applied Environmental Mechanics
- PESAT: Soil Atmosphere exchanges in peat bogs
- PESAA: Soil Atmosphere exchanges in Agricultural soils
- PRAT: Atmospheric Reactivity

The teams involved originate from BRGM (French Geological Survey), University of Orléans, CNRS (National Center for Scientific Research), INRA (National Institute for Agricultural Research), Antea Group (consulting and engineering), DREAM (cluster of enterprises) and LE STUDIUM (Loire Valley Institute for Advanced Studies).













# ARD 2020 INTELLIGENCE DES PATRIMOINES



THE INTELLIGENCE DES PATRIMOINES is an interdisciplinary and scientific research and innovation programme serving the tourism heritage economy in the Centre-Val de Loire and offering new education and employment perspectives. It consists in an unprecedented approach to the promotion of the territory combining the scientific research with the socio-economic world to design new innovative services and products. It reunites the efforts of forty laboratories and four hundred researchers from Tours and Orléans led by the Centre for Higher Studies of the Renaissance (CESR).

The Intelligence des Patrimoines programme is articulated around five major interdisciplinary research projects:

- Chambord Chateaux
- Vine and Wine
- Gastronomy, Health and Wellbeing
- Loire and Rivers
- Monuments. Parks and Urban Gardens

and proposes a transversal heterogenous digital data platform that will collect and present all developed activities and products. It offers new multidisciplinary and professional training courses (Master and Research Doctoral levels) and will plan for the creation of an open lab hosting a thematic academic incubator / accelerator for the development of startups on the regional territory.



















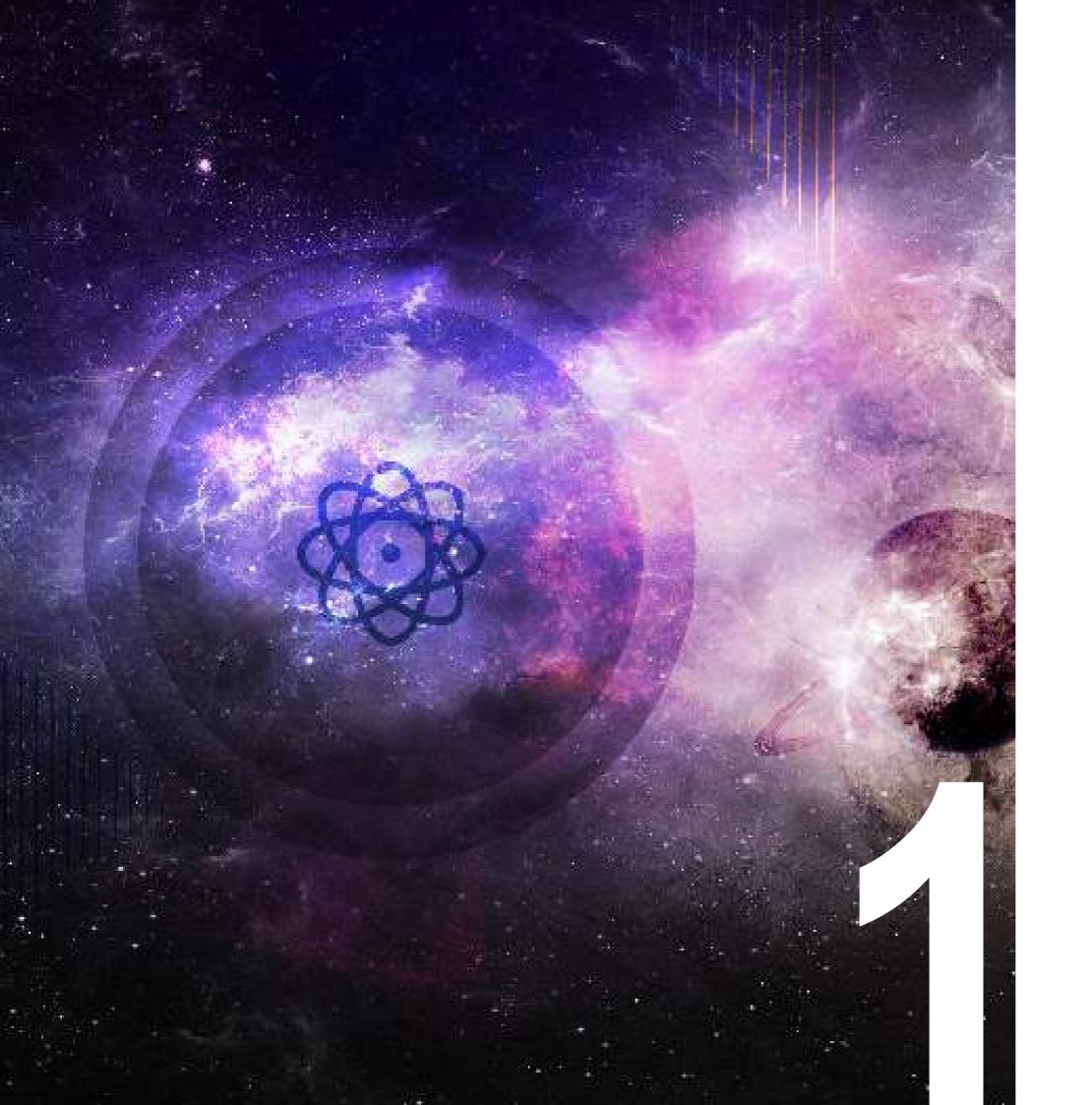




LE STUDIUM

Loire Valley
Institute for Advanced Studies





# MATERIALS & ENERGY SCIENCES

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# HOST LABORATORIES IN MATERIALS & ENERGY SCIENCES

# GROUPE DE RECHERCHE EN MATÉRIAUX, MICROÉLECTRONIQUE, ACOUSTIQUE ET NANOTECHNOLOGIES (GREMAN) -

**UMR 7347 - UNIVERSITÉ DE TOURS, CNRS, INSA-CVL** 



The GREMAN laboratory deals with the elaboration and characterization of materials, physics of condensed matter as well as nano- and microelectronics mainly focused on power electronics, RF electronics, MEMS for ultrasounds and energy harvesting. GREMAN

has a well-known expertise in all the aspects of piezoelectricity covering multidisciplinary competences in all the fields from material science to device development.

Since 2008, GREMAN has started the development of a new generation of piezoelectric generators based on ZnO nanowires, which has now reached the level of fabricated ZnO-based devices generating electrical power. The whole device is designed and fabricated at GREMAN: growth of the ZnO nanowires, device fabrication in clean room and characterisation, thanks to the CERTEM technological platform.







# LABORATOIRE DE PHYSIQUE ET CHIMIE DE L'ENVIRONNEMENT ET DE L'ESPACE (LPC2E) - UMR 7328 - UNIVERSITÉ D'ORLEANS, CNRS

The LPC2E is a joint research unit of the CNRS and the University of Orleans. In common with the ISTO (Institut des Sciences de la Terre d'Orléans) and the Station of Radioastronomy of Nançay, it is one of the founding laboratories of the OSUC (Observatoire des Sciences de l'Univers de la région Centre-Val de Loire).

The fields of activity of its four scientific teams range from the atmosphere to the most distant space: physicochemistry of the atmosphere, physics of space plasmas, planetology to study environment of planets and small bodies of the Solar System, pulsars and gravitation.

This research relies mainly on the scientific exploitation of instruments on board on satellites or space probes. The LPC2E is one of the CNRS-INSU (Institut National des Sciences de l'Univers) space laboratories, working in close partnership with the CNES (Centre National des Etudes Spatiales) to propose, design, build and operate these instruments, then make their data and observations and publish the results available to the scientist community.





### LABORATOIRE DE PHYSICO-CHIMIE DES MATÉRIAUX ET DES ELECTROLYTES POUR L'ENERGIE (PCM2E) -

### **EA6299 - UNIVERSITÉ DE TOURS**



The Laboratory of Physics and Chemistry of Materials and Electrolytes for Energy (PCM2E) was created in 2012 and works in the field of energy conversion and storage (batteries, supercapacitors, hybrid photovoltaic, ionic liquids), nanostructured materials and organic

electrochromic devices.

Located in Tours, The PCM2E laboratory has about 35 people including 14 assistant professors, three professors, a professor emeritus and a lecturer Excellence. It has been strongly renewed since the last four-year contract since nearly half of these members have been recruited since 2007.

The overall project of the laboratory is built around competences in electrochemistry, thermodynamics and chemistry of materials. The laboratory has three priority themes:

- **Y** Electrolytes, membranes and electrode materials for energy storage
- Organic semiconductors and nanostructured materials
- Ionic Liquids

In addition to the above mentioned directions of research, this laboratory is a unique research organisation owing to its in-depth focus on the design and development of novel electrolyte compositions. The electrolyte properties such as ionic conductivity, thermal behavior, potential range of stability, polarisability and dielectric constant fundamentally impact the performance of all types of batteries and form the core of the research activities.

The beneficial effect of choosing and designing novel materials and compositions of the electrolytes and applying appropriately to different battery systems has been demonstrated through numerous publications and patents at PCM2E.





### Pr EMRE ERDEM

From: University of Freiburg - Germany

In residence at: GREMAN, Tours

Nationality: Turkish

Dates: December 2017 - November 2018

Pr Emre Erdem was awarded the title "Privatdozent" from the Faculty of Chemistry and Pharmacy of the University of Freiburg in June 2017. The "Docent" title in Physics he obtained from the Universitelerarası Kurul Ankara in June

Having completed his PhD thesis at the University of Leipzig, Germany, in 2006 (magna cum laude), he has a strong background in diverse fields, such as materials physics, physical chemistry, atomic physics, solid-state physics, defect chemistry, studies of electronic properties of energy materials and, of course, the synthesis and characterization of nanocrystals (functional nanomaterials, piezoelectrics, supercapacitors and, in particular, semi-conducting quantum dots).

In addition, he has expertise not only in advanced spectroscopic methods, such as electron paramagnetic resonance (EPR), Raman spectroscopy, impedance spectroscopy, ultravioletvisible (UV-VIS) and photo-luminescence (PL) spectroscopies, but also on imaging techniques such as transmission/scanning (TEM/SEM) electron microscopy, both theoretically and experimentally.

Up to now, his research has resulted in more than 70 publications in internationally renowned, peerreviewed journals and books.

He is in editorial board member of Nature publication; Scientific Reports.

### INVESTIGATION OF INTRINSIC AND EXTRINSIC **DEFECT CENTERS OF ZnO NANOWIRES FOR NANO-GENERATORS**

Since the early 2000's, many new applications related to nomad electronics need "portable" electrical energy. Huge research efforts on Lithium based batteries have led to performances that made this technology the most popular for rechargeable batteries with the best energy densities. Recent efforts have also been done in order to charge them using renewable energy systems such as a photovoltaic cells, thermoelectric harvesters, or mechanical energy harvesters. Piezoelectric materials convert a physical pressure into the motion of electrons, and thus, the unused mechanical energy of our surroundings into electrical energy. Various technologies of piezoelectric harvesters have been tested for energy harvesting since the early 2000s. Since 2007, there is a tremendous interest for using onedimensional (1D) piezoelectric nanostructures (GaN, PZT, BatiO3, PVDF, CdS...) for mechanical energy harvesting. Among several materials, ZnO nanowires are promising candidates. They present high values of piezoelectric coefficients, can be grown at low temperature on almost any substrates, and finally are environmentally friendly.

The need for a more effective ZnO nanowire synthesis strategy has seen significant developments towards solution based hydrothermal reaction techniques below 100°C. As a result of the low temperature synthesis, such nanowires typically show unacceptable levels of defects (optical and electronic), rendering them inferior to their high temperature counterparts. The level of the excess free carriers in the material has been theorized to partly neutralise the induced piezoelectric potential, limiting hydrothermal ZnO nanowire-based nanogenerators performance.

In this context, the main objective of the project is the investigation of intrinsic and extrinsic defect centers of ZnO nanowires for nanogenerators. In particular, we intend to understand the defect structures of ZnO nanowires which are synthesized by hydrothermal method.

After characterizing the defect centers via spectroscopic methods such as electron paramagnetic resonance spectroscopy and photoluminescence spectroscopy, we will give effort to understand the effect of such defects on the electrical properties via impedance spectroscopy.

Then the nanogenerators will be manufactured and their performance will be examined using the dedicated test bench at GREMAN.

### **Dr GUYLAINE POULIN-VITTRANT**

### Laboratory Host Scientist



Dr Guylaine Poulin-Vittrant received the Agrégation in Electrical Engineering in 2000 from ENS Cachan (France), her MSc and PhD in Electrical Engineering respectively in 2001 from INP Toulouse (France) and in 2004 from Paris XI University (France) on human mechanical energy harvesting using bulk PZT ceramics. In 2005 she became full time researcher CNRS at Grenoble Electrical Engineering Laboratory and at GREMAN laboratory since 2008. Her research interests are experimental investigation and theoretical models development for piezoelectric materials and devices. She has participated and participates in European ("MIND" EU Network of Excellence, Piezo Institute, "EnSO" ECSEL JU project), national ("OVMI", "EVA", "FLEXIBLE" ANR projects) and regional ("CEZnO", "MEPS", "CELEZ") projects. She authored more than 40 articles referenced in international databases.



### Pr JOHNSON **IRUDAYARAJ**

From: St Joseph's college - India

In residence at: GREMAN. Blois

Nationality: Indian

Dates: November 2016 - June 2017

The researcher has 25 years of teaching (Academic experience) and 16 years of research experience.

He published nearly 50 research papers in peer reviewed journals and proceedings. He completed 3 major research projects in India. He guided 4 PhD candidates and is guiding 4 PhD candidates at present.

He completed his post doctoral studies at university of Coimbra, Portugal in the period of 2005 to 2006.

He was a visiting scientist to University of Zaragoza in 2007 under Indo-Spanish cultural exchange program.

He was a recipient of the American physical society Indo-US professorship award to deliver lectures at Utah State University in 2011.

He also organised an Indo-US workshop on Ultrasonics and Nanosonics and an International conference on Nanotechnology in India which has been sponsored by three international agencies IUSSTF, ICA and ICTP.

He was a Visiting scholar to KU Leuven in 2012 under Erasmus Mundus Nano program.

During this period he made invited talks and presentations at KU Leuven and Max Planck. Dresden.

He was a resource person for Indo-French conference on Acoustics (SFA and ASI) in 2013 at New Delhi and Royal society Indo-UK seminar in 2014 at Chennai.

His research fields include Acoustics, Energy, Material science and Nano materials for Energy and medical applications.

### **ENGINEERING AND SYSTEMS FOR RENEWABLE ENERGY**

In the olden days people used to say that No power is costlier than no power. But we are living in an era of seeking the cheapest and low cost ways to produce, save and redistribute energy. Mankind is also seeking for environmentally friendly ways to produce such energy.

Designing a proper curriculum on such energy program at Masters level with international cooperation and collaboration will be the need of the hour at INSA. Blois.

There are many ways to produce nanoparticles of energy and medical importance. But however producing such nanoparticles by Ultrasound and Green synthesis is more environmentally friendly and economically viable. Fine tuning and tailoring of nanoparticles is also possible.

Characterization of nano/micro thin films and materials by acoustical means is another interesting area which provides a non-invasive

The goals of the projects are :

- To help and coordinate the academic and scientific preparation for a new course at Masters level in Energy engineering
- To create and establish ways to sign M.O.U with leading universities for the above program since INSA-CVL wishes to develop students exchange and double degree programs.
- To be involved in research on Ultrasonics and Nanomaterials

Study of different syllabai and curriculum for different energy engineering program all over the world has been started. A detailed presentation will be done in the core group. Meeting of different Indian universities who are having Masters in Energy engineering has been

Identification of possible research collaboration in acoustical characterization of thin films and nanomaterials at Blois has been

### Pr MARC LETHIECQ



### Laboratory Host Scientist

Marc Lethiecg graduated in Electrical Engineering in 1984 and received the DEA (MSc) in acoustics followed by a Doctorat d'Ingénieur (PhD) in Non Destructive Testing in 1988, all from Institut National des Sciences Appliquées, Lyon, France. He has been with the University of Tours since 1990, first as an assistant professor and since 1994 as a professor, and has setup a research group on ultrasonic & piezoelectric devices. In 1988 and 1999 he worked as a research engineer on ultrasonic transducers for biological and medical applications for Vermon S.A. and CNTS. He has been teaching electronics, feedback control and courses related to his research activities since 1984 in several universities and engineering schools. He was scientific coordinator of a European Network of Excellence on piezoelectric materials & devices. He is a senior member of IEEE and member of SFA the French Society of Acoustics. He is director of GREMAN research laboratory and director of education at INSA Centre Val de Loire.



### **Dr SATYAJIT PHADKE**

LE STUDIUM Research Fellow ARD 2020 LAVOISIER

**From**: Customized Energy Solutions, India

In residence at: PCM2E, Tours

Nationality: Indian

Dates: January 2016 - June 2019

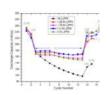
Dr Satvaiit Phadke completed his Bachelors (B.Tech.) in Metallurgical and Materials engineering from the Indian Institute of Technology (IIT) Roorkee in India. He obtained his PhD in Materials Science and Engineering from the University of Florida. His main interest area was the development of intermediate temperature proton conducting membranes for applications in PEM fuel cells. Thereafter he worked on an ARPA-E (Advanced Research Projects Agency for Energy) funded project as a postdoctoral associate at Massachusetts Institute of Technology (MIT). Here he pursued the development of a novel high temperature all liquid battery for stationary grid scale storage applications. He holds several patents from this work all of which have been licensed to a Cambridge based company Ambri, Inc. which is pursuing manufacturing and commercialization of this technology. During his position as a materials scientist at Alveo Energy, Inc which is a startup based in the Silicon Valley he worked on the development of Prussian Blue analogue battery materials. Additionally he has worked on the development of zinc alkaline batteries for transportation applications during his stay at Princeton University. He has also worked as a technical consultant for Customized Energy Solutions where he provided consultation services in his core area of energy storage and conversion technologies. Currently at the PCM2E laboratory his work is focused on development of novel electrolytes for next generation high energy density Lithium ion batteries which include Lithium rich cathodes, Lithium-sulfur and Lithium-air batteries. He is the author of several publications in the field of energy storage and conversion technologies. Recently, he was selected into the list of '50 Most Influential Indians in the Field of Energy Storage and Microgrids' awarded by India Energy Storage Association (IESA).

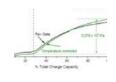
### **ENERGY STORAGE SYSTEMS**

The research project focuses on Energy Storage and Conversion Technologies and is supported by the ARD 2020 LAVOISIER Programme. The objective of the project is to develop novel materials (electrolytes, positive and negative electrodes) for advanced energy storage devices. The research work performed on Lithium-sulphur batteries has lead to the expansion of the project in the form of industry funding for the next 2 years (2017 - 2019) from Arkema.

Details about the topics of research and the progress made are listed below:

1. High energy NMC cathodes (HE-NMC): The high energy NMC cathodes have considerably higher energy density when compared to conventional lithium ion battery materials such as LCO, LMO, NMC, etc. These materials are very promising for transportation and portable electronics applications as the demand for long range on electric cars and longer life for portable electronics continues to grow. However, in order to achieve widespread commercialization some major technical challenges need to be overcome. These are namely high capacity fade, voltage fade and low coulombic efficiency on the first charge. Through work done over the last 12 months, specific electrolyte modification strategies have been demonstrated to significantly reduce the capacity fade in these cathodes. In this work supported by SAFT and UMICORE technologies we have reported a 10X improvement in the cycle life of the electrodes by optimising the composition of the electrolyte. We have also demonstrated the applicability of a completely new characterisation technique of in-situ pressure measurement during galvanostatic cycling which aids in the study of the HE-NMC materials.





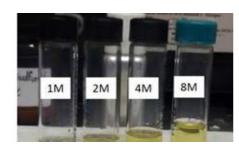


2. Lithium-sulfur (Li/S): Li/S batteries have an extremely high theoretical capacity density of about 1600 mAh/g due to which a very promising candidate for applications requiring lightweight batteries. By comparison, the conventionally used Lithium ion battery cathodes have a capacity density of 150-200 mAh/q. Thus the use of Li/S batteries has the potential to reduce the weight of batteries by 4-6X. The main challenges limiting its commercialization are low cycle life, low coulombic efficiency and high self-discharge. In previously published literature the micro-structural modification of the sulfur electrode has been the primary approach for performance improvement. Although significant progress has been made through this approach globally, most of the processes used are either difficult to scale up industrially or require the use of very expensive additives which increase the price significantly. We have shown that the electrolyte modification through the use of specific electrochemically active disulphide additives can not only significantly prolong the cycle life but also provide a very high coulombic efficiency. In addition, we have also shown that the additive modification technique can allow the batteries to operate at high c-rates opening the door for high power applications.

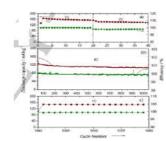
$$R_{2}S_{2} + e^{-} \rightarrow R_{2}S_{2}^{\bullet}$$

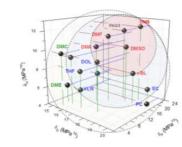
$$R_{2}S_{2}^{\bullet -} \rightarrow RS^{\bullet} + RS$$

$$RS^{\bullet} + RS^{\bullet} \rightarrow R_{2}S_{2}^{\bullet}$$

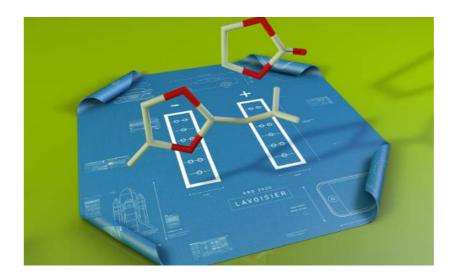


3. Organic electrodes: Organic polymer materials have attracted a lot of attention in last decade due to their favourable characteristics to serve as effective electrode materials. This is a new line of research initiated in the last 6 months at PCM2E. In this research we are focusing on the characterization of PAQS (poly anthraquinone sulphide) as a negative electrode (anode) material. The material was synthesized in the lab and its electrochemical performance was evaluated using standard coin cells. It shows excellent cycling stability with a high discharge capacity of 150 mAh/q and very fast redox kinetics. By increasing the cycling rate from 1C to 4C only a 25% reduction in capacity is observed which makes it suitable for high power applications. Owing to the excellent charge/discharge characteristics, the material will now be paired with activated carbon (for supercapacitors) and with conventional lithium ion cathode materials where PAQS can serve as a highly reversible and stable anode. Recent tests conducted using sodium and potassium intercalation show favourable cycling performance which opens avenues for the use of PAQS in sodium and potassium ion batteries also. Currently we are performing further investigation on the insertion/deinsertion kinetics of larger cations (potassium and sodium).





4. Measurement of gas solubility in electrolytes: The work is focused on the measurements of the solubility of gases in various electrolytes and solvents of interest. In addition to the solubility measurements this work permits the calculation the fundamental thermodynamic values of entropy, enthalpy and free energy of interaction of gases and liquids. Complimentary to these measurements are the pouch cell volume expansion studies and the pressure cell measurements. These studies together allow precise insitu determination of the evolution of gases during the cell cycling. Such studies focused on understanding the mechanisms of gas evolution in cells are essential for prolonging the cycle life of batteries.





Pr MERIEM ANOUTI
Laboratory Host Scientist
See page 27.

### AROUND THE PROJECT

### Oral Communications

- 1 Phadke, S. Self-healing high temperature batteries for high cycle life, Journées de la Section Régionale Centre – Ouest, Tours (France), February 2-3, 2017
- 2 Phadke, S. Organic electrode materials for energy storage applications, Energy Storage India (ESI) 2017, New Delhi (India), January 9-11, 2017

### Poster

Xionga, B. K.; Phadke, S.; Ulldemolinsb, M.; Tessier, C.; Anouti, M. Measurement of oxygen and hydrogen solubilities in electrolytes for lithium-ion batteries, 20th Topical Meeting of the International Society of Electrochemistry, Buenos Aires (Argentina), March 19-22, 2017

### Scientific Publications

- 1 Phadke, S.; Anouti, M. Effect of lithium salt concentration on the capacity retention of Lithium rich NMC cathodes, *Electrochimica Acta*, **2017**, *223*, 31-38.
- 2 Phadke, S.; Amara, S.; Anouti, M. Characterization of novel LiFSI-FMD electrolytes for supercapacitors: Measuring in-situ gas formation, *Chem. Phys. Chem.*, 2017, 18, 2364 – 2373.
- 3 Phadke, S.; Cadaou, E.; Anouti, M. Catholyte formulations for high energy Li-S batteries, Journal of Physical Chemistry Letters, 2017, 22 5007, 5017.



### Dr JÁN ŽABKA

From: Czech Academy of Sciences, Czech Republic

In residence at: LPC2E. Orléans

Nationality: Czech

Dates: July 2017 - June 2018

J. Žabka is a chemical physicist (J. Heyrovský Institute of Physical Chemistry of the CAS, v. v. i., Prague, Czech Republic) having an experience in ion/molecule chemistry using crossed-beam, guided-ion beam, ion traps, the SIFT instruments as well as Orbitrap aparatus and the synchrotron facilities (synchrotron SOLEIL, France). His major scientific interest is in the field of laboratory studies of ion/molecule reactions relevant to planetary atmospheres. He also has an expertise in design and construction of experimental setups. J. Žabka has been working in the field of planetary chemistry for many years, in cooperation with foreign partners in the framework of European programs (Astrochem 2010 -2013, XLIC 2013-2016, Origins 2014-2017) and project funded by the Grant Agency of the Academy of Sciences of the Czech Republic (Investigation of ion-molecule collision processes relevant to the atmosphere of Titan, the Czech Science Foundation, the Ministry of Education, Youth and Sports of the Czech

Co-author of 65 articles in journals, 878 citations (without self-citations), h-index 18



### **VERY HIGH RESOLUTION MASS SPECTROMETRY FOR SPACE APPLICATIONS**

The research project supported by LE STUDIUM is part of a central activity of the LPC2E Planetology team that has the objective to develop, optimize and test spacequalified, very-high-resolution mass spectrometers, based on the Orbitrap™ design. The goal is to reach mass resolutions that will permit in situ chemical analysis of the high mass, complex organic molecules observed or expected to be observed, on or near various Solar System bodies, and considered as possible building blocks of life. LPC2E leads a Consortium of 5 French laboratories developing for space applications the core of such instruments, consisting in an Orbitrap  $^{\text{TM}}$  cell and its immediate electronic and mechanical environment, and hereafter called Cosmorbitrap. The Consortium is supported by CNES, the French space agency, with additional funding from other sources. It has established, within two NASA and one H2020 proposals, prestigious collaborations with international partners who would develop front-ends appropriate for operation in diverse planetology contexts, leading to instruments that can be proposed on the next generation of in situ planetary missions. The leadership of LPC2E is based on its proven technical and scientific expertise as an established space sciences laboratory, e.g. actively involved in two instruments on board the Rosetta spacecraft. The Consortium works on the preparation of the scientific exploitation, characterizing and optimizing the science that can be obtained from the new family of instruments, and formulating goals and strategies they will make possible for the exploration of Solar System bodies.

One of the most important Consortium projects is to develop the interface coupling Orleans' laboratory prototype of Cosmorbitrap with the laboratory set-up LILBID (Laser Induced Liquid Bead Ion Desorption) of Frank Postberg in Heidelberg. The LILBID experiment has in particular allowed confirming the chemical nature of Enceladus plumes observed with the Cosmic Dust Analyzer (CDA) onboard the Cassini mission. This is a must-have experiment for calibrating such environments, as it will provide a much-higher mass resolution capability than what is currently available with CDA.

The research project supported by LE STUDIUM is planned to design, construct and subsequently experimentally test this implemented apparatus. During the first half of the project, an integration study simulation of the Orbitrap cell to the laboratory set-up LILBID was carried out. Based on this simulation it was decided to engineer a new prototype than to modify the original Orbitrap and LILBID apparatus. One of the arguments is to allow parallel research of various scientific goals.

### **Dr CHRISTELLE BRIOIS**

### Laboratory Host Scientist

Christelle Briois is associate professor (maître de conférences) at OSUC of University of Orléans, and a researcher at LPC2E in the Planetology team. In the last few years the main task of the team was to prepare for the operations and scientific exploitation of COSIMA (COmetray Secondary Ion Mass Analyzer), the mass spectrometer dedicated to the analysis of dust in the environment of comet 67P/Churyumov-Gerasimenko, on the Rosetta mission of ESA (launched in 2004). C. Briois is co-Principal Investigator of COSIMA. She is also co-Investigator of ROSINA (Rosetta Orbiter Spectrometer for Ion and Neutral Analysis), the suite of instruments analysing gases in the environment of the comet. This heavy and long term investment in instrumental science is now bearing its fruits, with the publication in Science, Nature and in other ranks journals of the first series of scientific papers presenting the results already obtained since Rosetta. Currently C. Briois is chair of the Comité Scientifique Orbitrap™, the French Consortium that has undertaken the development of a spacequalified Orbitrap™ core, for future in situ planetology applications.



### Pr MERIEM ANOUTI

**CONSORTIUM COORDINATOR** 

IF STUDIUM

ARD 2020 LAVOISIER

Professor Meriem Anouti is a Professor in the PCM2E laboratory at the University of Tours. Her research focuses of electrolytes for electrochemical energy storage (electrochemical capacitors, lithium-ion and sulfur batteries and hybrid systems) with a particular emphasis on room temperature molten salts (RTMS) as ionic liquids, deep eutectic solvents and their mixtures. She also applies ionic liquids for nanomaterials synthesis and studies fundamental properties including dissolution of gases. In all the applications the properties of RTMS are correlated with their structure and interactions. Based on the use of ionic liquids, she formulates electrolytes for improving the lifetime of energy storage systems, especially by enhancing the voltage and operating temperature range and by controlling the phenomena at the electrode/ electrolyte interface. She coordinates numerous ANR, regional funded and industrial research projects while also supervising PhD students. Her industrial research includes contracting with national and multinational companies. Her international collaborations include laboratories in Ireland, Canada, Germany and Poland.

### **DEVELOPING HIGH ENERGY DENSITY STORAGE TECHNOLOGIES** FOR PORTABLE AND TRANSPORTATION APPLICATIONS

The consortium was designed to encourage a long term scientific collaboration between carefully selected scientific peers working on closely related topics from around the world. The recently organised consortium meeting was held in Tours from December 12-16 and was attended by Pr Sagar Mitra from IIT Bombay (India) and Dr Roman Mysik (Spain). The combined expertise of the participants covers almost all areas of electrochemical energy storage technologies which includes Lithium ion Batteries, Lithium sulphur Batteries, Metal air Batteries, Lead acid Batteries, Supercapacitors, Flow and Hybrid Capacitors and High temperature Batteries. This free exchange of knowledge and combination of advances in technology and understanding in different parts of the world is crucial for enhancing the rate of development of these technologies. During this consortium the participants agreed to pursue joint development on four new research avenues in lithium ion, sodium ion and advanced lead carbon batteries.

### **PARTNERS**



Pr Sagar Mitra IIT Bombay - India



Dr Roman Mysyk CIC Energigune - Spain



Dr Satyajit Phadke PCM2E, University of Tours -France



# LIFE AND HEALTH SCIENCES

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# HOST LABORATORIES IN LIFE & HEALTH SCIENCES

### CENTRE DE BIOPHYSIQUE MOLÉCULAIRE (CBM) - UPR 4301 - CNRS

CBM

CBM is a key participant in the development of biophysics in France, and is one of the largest research laboratories in the region Centre-Val de Loire. It was founded in 1967 to set up interdisciplinary collaboration between chemists, biologists and physicists. Researchers at the CBM are investigating the structure, dynamics and interactions of biomacromolecules from the atomic level to the cell

and organism. This approach entails searching for the molecular causes of biological dysfunctions which trigger the development of diseases. The center is also recognized for its research in biomedical imaging. The laboratory has excellent facilities for small animal imaging. One key goal of CBM is to conceive new strategies in human therapy by combining innovative approaches in peptide/protein synthesis, biochemistry, bio-physics, molecular and computational biology. For this purpose, biomolecular interactions involving DNA, RNA, proteins and ligand are studied at the atomic and molecular level using a variety of experimental techniques. Moreover, some research projects are dedicated to the identification of new therapeutic targets and the development of innovative delivery systems for therapeutic and imaging agents in various pathologies such as cancer, cystic fibrosis and musculoskeletal defects. Biological targets are identified through the delineation of specific signaling pathways. Novel therapeutic strategies are developed using original nucleic acid delivery systems that combine chemical vectors and physical methods. One main area is the optimization of innovative vaccination based on messenger RNA coding for tumoral or viral antigens for cancer and viral infection, respectively.



# GÉNÉTIQUE, IMMUNOTHÉRAPIE, CHIMIE ET CANCER (GICC) – UMR 7292 – UNIVERSITÉ DE TOURS, CNRS



The GICC laboratory is focusing on the pathophysiological mechanisms of diseases, in order to set up and personalise therapeutics. The team PATCH (PhArmacology of TherapeutiC antibodies in Human; head Gilles Paintaud) aims at studying the mechanisms of action of monoclonal

antibodies in the context of chronic diseases, by combining biology and mathematics. This quantitative systems pharmacology approach evolves a pathophysiologic system, in combination with a mathematical model, to understand the mechanism of action of monoclonal antibodies that are used in immune-inflammatory diseases and in cancer.





# IMAGERIE ET CERVEAU (IC) - UMR U930 - INSERM, UNIVERSITÉ DE TOURS



"Imagerie et Cerveau" at University of Tours and Inserm is composed of 5 research teams. The Imaging and Ultrasound team led by Dr Ayache Bouakaz, dates back to the early 1970s with the pioneering work of Professor Léandre Pourcelot on clinical Doppler vascular imaging. Over the years, the team has developed various

industrial and medical ultrasound diagnostic imaging systems. Today, the activities of the Imaging and Ultrasound team are multidisciplinary and are primarily influenced by clinical need. Indeed the team's research goals which are concerned with the technical aspects of ultrasound diagnostic imaging and therapy are founded on strong theoretical (ultrasound propagation and generation, signal processing, interaction of ultrasound and complex media) and experimental (instrumentation, electronics) background. The objectives of Inserm U930 as a whole are concerned with normal and pathological brain development, from the perinatal period to adulthood. Their mission is the development, validation and use in clinical research, functional and structural brain imaging methods (MRI, PET, SPECT, EEG and ultrasound), in order to better characterise brain development and functioning, as well as understand and treat or alleviate brain disorders.





### INSTITUT DE CHIMIE ORGANIQUE ET ANALYTIQUE (ICOA) - UMR 7311 - UNIVERSITÉ D'ORLÉANS, CNRS



The host laboratory is part of the Institute of Organic and Analytical Chemistry of CNRS and University of Orléans: ICOA UMR7311, directed by Pr Pascal Bonnet. The main objective of the laboratory's research activities is the discovery, the

synthesis and the analysis of novel bioactive molecules having potential applications in drug discovery or in cosmetics. ICOA has numerous collaborations and partnerships in the Region Centre-Val de Loire, with many research laboratories such as CBM (CNRS UPR4301), forming with this laboratory a Research Federation (FR2708), with CEA (ICOA is Laboratorie de Recherche Correspondant LRC M09), with the Hospital of Orléans (CHRO), with many biotechs and large companies and through Clusters of Competitiveness such as LabEx SYNORG and IRON. In order to maximise human and financial ressources, the ICOA has recently created three focused strategic research axes: Therapeutic Innovation and Diagnostics, Molecular Diversity, and Bioactives and Cosmetics. Through these three axes, the research teams of the ICOA are working and publishing in many scientific areas such as molecular modeling, bioinformatics, glycochemistry, heterocyclic, nucleoside and green chemistry, molecular imaging, analytical strategies, metabolite identification, biomolecular interactions, etc.





# HOST LABORATORIES IN LIFE & HEALTH SCIENCES

# IMMUNOLOGIE ET NEUROGENETIQUE EXPERIMENTALES ET MOLECULAIRES (INEM) - UMR 7355 - UNIVERSITÉ D'ORLÉANS, CNRS

The research unit "Experimental and Molecular Immunology and Neurogenetics" (INEM), UMR7355 affiliated to CNRS and University of Orleans, is located on Orleans CNRS campus. Created in 2001, INEM is presently composed of 2 Teams, "Immune responses to infection and injury" led by V. Quesniaux/ I. Couillin, and "Neurogenetics" led by S. Briault / S. Mortaud, focusing on « Autism, mental deficiency and genetics » and « Developmental Neurotoxicity». A spin-off company Artimmune SAS was created in 2010 based on our immunology team expertise and research. A joined laboratory is being created with INEM (Site: http://www.artimmune.com/).

Upcoming public health challenges will have to integrate the constant increase of 1) asthma and lung pathologies, 2) neuropathologies such as autism due notably to pesticides neurotoxic effects, and 3) the emergence of drug resistant bacteria and parasites. Inflammatory responses, either exacerbated and pathogenic, or protecting and controlling infection, are central. Our strategy to contribute to these clinical challenges is multifold and transversal, by addressing novel regulatory mechanisms that are being unraveled and may concern these different pathologies. We aim at fostering the progress of the main research themes through common transversal approaches and research on mechanistic pathways, either *in silico* or *in vitro* when it is possible, but mainly through integrated *in vivo* approaches based on functional analysis of murine models.





### **NUTRITION, CROISSANCE ET CANCER (N2C)**

### - UMR 1069 - UNIVERSITÉ DE TOURS, INSERM

The mixed research unit of Inserm and the University of Tours has international recognition in research at the interface between cancer and nutrition. The team was the first to link diet-related changes in the lipidome of breast associated adipose tissue to breast cancer development and metastasis. The role of lipids on cancer development and progress is examined at the structural, metabolic and physiological levels. The laboratory is specialised in lipid biochemistry and metabolism as well as in breast and prostate cancer, cancers frequently associated with bone metastases. The research is multidisciplinary and focuses on the transversal interaction between medicine, pharmacology and sciences. The N2C researchers explore different modes of molecular and cellular actions and, the impact of specific lipids on mitochondrial function, cancer cell lines and, the relationships between tumor and its host. This knowledge may benefit patients who have chemical-resistant and/or metastasized cancers.





### **NANOMÉDICAMENTS ET NANOSONDES (NMNS)**

### - EA 6295 - UNIVERSITÉ DE TOURS



The Nanomedicine and nanoprobes laboratory is located in the faculty of pharmacy of Tours. It is directed by Pr I. Chourpa and groups 9 permanent senior researchers, also all university

lecturers. The research group started in 2008 and obtained his independency as an "Equipe d'Accueil" in 2012.

The main research topics of the team are the development of nanotechnologies for health and the development of analytical methods based on advanced separative or spectroscopic techniques. The first works were dedicated to the design of nanovectors able to deliver anticancer agent specifically to the tumor cells, leading to the decrease of the side effects of chemotherapy.

Over the years, the group diversified its activities and skills. Among the current funded projects, can be cited the development of theragnostic nanovectors dedicated to the diagnosis and treatment of breast cancer (InCA, Ligue contre le Cancer), the development of multimodal imaging nanoprobes (ERA-NET) or the development of encapsulation systems to increase the delivery of active molecules to the skin (Cosmetosciences program).

The team also focuses an important part of its energy on consolidating its national and international network, with academic or industrial actors.







### **Dr SOHAIL AKHTER**

From: Jamia Hamdard University, India

In residence at: CBM, Orléans

Nationality: Indian

Dates: June 2015 - June 2017

Dr Sohail Akhter is a professional Pharmacy graduate with specialization in Pharmaceutical nanomedicines. His past experience include senior Postdoc postions at U.S. Food and Drug Administration (US-FDA)/The Centre for Drug Evaluation and Research (CDER)/DPQR, USA and the Department Pharmaceutics, Utrecht Institute of pharmaceutical sciences, Utrecht University, Netherlands. He received team excellence award-2015; U.S. Food and Drug Administration (US-FDA)/CDER/DPQR for his work on novel nondestructive chemometric method/PAT tools and Nanomedicine European technology platform fellowship, 2013. Dr Akhter has authored more than 50 papers in high impact journals. His research interests involve nanomedicines design, application of bio-materials in drug delivery & targeting, biopharmaceutics, drug/nanoparticles metabolism/biodistribution and bioanalysis.

### SYNTHESIS AND BIOSYNTHESIS OF MOLECULES-**DEVELOPMENT OF MRNA CELLULAR FACTORIES**

Dr Sohail Akhter is working as Le Studium Research Fellow under ARD 2020 Biopharmaceuticals framework on the project entitled "Synthesis and biosynthesis of molecules-development of mRNA cellular factories" in a specific area "Intracellular delivery of nucleic acids to the dendritic cells (DCs) by non- viral nanovectors". The goal of this research is to develop and optimize the non-viral nanocarriers (for example-lipidic and polymeric nanoparticles) for selective intracellular delivery of mRNA to the dendritic cells to achieve specific anti- tumor immune responses.

The final goal is to develop novel biopharmaceutics that could be used for therapeutic vaccination against cancer. It is established that dendritic cells (DCs) play a key role in the development of immunotherapy against cancer. As sentinel of the immune components, DCs take up and process antigens to present them on either MHC class I, MHC class II molecules or both to T cells depending on the type of antigens. When DCs are modified to present tumor-associated antigens (TAAs), specific anti-tumor immune responses can be evoked. Messenger RNAs or plasmid DNA that encodes tumor antigens have been found as a safe mode of induction of tumor-specific immune responses after efficient transfection to the DCs.

mRNA being translated in the cytosol, it does not to be imported inside the nucleus and allows better transfection efficiency over plasmid DNA. The loading of mRNA to the DCs is challenging and requires the development of robust and smart delivery systems capable to reduce mRNA doses and/ or side effects. The nucleic acid delivery efficiency of viral vectors are, in general, higher to that of non-viral carriers. However, potential immunogenic adverse effects aftermath associated with viral vectors increasingly making non-viral gene delivery systems still relevant for gene therapy.

In our study, we are screening the transfection efficiency of mRNA lipoplexes and lipo-polyplexes made of different histidylated lipids and histidylated polymer to optimize a nanomedicine that can efficiently transfect and lead to high protein expression in large number of dendritic cells. We prepared new nanoformulations and evaluated the transfection efficiency of weakly basic imidazole with other N-head group variance containing amphiphilic lipids for improved mRNA & pDNA transfection in dendritic cells intended for cancer vaccination.

Cationic liposomes in a certain molar ratio of lipids were prepared by film hydration followed by sonication for the size reduction. he nanosized lipid vesicles had the size varied in between 80nm-150nm with the polydispersity index within 0.2.

Their zeta potential was ranging from 50mV to 80mV. The capacity of these formulations to complex with mRNA and pDNA were evaluated by gel retardation assay and ultimately their transfection efficiency in dendritic cells (DC2.4 cells) measured by flow cytometric analysis. The change in the size and shape/topography of lipoplex were observed by TEM and AFM and compared to cationic liposomes. We observed that imidazole or histidinecontaining lipids and polymer significantly improve the transfection up to 62%. Particularly, the expression of eGFP protein in these transfected cells goes remarkably high up to 1200 (indicated as MFI).

Further evaluation in animal (mice) showed that the in-vivo transfection is remarkably high and specific to the organs which are significant in immunotherapy. It indicates that our lipid and or polymer composition was efficient to overcome intracellular barriers and could be an excellent nanomedicine for DCs targeted based cancer immunotherapy.

At this stage, we are able to conclude that the tested lipids could be good candidates in designing cationic liposomes for mRNA and DNA delivery in dendritic cells.

### **MESSENGER RNA THERAPEUTICS: ADVANCES** AND PERSPECTIVES

In the framework of the regional Biopharmaceuticals ARD2020 Programme, LE STUDIUM Loire Valley Institute for Advanced Studies together with the Center for Molecular Biophysics are organising an international conference on mRNA therapeutics advances and perspectives.

The continuous research over a decade has led to excellent progress in the mRNA biology field and has extended our understanding of the distinctive features of mRNA. At this stage, researchers have learnt to stabilize and manipulate this biomolecule and now recent findings are actually transforming mRNA into new drugs category with many therapeutic applications. However, efforts on interdisciplinary biomedical approach are still required to translate the potentially commendable preclinical findings on mRNA therapeutics into the clinic. The conference will be held with the objective to discuss and exchange innovative ideas in the path of messenger RNA-based therapeutics. The presentations include internationally renowned biomedical researchers from the diverse area: vaccination, innovative therapies and delivery systems.

### DÉFI ET CHALLENGE DE LA MISE AU POINT D'UN VACCIN CONTRE LE VIRUS DE L'HÉPATITE C

The hepatitis C virus infects over 180 million people worldwide and about 250,000 people in France. It's a major cause of chronic liver disease, often leading to cirrhosis and liver cancer. New antiviral molecules have made it possible to combat this virus effectively, but they remain extremely expensive. In addition, many chronic carriers of the virus do not know they are infected. The World Health Organization (WHO) estimates that every year 3 to 4 million people are newly infected with this virus worldwide. If treatments are used too late, they are ineffective to prevent the liver from progressing to cirrhosis and liver cancer. The development of a vaccine against the hepatitis C virus is an important public health issue. Touraine has already been honored with the development of the first vaccine against hepatitis B, by the team of Professor Philippe Maupas, more than thirty years ago. In the continuation of this work, Philippe Roingeard and his team at Inserm Unit 966 established the concept of a modified hepatitis B vaccine, incorporating constituents of the hepatitis C virus, capable of inducing an immune response against both viruses. In his presentation, Dr P. Roingeard illustrated how basic research can lead to medical applications.

### Pr CHANTAL PICHON

Laboratory Host Scientist



Pr Chantal Pichon is a full Professor in Molecular and Cell Biology at the University of Orléans. She is currently the head of the Institute of Life Sciences and Chemistry for Life at the University of Orléans (6 lab units and 4 master degrees. She is performing her research activities at the Center for Molecular Biophysics of CNRS (Orléans, France) where she is leading the team Cell Biology and innovative therapies. One of main focus of the team is the development of chemical-based vectors for DNA, RNA (messenger RNA, replicons) and siRNA. The team is the pioneer of histidine-based nanomedicines for cellular transfection. In parallel with those investigations, the team is also involved in establishing specific cell tools and the identification of new targets for cancer and musculoskeletal tissue regeneration. Chantal Pichon has a trackrecord of 107 peer-reviewed publications, 10 patents and 21 grants inclunding regional grants (ARD 2020, APR), academic funding (ANR), European grants and funding from private companies.









### **Dr KRISTINA DJANASHVILI**

LE STUDIUM / Marie Skłodowska-Curie

From: Delft University of Technology, The Netherlands

In residence at: CBM. Orléans

Nationality: Dutch

Dates: January 2017 - January 2018

Kristina Djanashvili obtained her PhD in chemistry with honours in 2009 at the Delft University of Technology and has received DEWIS Award for the best PhD thesis of the year. A year later, she has started as a group leader within the Department of Biotechnology, while continuing being head of the NMR research facility. In 2011, she took up a position of Assistant Professor in the same department and in 2012 received a personal grant from the Dutch Organization for Scientific Research (NWO-VENI) for the research on nanotheranostic materials. Today, her research focuses on applied chemistry of probes for multimodal imaging and therapy exploiting versatile physical properties of lanthanides in combination with nanosystems. Recently, she has been awarded a High-Tech Systems and Materials (HTSM) grant (2018-2023) on brachytherapy with nanoparticles. She has published over 45 peer-reviewed papers and 2 book chapters. In 2017, she has arrived to Orléans with one year Le Studium Research Fellowship to work on one of her projects on porous nanodevices for MRI-PET applications in the group of Dr Éva Jakab Tóth (CNRS/Centre de Biophysique Moléculaire).



### **RESPONSIVE NANOZEOLITES: SMART POROSITY AND** SURFACE TAILORING FOR MULTIMODAL IMAGING AND THERAPY OF CANCER

Effective cancer treatment requires its early diagnosis and safe drug delivery systems. Up to date many therapeutics have failed due to their limited ability to reach the diseased site selectively without damaging healthy cells. Furthermore, none of the existing imaging techniques is absolutely reliable due to the differences in resolution and sensitivity. Therefore, synergistic combination of imaging modalities in one (typically nanodimensional) probe is the key strategy to benefit, for example from the sensitive and quantifiable PET signal and the high resolution of MRI. Nanozeolites are among the most promising candidates for realization of this concept due to their unique crystalline structure capable of stable binding with metal-ions with diagnostic and therapeutic properties. Even though, these materials have found many applications in various technologies, their medicinal potential still requires thorough investigations. This project aimed at the design, preparation and testing of novel nanostructured zeolitic materials that can be applied as personalized drugs for diagnostic and therapeutic

Loading of paramagnetic lanthanide-ions (GdIII) into the framework of nanozeolite LTL was exploited as a strategy for generation of a bright MRI contrast as a result of relaxivity (proton relaxation rate per mM Gd) as high as 38 s-1mM-1 (7 T and 25 °C). Furthermore, the extremely fast exchange between the water molecules directly bound to the GdIII ions inside the LTL zeolite pores with the bulk water was proved to follow a prototropic mechanism due to the unique arrangement of the long framework channels. This has resulted in a pH response of the MRI signal among the strongest reported so far. In the next step, the in vivo behaviour of the designed materials was evaluated, which was possible thanks to the excellent facilities provided by CNRS.

First of all, the surface of nanozeoltes was functionalised with long polyethylene glycol (PEG2000) chains in order to i) stabilise the particles and ii) prolong their blood-circulation time. We demonstrated that the presence of the PEG up to 6 wt% at the surface does not disturb the water exchange process and the relaxivity remains high. After injection of the colloidal solution of Gd-PEG-LTL into a nude mouse, a bright contrast was detected in the aorta that however vanished in time. At the same time, ICP analysis of liver, spleen, and lungs showed a significant accumulation of Gd. This phenomenon was further assessed by PET imaging, which in contrast to MRI does not rely on the water exchange, but on the presence of a radiotracer. For these experiments, we adjusted the loading procedure to the radioactive 89Zr, which represents a convenient radiotracer in terms of half-life (3d) and emission (b+) suitable for PET. An improved radiolabelling procedure compared to the conventionally used Zr-oxalate labelling was developed to ensure the incorporation of the tracer into the pores. This was possible by the introduction of an additional purification step, which allowed for removal of the toxic oxalate-ions that typically form large negatively charged complexes with Zr, preventing it from entering the small pores of 7.2 Å. The results of the post-injection imaging up to 4 days indicated a very strong accumulation in lungs, followed by the subsequent migration of the particles to the liver. Another ICP analysis demonstrated the intactness of the migrated particles by comparing the ratio of 89Zr, Gd and Si; the first two elements being loaded in the pores and the latter representing the zeolitic framework. The histological study will further clarify the mechanism of lung accumulation and possibly explain the rather untypical migration of the particles to the liver.

The results obtained in the course of the project so far open new perspectives for the application of nanozeolites as multimodal imaging probes. Demonstration of in vivo behaviour of the designed materials provide a clear view on the follow up research, which will be continued in the well-established collaboration with CNRS.

### IS MULTIMODAL IMAGING AN INVENTION WITH A **FUTURE? THE INPUT OF CHEMISTRY**

The conference, jointly organised by LE STUDIUM Loire Valley Institute for Advanced Studies and the Centre for Molecular Biophysics, has addressed the scientific concept of multimodal imaging that has been gaining momentum over the last decades. Given the intrinsic physical properties of each imaging technique available in the current clinical practice (MRI, CT, US, PET/SPECT or optical imaging), it is clear that none of these modalities alone is able to address all the questions in the search for a correct diagnosis or therapeutic follow-up. Today, many leading instrumental companies, supported by the physicists from academia, are investing in the design/improvement of multimodal scanners (e.g. PET-MRI). In parallel, chemists working in the field of imaging worldwide are gathering their efforts to create agents that combine various imaging reporters in a single probe. The conference has brought together the leading scientists in the field of medical imaging with the special focus on metal-based probes for MRI, optical and nuclear imaging modalities.

### LES NANOTECHNOLOGIES AU SERVICE DE LA SANTÉ BY Dr NATALIE MIGNET

Nanomedicine is an important application in nanotechnology that benefits from nanoscale size of the materials that allows for their interaction with biological entities such as cell proteins. The ability of nanoparticles of accommodate drug molecules, radiotraces, paramagnetic units etc. confers them high potential for imaging and therapy. Furthermore, the modifiable surface allows for grafting of functional groups that facilitate the delivery of nanosystems exclusively to the diseased sites. All these aspects make nanotechnology an interesting subject to the broad audience with the goal of elucidating the potential of the new approaches for the health care.





### Dr ÉVA JAKAB TÓTH

Laboratory Host Scientist

Éva Jakab Tóth (DR1 CNRS) is expert in the design, synthesis and characterisation of metal chelates related to imaging applications. After a PhD from the University of Debrecen, Hungary in lanthanide coordination chemistry, she occupied research positions at Ecole Polytechnique Fédérale de Lausanne and was appointed as CNRS research director in 2005. Since 2012, she is director of the Centre of Molecular Biophysics, CNRS UPR 4301, Orléans. She published over 150 original papers and edited "The Chemistry of Contrast Agents in Medical Magnetic Resonance Imaging", Wiley, 2001 and 2013 (2nd Ed.). She chaired the European COST Network "Metal-Based Systems for Molecular Imaging Applications". Her recent research focuses on imaging probes to detect enzymatic activities, neurotransmitters and amyloid peptides.

### AROUND THE PROJECT

### Scientific Publication

Zhang, W.; Martinelli, J.; Peters, J. A.; van Hengst, J. M. A.; Bouwmeester, H.; Kramer, E.; Bonnet, C. S.; Szeremeta, F.; Tóth, E.; Dianashvili, K. Surface PEG Grafting Density Determines Magnetic Relaxation Properties of Gd-Loaded Porous Nanoparticles for MR Imaging Applications, Appl. Mater. Interfaces, **2017**, *9*, 23458–23465.

### **Oral communications**

- 1 Djanashvili, K. Towards Multimodal Imaging with Porous Nanodevices, Le Studium Conference - Is Multimodal Imaging an Invention with a Future? The Input of Chemistry. Orléans (France), December 11-13,
- 2 Djanashvili, K. Responsive Nanozeolites Smart Porosity and Surface Tailoring for Multimodal Imaging and Therapy of Cancer, Seminar at Centre Biophysique Moléculaire (CBM-CNRS), Orléans (France), January 20,
- 3 Djanashvili, K. Challenges and Potential of Chemistry in Design of Theranostic Probes, Le Studium Thursday Seminar Series, Orléans (France) May 9 2017
- 4 Dianashvili, K. Responsive Nanozeolites Smart Porosity asd Surface Tailoring for Multimodal Imaging and Therapy of Cancer, Seminar at Conditions Extrêmes et Matériaux: Haute Température et Irradiation (CEMTHI-CNRS), Orléans (France), February 17, 2017.
- 5 Djanashvili, K. Porous Nanostructures as Versatile Stable Chelates for Complexation of Lanthanides for pH Responsive MR Imaging, International Symposium on Metal Complexes, ISMEC 2017, Dijon (France), June 11-15, 2017.
- 6 Djanashvili, K. Advances of Porous Nanomaterials Designed for Multimodal Imaging and Therapy, Annual Meeting of the Dutch Society for Matrix Biology (NVMB), Lunteren (The Netherlands), May 11-12, 2017.

### Posters

Putri Fauzia, R.: Ukun, R.: Soedianaatmadia, M. S.: Hardi Gunawan, A.; Djanashvili, K. Affinity Study on Gd-DTPA-PEG-Folate to Cervix Cancer Cells Overexpressing Folic Acid Receptors, Le Studium Conference – Is Multimodal Imaging an Invention with a Future? The Input of Chemistry, Orléans (France), December 11-13, 2017.





### **Dr JORGE GUTIERREZ**

LE STUDIUM Research Fellow
ARD 2020 BIOPHARMACEUTICALS

From: Columbia University New York, USA

In residence at: NCC, Tours

Nationality: Peruvian

Dates: November 2014 - June 2017

Jorge L. Gutierrez-Pajares worked at Columbia University (New York, USA) conducting cancer research in a multidisciplinary environment. His collaborative work with the Institute for Cancer Genetics, the Stem Cell Initiative, the Molecular Genetic Pathology, and the Center for Computational Biology and Bioinformatics has allowed him to gain experience in the fields of cell signaling, epigenetics, high-throughput sequencing, and system biology focused on understanding the behavior of complex biological networks. His research takes advantage of epigenetic and genomic analysis of cancer tissues and established gastric cancer cell lines. He was awarded a Columbia University - University of Glasgow fellowship to the Institute of Cancer Sciences (Glasgow, UK). In 2009, he was also awarded a fellowship from American Association for Cancer Research - Avon presented at 100th Annual Meeting of the AACR in Denver, USA.

### CHOLESTEROL AND CANCER, LIPIDS AS MODULATORS OF THE RESPONSE TO BIODRUGS

The team's scientific project is multidisciplinary (biology, biochemistry, physiology, metabolism, nutrition and cancerology) and focuses on the transverse interaction of resources for research (medicine, pharmacology, sciences, University Institute of Technology).

We investigate the different modes of molecular and cellular actions and the impact of specific lipids on mitochondrial function, cancer cell lines, and the relationship between tumour and its host.

The goals of the project are to better understand the metabolism of cholesterol and use this knowledge to develop new methods to target the development of tumors.

This project provides the opportunity to work in a network of nationally and internationally recognized laboratories of the region. Benefiting from the international scientific environment of region Centre-Val de Loire and work under the leadership of the UMR 1069 «Nutrition, Growth and Cancer» research unit, University Francois- Rabelais in Tours.

During this year we started the development of a biopharmaceutical particle composed of apolipoprotein AI (ApoAI), phospholipids and cholesterol or phytosterols (PS), named reconstituted high-density lipoproteins (rHDL).

Given that breast cancer over-expresses the SR-BI receptor that specifically binds to ApoAI, this rHDL will be specifically delivered to breast cancer tumors. We hypothesize that PS will compete with endogenous cholesterol and interfere with key cellular processes, such as migration and proliferation. We were able to demonstrate that, two of our new rHDL were able to block breast cancer cell migration.

In addition, we have tested more than 100 compounds to identify modulators of lipid uptake. By using the CHO-LdlA7-SR-BI cells that over-express SR-BI, we have discovered new compounds that promote or prevent HDL-mediated lipid uptake. This data will be further used to develop drugs with application in cancer and cardiovascular diseases.

### Dr PHILIPPE G. FRANK

### Laboratory Host Scientist



Philippe G. Frank obtained his PhD in 1998 at the University of Ottawa, in Ontario, Canada in lipoprotein studies. He then joined the Albert Einstein College of Medicine as a post-doctoral fellow. There, his work focused on the role of caveolin proteins in cancer and atherosclerosis, in addition to lipoprotein and cholesterol metabolism. In 2006, he joined the Kimmel Cancer Center as Assistant Professor at Thomas Jefferson University in Philadelphia, Pennsylvania where he started a program to examine the role of lipoproteins and cholesterol during cancer development and progression. Later, he was appointed as a senior research investigator at the University of Tours to build on and extend the ARD 2020 Biopharmaceuticals funded initiative of Region Centre-Val de Loire, in the research project entitled «Lipids as modulators of the response to biodrugs». His research project is hosted within the Nutrition, Croissance et Cancer (N2C) Inserm research team of Professor Stephane Chevalier. He is currently serving as Associate Editor of The American Journal of Pathology and of Frontiers in Cardiovascular Medicine (Lipidology and Metabolism).



### **Dr WILLIAM HORSNELL**

LE STUDIUM / Marie Skłodowska-Curie Research Fellow

From: University of Cape Town, South Africa

In residence at: INEM, Orléans

Nationality: British

Dates: July 2017 - June 2018

His research investigates how immune responses control parasitic worm infections, how parasitic worms influence this immunity and how these immune responses help us understand other diseases. This has resulted in the identification of novel mediators of protective immunity against worms and shed new understanding on how these mediators change our immunity to other infections. In particular he is interested in these effects in the lung. His work is published in peer reviewed journals and, where relevant, patented for future commercial explotation. Components of our work addressing relationships between worms and bacterial infection were awarded a Harry Crossley Research Prize. All research activities are currently supported by multi-year grants from the National Research Foundation (South Africa), Poliomyelitis Research Foundation (South Africa) and the Deutsche Forschungsgemeinschaft (Germany). An important new activity in Cape Town and Birmingham is the development of senior researcher capacity at the Mangosuthu University of Technology, kwaZulu Natal, South Africa (supported by the South African Department of Science and Technology)



### TARGETING ACETYLCHOLINE RECEPTORS TO ENHANCE IMMUNITY TO ACUTE VIRAL INFECTION

Recently studies have shown that acetylcholine (ACh), a neuro-transmitter, which regulates nerve and muscle functions, also strongly regulates the immune system. Immune cells can produce and release ACh to control local immune responses independently of the nervous system. The understanding of ACh mediated immunoregulation in disease is very limited. Here we will build on recent discoveries made by us that blocking ACh signaling can boost the ability of the immune system to control a viral infection in the lung. The infection we are studying is known as RSV and is the main cause of small children being hospitalised for breathing difficulties.

Our project will show how blocking ACh can be used to develop new treatments for this and similar diseases such as influenza established in the host laboratory.

To date our work at INEM has resulted in the generation of two novel mouse strains. These are mice with targeted disruption of expression of the enzyme required to generate ACh; choline acetyl transferase (ChAT). We have targeted disruption of ChAT in two populations of innate lymphoid cells (ILC) known to contribute pulmonary inflammation in a range of disease settings, including viral infection. We are currently establishing the integrity of this Cre mediated disruption and testing for phenotype in a range of pulmonary inflammation models.

Additionally, we are testing the effects of pharmacological inhibitors of ACh on lung inflammation.

Together this work will establish the contribution of ILC derived ACh in pulmonary inflammation and how drugs can manipulate these ACh responses.

### Dr BERNHARD RYFFEL





Bernhard Ryffel's research interests primarily lie in understanding the mechanisms of pulmonary inflammation and repair of resulting lung injury. He has published over 400 papers and has H factor of 75. In addition to his position at CNRS he also holds chairs in Shangai and Cape Town. He currently holds a number of major international grants supporting this work. In addition to his academic achievements Bernhard has excellent links with industry, has played key roles in the founding of PhenoTec AG and ArtImmune and consults widely.



—— Life & Health Sciences



### Dr NORINNE LACERDA-QUEIROZ

LE STUDIUM / Marie Skłodowska-Curie Research Fellow

**From**: National Institute of Health (NIH), USA

In residence at: INEM, Orléans

Nationality: Brazilian

Dates: October 2017 - October 2018

Norinne Lacerda Queiroz received her PhD in cell biology in 2011 from the Universidade Federal de Minas Gerais (UFMG) in Brazil. From 2012 to 2017, she was a postdoctoral fellow at the National Institutes of Health (NIH), working in the Laboratory of Malaria and Vector Research (LMVR). Norinne mostly focused on studying malaria pathogenesis and host-parasite interactions in murine models. She has experience in the area of parasitology, cell biology and immunology. She authored over 10 publications in the field of malaria, including collaborations. Currently, her research focuses on systemic damage during experimental severe malaria and especially in pulmonary pathology. A better understanding of severe manifestations during malaria might contribute to the development of new therapeutic approaches, for those often-lethal complications.

### AROUND THE PROJECT

### Oral communication

Reverchon, F.; Mortaud, S.; Maillet, I.; Laugeray, A.; Palomo, J.; Montécot, C.; Ryffel, B.; Menuet, A.; Quesniaux, V.F.J. IL-33/ST2 pathway in cerebral malaria and induced cognition defects, ICGEB Workshop "Host-directed therapeutic strategies for infectious diseases", Cape Town (South Africa), September 18-21, 2017.

### Scientific publication

Reverchon, F.; Mortaud, S.; Sivoyon, M.; Maillet, I.; Laugeray, A.; Palomo, J.; Montécot, C.; Herzine, A.; Meme, S.; Meme, W.; Erard, F.; Ryffel, B.; Menuet, A.; Quesniaux, V.F.J. IL-33 receptor ST2 regulates the cognitive impairments associated with experimental cerebral malaria, *PLOS Path.*, **2017**, *13*, e1006322.

### STUDY OF PULMONARY DAMAGE IN EXPERIMENTAL SEVERE MALARIA: MALARIA-ASSOCIATED ACUTE RESPIRATORY DISTRESS SYNDROME (MA-ARDS) AND MALARIA SEPSIS INDUCED BY SECONDARY BACTERIAL INFECTION

Plasmodium parasites annually infect hundreds of millions of people and complications known as severe malaria lead to half a million deaths. Severe malaria includes cerebral malaria (CM), acute respiratory distress syndrome (ARDS), and severe anemia. Experimental malaria models are relevant to study severe malaria-associated syndromes, respecting the complexity and diversity of those manifestations.

The main goal of this project is to investigate the immunopathology of two pulmonary often-lethal major but neglected complications: malaria-associated acute respiratory distress syndrome (MA-ARDS) and malaria sepsis induced by secondary bacterial infection. It has been demonstrated that patients with malaria may develop MA-ARDS after the start of antimalarial chemotherapy, as well as succumb from hypersensitivity to secondary bacterial infection, due to exacerbated inflammatory response. As a first approach, we aim to characterise the endothelial-leukocyte interactions in a rodent model of MA-ARDS, and the detrimental role of CD8+ T cells in the context of pulmonary damage, through the involvement of adhesion molecules (LFA-1 and VLA-4) and granzyme release. In a second part, we are planning to examine the mechanisms of pulmonary damage in the context of secondary bacterial challenge, focusing on the role of free heme-associated cell death and neutrophil dysfunction.

Altogether, this study ambitions to better characterise the pathogenesis of MA-ARDS and malaria sepsis, investigating cellular and molecular mechanisms involved in the pulmonary damage and endothelial leukocyte interactions. An understanding of the mechanisms underlying the disease pathogenesis is essential for the development of new therapeutic approaches, especially adjunctive therapy, for those often-lethal complications.

### Dr VALÉRIE QUESNIAUX

### Laboratory Host Scientist

After a PhD in Biochemistry in France and post-doctoral fellowships at the Max Planck Institute for Immunobiology, Freiburg, Germany, she worked for 12 years at Novartis Pharma Basel, Switzerland on immunosuppressants and anti-inflammatory drugs. Back to public research in 2000, she is now Research Director and heading the research unit UMR7355 'Experimental and Molecular Immunology and Neurogenetics" at CNRS, Orleans, France, she extended her field of interest to the immune responses involved in lung inflammation, and host-pathogen interactions, in particular in tuberculosis and experimental severe malaria. We analyzed the role of TLRs, inflammasomes, TNF, IL-1, IL-17 and, more recently IL-33 in these conditions. Former coordinator of the European project "TB REACT", she contributes to several European, national or international research projects, including an International Associated Laboratory (LIA) "TB Immunity" with the University of Cape Town, South-Africa (2007-2014), and a second "LIA" on "Lung Inflammation" with the University of Sao Paulo, Brazil (since 2012).





### Pr MAREK ŁOS

LE STUDIUM / Marie Skłodowska-Curie Research Fellow

From: Jagiellonian University, Poland

In residence at: CBM. Orléans

Nationality: Polish

Dates: October 2017 - October 2018

Pr Łos holds a 2 visiting professorships, and 2 adjunctprofessorships at Polish universities and a 'Senior Scientific Adviser' position at Linkocare AB, Linköping, Sweden. In 2003, he received the prestigious Canada Research Chair career award. Pr Łos (co-)authors about 150 scientific papers and 7 patents, edited several books and volumes. His Hirsch is currently 50, and his work research papers have been cited about 11000 times. He has been serving as member of a number of editorial boards of scientific journals, as well as on grant review committees in the Europe and in Canada. Pr Łos pursues various research projects within area of oncology, targeted cancer therapies and regenerative medicine. His most important scientific achievements were the description of involvement of caspases in CD95 mediated apoptosis, (Los et al., 1995; Nature 375: 81-83), and the discovery of the role of kinase Akt both in the regulation of cell survival and cell death (Maddika et al., 2008, J. Cell Sci.; Maddika et al., 2009, Mol. Cell. Biol.).

### AROUND THE PROJECT

### Oral communication

Łos, M. J. Cancer Stem Cells – salinomycin as an example of targeted therapy directed agains cancer stem cells, 70th anniversary of the existence of the Oncology Center in Glivic & VIIth Congress of Polish Radiotherapy society, Glivice (Poland), October 26, 2017.

### Scientific publication

Skubis, A.; Gola, J.; Sikora, B.; Hybiak, J.; Mazurek, U.; Łos, M. J. Impact of antibiotics on the proliferation and differentiation of human adipose-derived mesenhymal stem cells, *Int. J. Mol. Sci.*, **2017**, *18*, 2522.

### Books or book chapters:

Several book chapters are in preparation. They will form the back-bone of the book "Biomaterials, Stem Cells & Regenerative Medicine" that is being edited for Elsevier. The book should be finalized in mid-2018.

### EFFECTS OF ELECTRO-CONDUCTIVE, BIOMATERIAL-BASED TISSUE SCAFFOLDS ON STEM CELLS AND TRANSDIFFERENTIATION-DERIVED SOMATIC CELLS

The project focuses on the development of novel engineered artificial electro-conductive extracellular matrix materials, and characterization of their compatibility and interactions with stem cells, both under normal condition and upon stimulation with 0,2-1V, and 0,05-2,0 Hz oscillations. The engineered extracellular matrices will be obtained from combination of biodegradable polymers like for example PLGA, PCI\_PLA with

I – conductive polymers like i.e. PPy, PEDOT, PANI, in order to make the combined polymers electro-conductive,

II – carbon-based nanomaterials, like single-wall carbon nanotubes (SWCNT), and/or multi-wall carbon nanotubes (MWCNT), in order to make the combined polymers electro-conductive,

III – combination of conductive polymers, carbon-based nanomaterials, and bioactive elements, in order to achieve controlled drug release.

The nanomaterials will then be tested for biocompatibility and for other potential biologic properties, on primary somatic cells obtained either by transdifferentiation or by reprogramming with subsequent differentiation to selected cell types. Such tests will be performed both under normoxic and under hypoxic conditions. Furthermore, since natural extracellular matrix (ECM) is electroconductive, and several cell types, including muscle cells, cardiac-muscle cells and neurons are routinely exposed to electric currents, selected biocompatibility tests will also be performed under electrostimulation (0,2-1V, and 0,05-2,0 Hz oscillations).

### **Dr CATHERINE GRILLON**





Dr Catherine Grillon is a CNRS researcher at the Center for Molecular Biophysics in Orleans. She has long-standing expertise in skin biology, oxidative stress, angiogenesis, physio-pathological cell microenvironment and cell interactions. She has contributed to the discovery of lectins on skin cells and lymphocytes, to the study of the role of the tetrapeptide AcSDKP in protecting stem/progenitor cells against cytotoxicity of chemotherapeutic agents. She has studied the importance of oxygen level really present in the microenvironment for skin cell activity and developed in vitro skin models respecting physioxia. Now, she is developping several projects mainly in skin biology with the aim to prevent or treat skin aging. She is co-author of 34 publications + 3 patents, is now co-leader of the axis "Skin biology", co-leader of a group of 14 people and co-responsible of the CBM P@CYFIC plateform (cytometry and cell imaging). Main scientific skills: cell biology, angiogenesis, cell dynamics, hypoxia/physioxia, cytofluorimetry, biochemistry





### Pr SALVATORE MAGAZÙ

From: University of Messina, Italy

In residence at: CBM, Orléans

Nationality: Italian

Dates: July 2016 - July 2017

Salvatore Magazù is Professor of Experimental Physics since 2002 at the Department of Mathematical and Computer Science, Physical Sciences and Earth Sciences of the Messina University in Italy. He is currently President of the Interuniversity Consortium for Applied Physics. He was chairman of the Scientific Committee on Glass Forming Systems at the European Synchrotron Radiation Facility (ESRF, Grenoble) and member of several Scientific Committees at ESRF and Institute Laue Langevin (ILL, Grenoble). At present, he is engaged in a project for the European Spallation Source. He has received several international and national prizes, such as the Scientia Europaea 2000 Prize by the French Academy of Sciences and by Aventis. His research activity concerns the structural and dynamic characterization of disordered systems of biophysical interest such as bioprotective systems, biomolecules (proteins, antioxidants) and water. Its transdisciplinary approach relies on the integrated use of complementary spectroscopic techniques such as neutron scattering, synchrotron radiation and optical spectroscopies.



### FROM SUGARS AND POLYOLS TO INNOVATIVE **COSMETIC FORMULATIONS AND TECHNOLOGIES: MOLECULAR MECHANISMS AND NANOSCOPIC CHARACTERISATION**

The project is mainly focused on innovative cosmetic formulation processes based on natural molecules, as oligosaccharides (e.g. trehalose and its homologues maltose and sucrose) and polyols (e.g. glycerol and sorbitol). Such natural molecules have received in the last years a growing attention both from the scientific and applicative points of view. The interest is due not only to their effectiveness as bio-protecting systems conferring to biomolecules a higher stability and resistance under stress conditions but also to their nature of glass-forming systems characterised by phases of different specific density and entropy but identical composition (polvamorphism).

The project is based on two main interplaying driving directions:

- 1. the understanding of the chemical physical mechanisms responsible for the bioprotectant function of natural molecules;
- 2. the nanoscopic characterisation of confinement and crowding effects of such natural active ingredients when encapsulated in delivering systems. The research activity has been so far mainly focused on the study of structural and dynamical properties of disaccharide and polyol mixtures of cosmetic interest by spectroscopic techniques. A special attention has been paid to large scale facilities, such as neutron and synchrotron radiation spectroscopy facilities, whose instrumental performances provide an added value to the cosmetic field.

### AROUND THE PROJECT

- 1 Magazù, S. Biophysics of life under extreme conditions, Le Studium Thursday. Orléans (France), January 5, 2017.
- 2 Magazù, S. Molecular origins of bio-inspired cosmetics, Recent advances in basic & applied science in cosmetics - Le Studium Conferences, Tours (France), July 3-5, 2017.

- 1 Magazù, S.; Mezei, F.; Falus, P.; Farago, B.; Mamontov, E.; Russina, M.; Migliardo, F. Protein dynamics as seen by (quasi) elastic neutron scattering, Biochimica et Biophysica Acta - General Subjects, 2017, 1861, 3504-3512.
- 2 Angell, C.A.; Magazù, S.; Migliardo, F. Science for life Recent advances in biochemical and biophysical methods, Biochimica et Biophysica Acta - General Subjects. 2017. 1861. 3501-3503.
- 3 Migliardo, F.; Magazù, S.; Angell, C. A. Contrasting dynamics of fragile and nonfragile polyalcohols through the glass, and dynamical, transitions: A comparison of neutron scattering and dielectric relaxation data for sorbitol and glycerol, Biochimica et Biophysica Acta - General Subjects, 2017, 1861, 3540-3545.

### Pr FRANCESCO PIAZZA

### Laboratory Host Scientist



Francesco Piazza is Professor at the CNRS laboratory, Centre for Molecular Biophysics, affiliated with the University of Orléans. A physics graduate of the University of Florence in Italy, he obtained his PhD at Heriot-Watt University, Edinburgh, UK in 2002. He was a research and teaching associate at the Ecole Polytechnique Fédérale de Lausanne in the Statistical Biophysics group, from 2003 to 2009. Professor Piazza uses quantum biology to elucidate the functioning of efficient light- harvesting molecular complexes; studies allosteric communication in proteins using coarse-grained models of protein dynamics; models diffusion-limited reactions among complex macromolecules or within complex environments and studies macromolecular crowding where the interior of the cell shares many properties with the liquid state of matter.



### **Dr SIVAKUMAR PONNURENGAM MALLIAPPAN**

From: RIKEN, Japan

In residence at: NMNS. Tours

Nationality: Indian

Dates: November 2016 - November 2017

Sivakumar Ponnurengam Malliappan was awarded doctorate degree from the Department of Biotechnology, Indian Institute of Technology Madras, India. He has also received prestigious postdoctoral fellowships like JSPS (Japanese Science Promotion Society) research fellow and FPR (Foreign Postdoctoral Researcher), worked at RIKEN laboratories, Wako-shi, Japan. He also acquired postdoctoral trainings from University of Pisa, Pisa, Italy and Indian Institute of Technology Madras, Chennai, India. At present, he also serves as editorial board member and as reviewer for several journals. His major research interests include nanoparticle synthesis, drug delivery, biomaterials and biofilm prevention. He authored and co-authored more than 38 internationally peer reviewed journal papers, edited 3 books with international publishers and contributed to ten invited book chapters.

### AROUND THE PROJECT

- 1 Ponnurengam Malliappan, S. Nanotechnology in Cosmetics, LE STUDIUM Thursday Seminar, Orleans (France), January 5, 2017.
- 2 Ponnurengam Malliappan, S. Nanotechnology in Targeted Cancer Drug Delivery, HIPER, Nadaun (India), February 26, 2017.
- 3 Ponnurengam Malliappan, S. Impact of Nanotechnological formulations in cosmetics, Recent advances in basic & applied science in cosmetics - Le Studium Conferences, Tours (France), July 3-5, 2017.
- 4 Ponnurengam Malliappan, S. Recent Advances in Cosmetic Technology, Seminar at Dr. APJ Abdul Kalam University, Indore (India), September 14, 2017.

### INNOVATIVE NANOCARRIER DELIVERY SYSTEM FOR ACTIVE COSMETIC INGREDIENTS (ACI) AND IN VITRO MODEL DEVELOPMENT FOR **EPIDERMIS**

Stratum corneum is considered to be a barrier for the diffusion of drugs. The stratum corneum is found to be of approximately 15 µm thickness and contributes to the Outer most part of the epidermis. Stratum corneum contains fatty acids in free form, cholesterol and ceramides as lipid multilayers which limits the penetration of the drug molecules. Nano delivery systems can be used to improve the drug penetration to the skin. Intracellular lipid route is important for the nanoparticle based drug

Nano delivery system for Active Cosmetic Ingredients (ACI) has been used as nanomaterials in order to:

- 1. improve their UV protection,
- 2. skin penetration,
- 3. site directed delivery of ingredients,
- 4. long term persistence/ controlled release of ingredients,
- **5.** Stability of ingredients
- 6. solubility
- 7. and to minimize toxicity.

Several physiochemical characteristics are pre-requisite for the nanocarrier delivery systems like hydrophobicity, rigidity, size and their mechanism of skin penetration. Polymeric nanoparticles are stable due to their rigid matrix; their size and hydrophobicity are tunable. Hence we propose polymeric nanoparticles as nanocarrier system for Active Cosmetic Ingredients. Our objective is to develop a novel nanocarrier delivery system for Active Cosmetic Ingredients (ACI) and evaluation of their effective delivery/penetration to stratum corneum by developing In vitro epidermis model. This project includes two steps namely,

- 1. Development of novel nanocarrier system using polymeric nanoparticles 2. In vitro model development for epidermis. The prepared and evaluated nanoparticles are then used for cosmetic applications.
- Poster

Buchy, E.; Darner, L.; Ponnurengam Malliappan, S.; Soucé, M.; Chourpa, I.; Munnier, E. Design, synthesis and nanoparticular formulation of a lipophilic bioconjugate of pyroglutamic acid with auto-assembling properties derivated from pyroglutamic acid, Recent advances in basic & applied science in cosmetics - Le Studium Conferences, Tours (France), July 3-5, 2017.

### **Dr EMILIE MUNNIER**

### Laboratory Host Scientist



Emilie Munnier is an assistant professor in pharmaceutical technology and cosmetology at the faculty of Pharmacy of Tours and a senior researcher in the research team Nanomedicines et Nanoprobes. After her Pharm D, she obtained a PhD in Life and health sciences at the University of Tours, dealing with nanotechnologies applied to cancer treatment, and finally her HDR in 2016. Using her skills in formulation and analytical chemistry, she now dedicates herself to the encapsulation of active molecules to improve their delivery in the skin and their interaction with the skin or with the ingredients of a pharmaceutical/cosmetic final product. She has been the coordinator of several national research projects implying actors of the cosmetic industry, among them the COSMICC project, part of the Cosmetosciences regional research program. The aim is to first to develop innovative stimuliresponsive encapsulation systems for the delivery of cosmetic ingredients, then to improve the analysis of biological tissues by vibrational spectroscopy methods to elucidate their mechanism of action and measure their efficacy. 43

### RECENT ADVANCES IN BASIC AND APPLIED SCIENCE IN COSMETICS

The International Interdisciplinary Conference titled Recent advances in basic and applied science in cosmetics was held from 3rd to 5th of July 2017 in Tours. The Conference aimed to update the knowledge in the fields of biophysics, chemistry, biochemistry and imaging applied to skin and cosmetics. This event gathered renowned academy and industry experts and offered a unique chance to debate the latest topics, issues, trends and challenges in the cosmetics and dermatology field. For this purpose, the scientific programme crossed both fundamental research fields, such as physical and chemical properties of systems of cosmetic interest, bioprotection molecular mechanisms and interface chemical processes, and advanced analytical, imaging and simulation techniques. Another goal of the Conference was to build cross-disciplinary collaborations to create a scientific value chain, leading to the emergence of new innovative collaborative research activities and to significant socioeconomic impacts. The Conference was held in Tours in the heart of the territory covered by Cosmetic Valley which supports growth in the cosmetics sector by means of research, training and development activities and services.

### L'EFFICACITÉ DES COSMÉTIQUES : COMMENT EST-ELLE DÉMONTRÉE ?

European regulation of cosmetics (Regulation (EC) No 1223/2009) requires the demonstration of the effectiveness of any cosmetic product marketed on European soil. It also prohibits any experimentation on animals. The Loire Valley Region, and more specifically the city of Tours, is a pioneering region in the development of so-called objectivation tests of cosmetic claims. Through concrete examples, a duo made up of an academic researcher and an industrialist specialising in the evaluation of cosmetics, has presented the different stages of the demonstration of the effectiveness of a cosmetic, *in vitro* tests, in test tubes or on cell cultures, *in vivo* tests on healthy volunteers. An incursion into the methods of the future will close the conference.











### **Dr MAURO MANNO**

LE STUDIUM / Marie Skłodowska-Curie Research Fellow

From: National Research Council, Italy

In residence at: ICOA, Orléans

Nationality: Italian

Dates: October 2016 - October 2017

Mauro Manno is researcher at the National Research Council of Italy, Institute of Biophysics, Palermo. He is author of one patent, and several I.S.I. publications, most as first or corresponding author, as well as book chapters, abstract or articles on conference proceedings, invited talks.

In the last 5 years, he was involved in different projects, and responsible of two projects related to Serpinopathies funded by Telethon Foundation (Italy) and Cariplo Foundation (Italy).

He worked on several projects at large European facilities: ILL (Grenoble), synchroton Soleil (Paris), Elettra (Trieste), ESRF (Grenoble).

Current research focuses on the thermodynamic and conformational stability of protein in solutions and on the common pathways of self-assembly leading to different biologically relevant structures, including amyloid fibrils, proteins clustering on the membrane of extracellular vesicles, polymers of serpin proteins.



# THE ROLE OF GLYCOSYLATION IN THE FUNCTIONAL ACTIVITY AND PATHOLOGICAL CONSEQUENCES OF SERPIN PROTEINS

The goal is to shed light into the molecular basis of a peculiar class of conformational diseases, called Serpinopathies, with a special emphasis to glycosylation, an important post-translational modification which rules the functional and pathological behaviour of the proteins responsible for the diseases. Serpinopathies are a class of genetic diseases related to the deficiency of a serpin (SERin Protease Inhibitor) and/or its accumulation as polymer chain in the cell of synthesis.

For instance, the best-known a-antitrypsin deficiency is caused by mutations in alpha1-antitrypsin determining polymer accumulation in the hepatocytes and lack of inhibition of lung proteases; the Hereditary Angio-Edema is caused by a poor activity of mutated C1-Inhibitor; and the Familial Encephalopathy with Neuroserpin Inclusion Bodies (FENIB) is related to the accumulation of neuroserpin polymers within neuron endoplasmic reticulum.

FENIB and in general all serpinopathies are incurable disorders also due to the incomplete understanding of polymer structure and formation, which makes it difficult to develop a successful therapeutic approach based on polymerisation inhibitors.

To date, all the biochemical and biophysical research performed on neuroserpin has been carried out using recombinant neuroserpin expressed in bacteria, thus non-glycosylated.

However, our recent data indicate that neuroserpin polymerisation is hindered by the presence of glycosidic chains at two sites that are glycosylated when expressed in mammalian cells.

Also, preliminary experiments show that N-linked glycosylation relates to the stability and polymerisation of alpha1-antitrypsin, as well as to the molecular conformation of the unstructured domain of C1-inhibitor.

The main aim of the present project is to highlight the role of glycosylation in the conformational stability, functional activity and polymerisation propensity of neuroserpin and C1-inhibitor.

This aim has been pursued by implementing serpin production in a novel expression system: Leishmania Expression System (LEXSY), based on the protozoan host Leishmania tarentolae, that is able to generate complex glycosylation patterns in proteins.

In collaboration with our collaborators from the University of Milan, the sequence of human neuroserpin and human C1-inhibitor were cloned into LEXSY plasmid. A his-tag for protein purification was also inserted at the N-terminus of the proteins, since the C-terminus is known to be important for serpin function and stability.

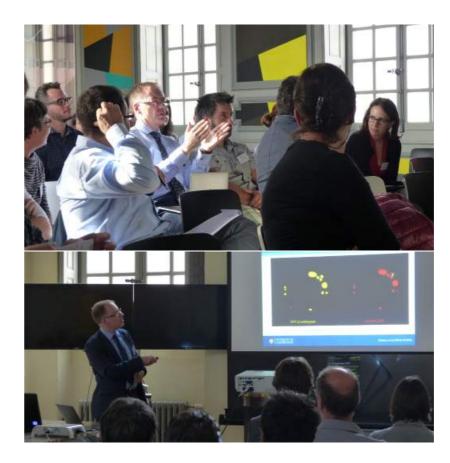
Then, a stable cell line, transfected with the neuroserpin coding plasmid, was established.

The cells were verified to produce glycosylated neuroserpin and a first purification protocol was prepared. The work will continue with further tests on glycosylated neuroserpin and with the optimization of the purification protocol, as well with the production of new cell lines for the expression of C1-Inhibitor, and eventually of alpha1-antytripsin (the latter in collaboration with our collaborators at University College of London.

### THE ROLE OF GLYCOSYLATION ON SERPIN BIOLOGY AND CONFORMATIONAL DISEASES

The aim of the conference was to bring together scientists working on the molecular aspects of protein conformational disease, specifically on serpinopathies, and on the role of glycosylation on the folding, stability, function and cellular fate of serpin proteins. Although this topic is recognised as an important aspect in the field, it has not been the focus of a dedicated conference so far. This event aimed to be a milestone in the broader topic of the role of glycosylation on conformational disease, devoting a substantial time to open discussion with the intention of fostering collaborations and promoting new ideas.

The conference has seen the participation of speakers with different background, from medical doctors to molecular biophysicists. The success of the conference drove the participants to plan a series of conferences modelled on this one.



### Pr RICHARD DANIELLOU

Laboratory Host Scientist

Internationally recognized expert in Glycosciences, Pr Richard Daniellou received a degree in Biochemistry and a PhD (2003) in Organic Chemistry from the University of Paris XI. After two years as a postdoctoral researcher at the University of Saskatchewan (Canada), he was offered an Assistant Professor position at the ENSC of Rennes (France). In 2010 he defended a habilitation and was promoted Full Professor of Biochemistry at the Organic and Analytical Chemistry Institute of Orléans (France) in 2011. His main interest for carbohydrate-active enzymes as biocatalysts for chemo-enzymatic synthesis of glycoconjugates led him to the creation of the research group named Enzymology and Glycobiochemistry. He is currently co-author of 55 publications and 3 patents. He was awarded in 2016 the prize of the French Group of Glycosciencess in recognition of his young but talented career.

### AROUND THE PROJECT

### Oral communications

- 1 Manno, M. Non-Classical Polymers of alpha1-antitrypsin: A multidisciplinary approach, 1st Italian Meeting on the research on Alpha1-Antitrypsin Deficiency, Brescia (Italy), February 25, 2017.
- 2 Manno, M. Serpin conformational diseases: From molecular studies to therapeutic intervention, 15th ADOC Conference-Colloque on "Fundamental research, Orléans (France), May 4, 2017.

### Poster

Manno, M.; Randazzo, L.; Raccosta, S.; Noto, R.; Mangione, M. R.; Ati, J.; Lafite, P.; Daniellou, R.; Miranda, E.; Russo, R.; Barbiroli, A.; Bolognesi, M.; Ricagno, S.; Martorana, V. The well-tempered polymerization of human neuroserpin: The mechanism and its prevention in related pathologies, Conference on "Biophysical Approaches to Protein Folding and Disease", Edinburgh (United Kingdom), July 20-21, 2017.





### Pr MICHIEL POSTEMA

LE STUDIUM / Marie Skłodowska-Curie Research Fellow

From: University of Bergen - Norway

In residence at: Imagerie & Cerveau, Tours

Nationality: Dutch

Dates: February 2017 - January 2018

Michiel Postema graduated in Geophysics from Utrecht University. Following a Doctorate in the Physics of Fluids (Twente), he worked in research positions across the globe concentrating on medical and nonmedical microbubble behaviour in sound fields.

He was appointed Professor of Experimental Acoustics at the University of Bergen in 2010, Erasmus Visiting Professor of Astrophysics at the University of Dundee in 2012, Visiting Professor of Electrical Engineering at the University of the Witwatersrand in 2015, Ordinary Professor of Ultrasound at the Polish Academy of Sciences in 2016, and Distinguished Professor of Biomedical Engineering at the University of the Witwatersrand in 2017.

As part of the Le Studium Fellowship, Michiel successfully defended a Habilitation on the topic acoustic cells and antibubbles at the University of Tours.

### SONIC ANTIBUBBLES IN HARMONIC IMAGING AND THERAPY

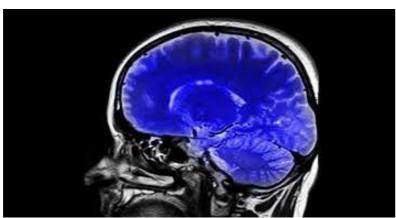
Bubbles are gaseous or vaporous voids, surrounded by liquid. Owing to the Laplace surface pressure, bubbles tend to be spherical of form. Bubbles smaller than 10 µm are referred to as microbubbles. When subjected to a sound wave, microbubbles oscillate, i.e., they repeatedly contract and expand. A microbubble oscillation radiates a sound field itself, which can be detected by a transducer or a hydrophone. So-called ultrasound contrast agents consist of microbubbles, encapsulated by elastic shells. These agents are commonly used in clinical diagnostic imaging but are also of interest in therapeutic settings. The encapsulating shells prevent the microbubbles from dissolving quickly after having been administered intravascularly into a patient.

Studying the dynamic behaviour of acoustic microbubbles has been the primary research topic of the host laboratory and the guest scientist. Specifically, we have used high-speed photography to observe microbubbles under sonication. Furthermore, we have worked on optical and acoustical theory to model and predict encapsulated microbubble dynamics.

In order to enhance ultrasound imaging, we investigated pulse forms before administering bubbles. These findings have been published.

For diagnostic imaging and drug delivery application, the dynamic behaviour of antibubbles under sonication needed to be predicted in greater detail, with a focus on harmonics generation and antibubble disruption.

An objective was to generate a mathematical model of antibubble dynamics, incorporating solid and viscoelastic shells. Furthermore, the harmonic response of antibubbles was to be studied experimentally using multifrequency probes.





# ACOUSTIC BUBBLES IN THERAPY: RECENT ADVANCES WITH MEDICAL MICROBUBBLES, CLOUDS AND HARMONIC ANTIBUBBLES.

LE STUDIUM Loire Valley Institute for Advanced Studies and Inserm Research unit U930: Imaging and Brain at University of Tours organised an international conference on acoustic bubbles in therapy, visited by over 80 participants.

Although the use of microbubbles has become common in ultrasound diagnostics, they are not that often seen in therapeutic applications. This conference focusses on recent advances in the development and application of microbubbles in therapy.

Plenary sessions included the following topics: bubble physics, bubble physical phenomena, bubble engineering and design, in-vitro evaluation, preclinical validations, and clinical studies. Invited speakers included Pr Kimmel (Technion), Pr Kudo (Hokkaidō), Pr Huang (Zhejiang), Pr Freear (Leeds), Dr van Wamel (NTNU), Dr Kotopoulis (Bergen), and Dr Prentice (Glasgow).

### DÉTECTER, VOIR ET SOIGNER: DES ULTRASONS AUX MULTIPLES FACETTES

This presentation will highlight how, over the last decades, ultrasound has benefited from remarkable and renewed concepts and scientific and technical innovations. A favorable physical situation for ultrasound in tissues, advantages of multidisciplinary medical employment creating a buoyant market, advances in miniaturization in mechanics and electronics, these are the main factors that made these advances possible. We now have powerful diagnostic tools and many research teams are opening the door to therapeutic ultrasound.





**Dr AYACHE BOUAKAZ**Laboratory Host Scientist
See page 53.

### AROUND THE PROJECT

### Oral communication

Postema, M. Science fiction technology in biomedical science, Le StudiumThursday series, Tours (France), March 2, 2017.

### **Scientific Publications**

- 1 Van Leusden, P.; den Hartog, G. J. M.; Bast,
- A.; Postema, M.; van der Linden, E.; Sagis, L. M. C. Effect of salt and processing conditions on the permeation of probe molecules into alginate microbeads prepared by W/O emulsification, Food Hydrocolloids, 2017, 73,
- 255-261.
  2 Postema, M.; Abraham, H.; Assefa, D. Size determination of microbubbles in optical microscopy: a best-case scenario, *Optics Express*, 2017, 25, 33588-33601.





### Dr EMMANUEL SARIDAKIS

LE STUDIUM / Marie Skłodowska-Curie Research Fellow

**From**: Institute of Nanoscience and Nanotechnology «DEMOKRITOS», Greece

In residence at: CBM, Orléans

Nationality: Greek

Dates: January 2017 - January 2018

Emmanuel Saridakis is Principal Researcher at the Institute of Nanoscience and Nanotechnology, National Centre for Scientific Research "Demokritos", Athens, and an Honorary Research Fellow at the Faculty of Medicine, Imperial College London. Since January 2017, he works as a Le Studium Fellow, hosted by the "Aspects Moléculaires du Vivant" team at the CBM, CNRS-Orléans. He obtained his Ph.D. in 1995 at the Biophysics Group, Physics Department, Imperial College London. He is a protein X-ray crystallographer, focusing his research on the theory and methodology of macromolecular crystallogenesis, as well as on solving crystal structures of proteins of biomedical interest. His current projects include crystal nucleation on porous and functionalised nanomaterials, thermodynamics aspects of crystallisation, and structure determination of proteins and complexes of medical interest, with a view to rational drug design. He has 42 publications in peer-reviewed international journals (>1400 citations, h-factor 21).



### NEW CRYSTALLISATION STRATEGIES FOR STRUCTURE-GUIDED PHARMACOLOGICAL DEVELOPMENT – LARGE BIOLOGICAL ASSEMBLIES FOR RNA METABOLISM

The project aims at the elucidation of the three-dimensional structure of a complex cellular molecular machine, namely the transcription termination factor Rho. Rho is a key regulator of RNA metabolism in the cell, being thus at the heart of protein expression programs. It is quasi-ubiquitous in bacteria but absent from eukaryotic organisms, which makes it a very interesting potential antibacterial pharmacological target. Besides contributing to the punctuation of transcription units in the genome, Rho mediates riboswitch-dependent gene regulation, maintains chromosomal integrity by disrupting transcriptional R-loops and by preventing conflicts between transcription and DNA replication, and suppresses expression of harmful horizontally-acquired genes.

The functional Rho is a homohexamer, comprising six tightly regulated ATP hydrolysis pockets and multiple RNA-binding sites (which can also bind DNA). These features make its crystallisation an intricate and highly multi-parametric undertaking. A handful of structures of Rho from E.coli and Th. maritima have already been solved by other groups, but they have not always led to consensus on various central features of the molecular mechanisms involving Rho. In this project, we are focusing on a different organism of obvious medical interest, Mycobacterium tuberculosis, the Rho factor of which presents distinct characteristics, in its primary structure (it contains a large N-terminal insertion compared to E. coli Rho) as well as its functionality (it is for example refractory to the natural antibiotic bicyclomycin, the only available Rho-targeting drug).

The project has therefore a fundamental research aspect, namely the better and more detailed understanding of a key bacterial transcription molecular mechanism, and a long-term applied aspect, namely the development and/ or optimisation of novel antibacterial drugs. As a side-benefit of this project, relevant to the crystallogenesis methodological interests of the researcher in residence, it provides a challenging stimulus for the development and application of more unconventional and novel crystallisation techniques and approaches. These will be further pursued at the Fellow's home laboratory after his return.

Our work to date has resulted in the crystallisation of a single-point mutant (T501K) of M. tuberculosis Rho, and the collection of a full X-ray dataset at low resolution (6.5 Å), at the SOLEIL synchrotron. The wild type Rho has also been crystallised, but crystals were smaller. Crystallisation was possible only after removal of a likely disordered domain of the macromolecule, by in situ proteolysis. In the process of screening for potential crystallisation conditions, thermal shift assays, dynamic light scattering trials, as well as crystallisation screenings were conducted, which led to the discovery of optimal ligands (ATP-analogues and oligonucleotides) for the M. tuberculosis Rho. The quality of the crystals to date is not sufficient for obtaining an X-ray crystallographic structure to sufficient resolution, so crystal optimisation is now being pursued in the last phase of the project.



### STRUCTURAL BIOLOGY AND BIOPHYSICS OF PROTEIN-RNA COMPLEXES

The Conference, brought together several international leaders at the cutting edge of research on protein-RNA complexes. It aimed to approach the field of RNA-protein complexes from many different angles in terms of methodology (X-ray crystallography, NMR spectroscopy, cryo-electron microscopy, single molecule imaging and nanomanipulation techniques), but with a common emphasis on the acquisition of structural knowledge at the molecular level. The conference involved the presentation of the latest results of several research groups as well as more wide-scope overviews of the field, it allowed fruitful cross-disciplinary exchanges, and the interaction of younger researchers with established authorities. The Studium Fellow also established contacts with two french research groups (Prof. N. Leulliot, Université Paris Descartes; Dr. E. Margeat, CNRS-Montpellier) during the Conference, with a view to longer-term collaboration.

### L'UNIVERS EN EXPANSION DES VIRUS GÉANTS

The public Le Studium Lecture, entitled The expanding universe of giant viruses, was given by Dr Chantal Abergel, of the Information Génomique et Structurale (IGS) Laboratory, CNRS, Institut de Microbiologie de la Méditerranée, Aix-Marseille Université. Dr Abergel is the author of more than 100 peer-reviewed papers and has solved ca. 50 protein structures. She is a leading international authority in virology, and one of the discoverers of several previously unknown families of viruses, collectively labelled as giant viruses. She is a laureate of the CNRS Silver Medal and a Chevalier de la Légion d'honneur. Her work sheds light and has revolutionary implications on the understanding of the origins of life on Earth.



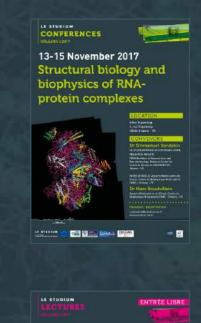
### Dr MARC BOUDVILLAIN Laboratory Host Scientist

Marc Boudvillain is a Research Director with CNRS and a Principal Investigator at Centre de Biophysique Moléculaire (CBM) in Orléans. Educated as a chemist, he obtained a PhD in Molecular Biology and Biophysics from the University of Orléans in 1996 for his work on Platinum(III) –based metalloribozymes. From 1996 to 1999, he was a postdoctoral Research Scientist at Columbia University and Howard Hughes Medical Institute in New York, working with Anna Marie Pyle on the structural basis of RNA catalysis by group II introns. Since 2000, he is a tenured CNRS scientist at CBM where he is now coordinating the activities of the team "Aspects Moléculaires du Vivant" and is heading its RNA biochemistry research group. His main research interests revolve around structure-function relationships in RNA-based systems with a particular focus on RNA remodeling by RNA helicases. Most of his recent work has been devoted to the transcription termination factor Rho, a bacterial RNA helicase, and to the development of combinatorial RNA biochemistry tools to probe the structure and mechanisms of RNA-protein complexes.

### AROUND THE PROJECT

### Oral communications

- 1 Saridakis, E. From crystals to drugs Methodology and applications of macromolecular crystallogenesis, Séminaire externe CBM, Orléans [France], April 28, 2017.
- 2 Saridakis, E. Towards crystallisation of the transcription termination factor Rho from Mycobacterium tuberculosis, Le Studium Conference: Structural biology and biophysics of protein-RNA complexes, Orléans (France), November 13-15, 2017.
- 3 Saridakis, E. Méthodes d'optimisation pour les cristaux de macromolecules, Séminaires Scientifiques à la Faculté de Pharmacie, Paris (France), December 8, 2017.





Lundi 13 Novembre 2017 - 18h30

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### Dr VOLODYMYR SUKACH

LE STUDIUM / Marie Skłodowska-Curie Research Fellow

**From**: National Academy of Sciences, Ukraine

In residence at: ICOA, Orléans

Nationality: Ukrainian

Dates: November 2017 - November 2018

Volodymyr Sukach graduated from the Chemistry Department of Taras Shevchenko National University of Kyiv and received his PhD in 2007 at the Institute of Organic Chemistry (IOCh), National Academy of Sciences of Ukraine. He was appointed a permanent position as senior research scientist (2010-2017) at IOCh. Dr V. Sukach is an author of 36 journal publications, 3 book chapters, 3 patents and 27 communications in conferences. For his expertise in organofluorine chemistry, he was invited to work as a visiting scientist at Jacobs University Bremen (DFG grant "Initiation of International Collaboration", Germany, 2014). His main research activities concern the development of asymmetric organocatalytic methodologies for the preparation of chiral fluoroalkyl substituted small synthetic building blocks and heterocyclic compounds with a special focus on fluoroalkyl ketimine chemistry and medicinal chemistry.

### AROUND THE PROJECT

### **Scientific Publications**

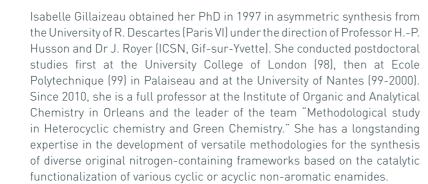
- 1 Melnykov, S. V.; Pataman, A. S, Dmytriv, Y. V.; Shishkina, S. .; Vovk, M. V.; Sukach, V. A. Regioselective decarboxylative addition of malonic acid and its half(thio) esters to 4-trifluoromethylpyrimidin-2(1H)-ones, *Beil. J. Org. Chem.*, 2017, 13, 2617-2625.
- **2** Tkachuk, V. M.; Melnykov, S. V.; Sukach, V. A.; Vovk, M. V. The addition of β-ketoacids to 4-(trifluoromethyl) pyrimidin-2(1H)-ones with decarboxylation: an effective method for the synthesis of 4-(2-oxoalkyl)-6-(trifluoromethyl)-3,4-dihydropyrimidin-2-ones, *Chem. Heterocycl. Comp.*, **2017**, *53*, 1124-1127.

# EXPLORING THE EFFECTS OF TRIFLUOROMETHYL GROUP IN THE DESIGN OF ORGANOCATALYSTS, ENZYME INHIBITORS AND IN THE CONFORMATIONAL CONTROL OF SATURATED NITROGEN-CONTAINING HETEROCYCLES

The trifluoromethyl group plays an important role in the design of novel pharmacologically active agents since its introduction into organic compounds often leads to improved potency, stability and activity in vivo. Our objective is to propose an interdisciplinary project including methodological studies, structure investigations, and organocatalytic transformations of a range of trifluoromethyl-containing ketimine derivatives with potent biological activity. We focus on the study of specific effects of trifluoromethyl group that could provide novel tools in molecular design of more efficient organocatalysts for asymmetric synthesis and pharmacologically promising nitrogen containing heterocyclic compounds. These effects include activation of NH-ketimine function for addition of nucleophiles giving rise to previously unknown "organoinhibition" phenomena and stabilisation of transition state-like structures in enzyme inhibitors. In addition, a rare intramolecular through-space interaction of fluorine atom of trifluoromethyl group with electrophilic sp2-hybridized carbon atom will be systematically studied. For this aim a new series of trifluoromethyl substituted nitrogen containing heterocycles possessing various electrophilic functional groups will be synthesized and characterized as model compounds by X-ray diffraction and NMR methods. The obtained results will provide better insight into a nature of this interaction which is of particular importance in rational drug design. The work will be conducted in collaboration with experienced scientists in the area of computational chemistry and methodological synthesis representing both IOCH NAS of Ukraine and ICOA, University of Orleans in France. In the first two months we synthesised and characterised by NMR method the first representatives of novel 6-(trifluoromethyl)hexahydropyrimidin-2(1H)-ones functionalised with 2-imidazolinyl substituent at position 4 of the pyrimidine ring. These structures perfectly fulfill the requirements for a strong orthogonal through-space interaction between the fluorine atoms of trifluoromethyl group and the carbon atom of the corresponding electrophilic counterpart represented by protonated C=N function from heterocyclic ring. In collaboration with Pr A. Rozhenko (Institute of Organic Chemistry, NAS of Ukraine) we calculated conformation energies by DFT and ab initio methods. The results supported the plausible axial-axial conformation preference due to the mainly electrostatic orthogonal dipolar interaction.

### Pr ISABELLE GILLAIZEAU

Laboratory Host Scientist







### Dr AYACHE BOUAKAZ

CONSORTIUM COORDINATOR

CONSORTIUM

SMART LOIRE VALLEY

Ayache Bouakaz is a Research Director and Team Leader at "Imagerie & Cerveau" joint research unit U930, Inserm, University of Tours. His research focuses on imaging and therapeutic applications of ultrasound, microbubble contrast agents and transducer design. He graduated from the University of Sétif, Algeria, and obtained a PhD at the Institut National des Sciences Appliquées de Lyon, France. In 1998, he joined the Bioengineering Department at The Pennsylvania State University (USA) and later moved to the Erasmus University Medical Center of Rotterdam in the Netherlands. He is Associate editor for IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control, a member of the editorial board of the Journal of Ultrasound in Medicine and Biology, and a Member of the technical committee of the IEEE Ultrasonics International Symposium.

### SONOPORATION FOR THERAPY: FROM IN-VITRO, TO IN-VIVO TO PATIENTS

Although cancer specialists can call on a plethora of treatment approaches, current treatment outcomes and patient survival rates remain modest. Sonoporation is a delivery technique for which high-frequency sound is used in conjunction with microbubbles to enhance the permeability of biological barriers while allowing co-administered therapeutic drugs or genes to be introduced into target tumours. Although sonoporation offers promise as a drug delivery tool with potential of alleviating the suffering brought on by the ravages of various disorders it has not been adopted as a clinical tool because its safety has not been evaluated and the relevant protocols leading to its efficient use in humans remains poorly defined and thus broadly unregulated. This Consortium proposes to establish a framework for the safe and effective use of sonoporation as a tool for selective drug delivery in order to enhance drug bioavailability in tumor tissue. This multidisciplinary team has been constituted with the express purpose of creating a research network addressing key challenges facing clinical translation of sonoporation (preclinical studies of sonoporation in animals, imaging protocols necessary to evaluate sonoporation efficiency...)

### PARTNERS COLLABORATOR



Pr Mike Averkiou
University of
Washington - USA



**Pr Nico de Jong** Erasmus University -The Netherlands



Pr Chrit Moonen
University Medical
Center Utrecht The Netherlands



The Netherlands

Pr Hanneke W.M.

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Medical Oncology

Academic & Medical

Centre -



Dr Charles
Sennoga
Imagerie & Cerveau
University of Tours France

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### Pr DENIS MULLEMAN

**CONSORTIUM COORDINATOR** 

LE STUDIUM

**SMART LOIRE VALLEY** 

Denis Mulleman is Professor of Rheumatology at the University François- Rabelais of Tours, member of the PATCH (PhArmacology of TherapeutiC antibodies in Human) team; head Gilles Paintaud. His research aims to characterise the concentration-response relationship of monoclonal antibodies used in inflammatory diseases, to help clinicians to individualise dosages, enabling personalised therapeutic drug monitoring. He is involved in numerous research projects using anti- TNF mAbs and Fc- containing fusion proteins, among them an Innovative Medicine Initiative [IMI] European project dedicated to the immunogenicity of biopharmaceuticals. His group has been deeply involved in the development of validated ELISA techniques allowing the quantification of serum concentrations of therapeutic antibodies. He is coordinator of designed clinical drug trials enabling population pharmacokinetic and pharmacokineticpharmacodynamic (PK-PD) modelling to quantify the different sources of the response interindividual variability.

### MONITORING OF MONOCLONAL ANTIBODIES GROUP IN EUROPE (MAGE) FOR **INFLAMMATORY DISEASES**

Biopharmaceuticals, in particular monoclonal antibodies, have radically transformed the course of various conditions, from malignancies to inflammatory diseases. Considerable inter-individual variability in the clinical response has been documented. It has been shown that pharmacokinetics (drug concentration versus time) is highly variable between patients and is related to clinical response, patients with high concentrations of the drug being more likely to respond than those who have low concentrations. Pharmacokinetic and pharmacokinetic- pharmacodynamic (PK-PD) modelling allows a description of the dose-response relationship to identify the sources of inter-individual variability, for both PK and PD-PD relationship. The team is seeking to explain this variability by studing the sources of the interindividual variability that is observed in the response to monoclonal antibodies. Our work is based on both in vitro and preclinical models and on patient studies. Mathematical models are also used to quantify the influence of the individual sources of variability, to describe biological phenomena, and to design personalised dosage regimens for therapeutic antibodies. Over the last few years, academic groups have developed tools to monitor the pharmacological effect of therapeutic antibodies by means of measuring trough concentrations and biomarkers of disease activity. This practice called therapeutic drug monitoring (TDM), involves the measurement in sera of the concentration of the drug, often in combination with anti-drug antibodies (ADA) detection on the one hand, and the disease activity of patients on the other hand. TDM may help clinicians to adjust the dose regimen according to individual characteristics to improve clinical outcomes and avoid adverse events related to unnecessary overexposure. This strategy is relevant considering the economic burden of inflammatory chronic disease such as rheumatoid arthritis, Crohn's disease and multiple sclerosis. However, although TDM of biopharmaceuticals seems promising, its implementation in clinical settings deserves further research to develop reliable and standardised assays, mathematical modelling (population approaches to analyse databases, mechanistic PK-PD modelling, clinical trial simulation) and clinical expertise.

The main aim of the MAGE consortium is to examine the scientific bases of the TDM of monoclonal antibodies in inflammatory diseases. This will be facilitated:

- 1.to standardize assays for drug measurement,
- 2.to perform analyses in partnership to develop models for TDM,
- 3. to design comparative effectiveness research to validate these tools.

### **PARTNERS**



Pr Mike Averkiou University of Washington - USA



Pr Nico de Jona Erasmus University - The Netherlands



Pr Chrit Moonen University Medical Center Utrecht -The Netherlands



Pr Hanneke W.M. van Laarhoven Medical Oncology Academic & Medical Centre -The Netherlands

### Scientific Publications

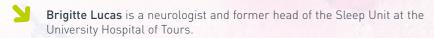
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- 4 Bloem K, Hernández-Breijo B, Martínez-Feito A, Rispens T. Immunogenicity of Therapeutic Antibodies: Monitoring Antidrug Antibodies in a Clinical Context. *Ther Drug Monit.* 2017, 39, 327-332.
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- 7 Caldano, M.; Raoul, W.; Rispens, T.; Bertolotto, A. Drug Efficacy Monitoring in Pharmacotherapy of Multiple Sclerosis With Biological Agents, Ther. Drug Monit., 2017, 39, 350-355.
- 8 Hermans, C.; Herranz, P.; Segaert, S.; Gils, A. Current Practice of Therapeutic Drug Monitoring of Biopharmaceuticals in Psoriasis Patients, Ther. Drug Monit., 2017, 39, 356-359
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- 11 Murias, S.; Magallares, L.; Albizuri, F.; Pascual-Salcedo, D.; Dreesen, E.; Mulleman, D. Current Practices for Therapeutic Drug Monitoring of Biopharmaceuticals in Pediatrics, Ther. Drug Monit., 2017, 39, 370-378.
- 12 Dreesen, E.; Bossuyt, P.; Mulleman, D.; Gils, A.; Pascual-Salcedo, D. Practical recommendations for the use of therapeutic drug monitoring of biopharmaceuticals in inflammatory diseases, Clin. Pharmacol., 2017, 9, 101-111.

## SLEEP PATHOLOGIES, RESEARCH & THERAPIES

For the past 10 years, the Rotary International's Clubs launch an annual campaign «Espoir en Tête», an initiative that raises funds to support the Brain Research Foundation (FRC) research activities. Funds have been targeted to fund many equipments used in research for Alzheimer's disease, Parkinson's disease, multiple sclerosis, autism, cerebrovascular accidents. LE STUDIUM is pleased to collaborate with the International Rotary Loiret Clubs to support their fundraising efforts and offer the general public instructive scientific conferences. This year, the Rencontre Leonardo offered two fascinating presentations focusing on sleep disorders and mechanisms.

### **SPEAKERS**

Karim Benchenane, researcher at CNRS / ESPCI in Paris is one of the 2016 Espoir en Tête winners for his project Using Sleep in the Treatment of Posttraumatic Stress.



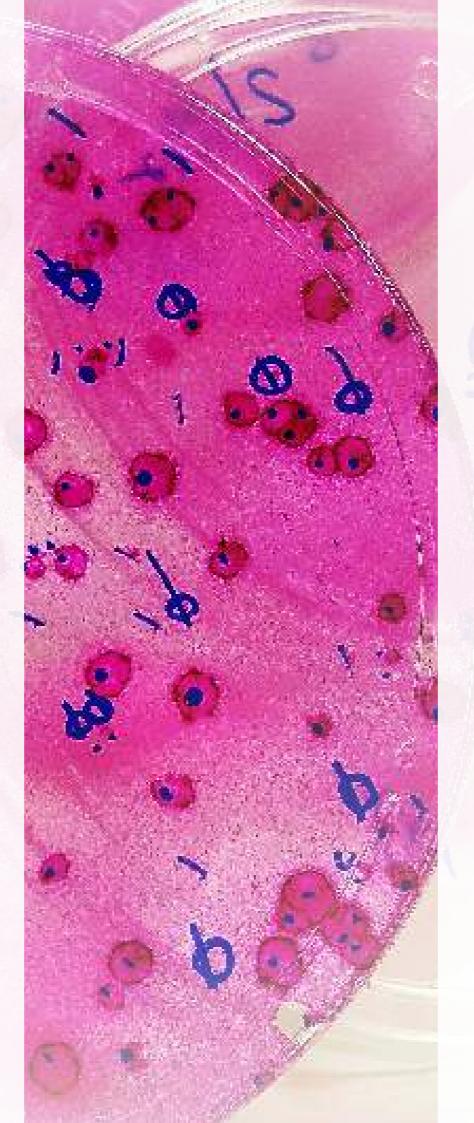
### SLEEP OVER TIME & CREATION OF ARTIFICIAL MEMORIES DURING SLEEP: A TOOL TO UNDERSTAND THE MEMORY

Sleep occupies one-third of our life is a key factor to recover on the physical and psychological levels, to consolidate the defenses but also necessary to have a good memory. Sleep disorders (insomnia hypersomnia, parasomnia...) affect the quality of life. Recent discoveries highight the understanding of the memory processes during the awakening phase and the memory consolidation happening during sleep phases.

### **IMMUNOSHAPE MEETING**

GLYcoDiag is a French research start-up (SME) specialised in glycosciences projects and products (www.glycodiag.com). GLYcoDiag's technology serves the determination of interaction profiles with lectins allowing to identify glycans signatures on the surface of molecules, cells or conversely, to study the interactions with carbohydrates binding proteins expressed by cells. The activities are linked to the recombinant protein development and glyco-proteomic analysis in biotechnology and pharmaceuticals, and apply as well to other fields like cosmetics, veterinary, diagnostics and environment. GLYcoDiag was in charge of the organisation of the 4th Immunoshape meeting in Orleans. Immunoshape is intended to provide with multidisciplinary and multisectorial training in biomedical glycoscience and its industrial applications to a new generation of young scientists.

LE STUDIUM supported the organisation of this 4th session of the Immunoshape Marie Curie European International Training Network dedicated to Entrepreneuship and Intellectual property in pharmaceutical and diagnostic product development.



# ELISE European, Life Science Ecosystems

ELISE is an European Interreg programme that focuses on improving public policies supporting innovation in the healthcare application of Life Sciences, covering largely three core sectors: biotechnology, medical devices, and pharmaceuticals. Life Sciences are defined as all sciences that have to do with organisms, such as plants, animals and human beings. It reunites 8 members:

Kaunas University of Technology - Lithuania

ASTER Innovatione Attiva - Italy

Cassovia Life Sciences - Slovakia

Kosice Self-governing region - Slovakia

BioCon Valley Association - Germany

Lubelskie Voivodeship - Poland

Région Centre-Val de Loire - France

Life Science Nord - Germany

Life Sciences for healthcare are characterised by a diversity of products types, outcomes and lifecycles. The global Life Science sector is in the midst of significant and rapid change which presents both opportunities and challenges. Progress in the health sector is driven by supply and demand pressures, lifestyle choices, longevity and a rise in chronic conditions (e.g. diabetes, obesity, dementia). Innovative technology and materials for healthcare is a growing and exciting market, including Key Enabling Technologies (KET): biotechnology (e.g. prosthesis and artificial limbs), but also nanotechnology (e.g. for medical devices) and ICT.

As an active member of the regional ARD 2020 Biopharmaceuticals Programme in charge of the international partnership dynamics, LE STUDIUM is invited by the Region Centre-Val de Loire to participate in all meetings organised in the ELISE Programme. LE STUDIUM brought his support to welcome all project's partners in Tours on 22nd-23rd November 2017: formal presentations meetings at the University of Tours, visits of laboratories at Inra Centre-Val de Loire and at the Bio3 Institute of Tours, cultural visits of Vouvray vineyard, the new modern contemporary 0. Debré art centre and the International Gastronomy Centre in Tours were programmed.





# EARTH ECOLOGY & ENVIRONMENT SCIENCES

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# **HOST LABORATORIES IN EARTH ECOLOGY & ENVIRONMENT SCIENCES**

### **UNITES ISOTOPES - BRGM**

The BRGM is a public institution, created in 1959, acting as French Geological Survey since 1968. In addition to contributing to the advancement of fundamental knowledge in the field of earth sciences and resources management, its research activities aim to provide support for public policies and decision making, and also to contribute the development of innovative technologies in public-private partnership. With a staff of 1050, BRGM combines the experience and skills of specialists in the following fields: earth modelling, management of water and mineral resources, natural hazards, industrial environment and processing procedures, energy (geothermics - underground storage), environmental metrology and environmental economics.



### **BIOLOGIE INTÉGRÉE POUR LA VALORISATION DE LA DIVERSITÉ** DES ARBRES ET DE LA FORÊT (BioForA) - UMR 0588 - CENTRE **INRA VAL DE LOIRE. ONF**

The UMR 0588 BioForA (ex-AGPF) is an INRA Research Unit belonging to INRA Val de Loire and located near the Orléans University campus. BioForA depends on the INRA EFPA department BioForA (Ecologie des Forêts, des Prairies et des milieux Aquatiques), which coordinates environmental studies carried out on forests, grassland and fresh waters. BioForA brings together specific skills in breeding, genetics, genomics, physiology and wood sciences applied to forest trees. BioForA develops integrative biological approaches to produce knowledge on the genetic determinism of complex traits involved in tree development (phenology, growth, wood properties) and on the mechanisms of tree adaptation to environmental constraints, such as resistances to pathogens, climate, including, through collaborations, resistance to drought. In BioForA, the breeding programs developed on different forest tree species (poplar, Douglas-fir, larch, ash, Scots pine and wild cherry) rely on innovative strategies for the selection and dissemination of genetic gains. In addition, BioForA scientists assess and manage forest tree genetic diversity to define the most effective strategies for combining short-term adaptation towards environmental and economic challenges and preserving long-term conservation of the genetic resources. Therefore, the research leads to a variety of scientific productions ranging from scientific papers to new forest varieties.





### CITÉS, TERITOIRES, ENVIRONNEMENT, ET SOCIETÉS (CITERES) - UMR 7324 -UNIVERSITÉ DE TOURS, CNRS

citeres was created in 2004 with a focus on cities and territories, today more than 100 permanent researchers, ca. 80 PhD students and 20 other

staff contribute to four study groups. Its objective is analysis of the spatial and territorial dynamics and of social groups.

CITERES' four principal fields are urban research, environmental research, and studies of territories and of contemporary social dynamics, including archeology. The research includes exploring the transformation of natural environments and human impact on the organisation of space, and the scientific baselines for sustainable management and policies for urban and landscape development. The city, in terms of material and cultural circulation in the urban space, is also a domain of research, with a special focus on the Arab world and the European part of the Mediterranean. The work group on environmental dynamics (DATE) to which the coordinators of the Consortium belong, works i.a. on the restoration and management of





### INSTITUT DE COMBUSTION AEROTHERMIQUE REACTIVITE ET ENVIRONNEMENT (ICARE) -

**UPR 3021 - CNRS** 



ICARE was founded on January 1st, 2007. It is an intramural laboratory, fully funded and managed by CNRS it depends on the Institute for Engineering and Systems Sciences (INSIS).

It is the result of the merger of two laboratories : the "Laboratorie d'Aérothermique" and the "Laboratoire de Combustion et Systèmes Réactifs".

Today, ICARE is a major player in the field of reactive systems, with leading experimental facilities, at national and even global level.

The main areas of research concern the chemical transformation of energy, the environment, propulsion and space. The laboratory develops four main research themes:

- Chemical kinetics of combustion and reactive systems
- Dynamics of combustion and reactive systems
- Atmospheric reactivity
- Space propulsion and high speed flows





### INTERFACES, CONFINEMENT, MATÉRIAUX **ET NANOSTRUCTURES (ICMN) - UMR 7374** - UNIVERSITÉ D'ORLÉANS, CNRS



The Research Center on Divided Materials (CRMD) was originally created  $M_N$  as a CNRS unit in 1991. The institute is today a research unit shared by CNRS and University of Orléans including 30 permanent researchers and around 25 PhD students and postdocs. On 1st January 2015, CMRD changed

its name to become Interfaces, Containment, Materials and Nanostructures (ICMN). The ICMN laboratory is involved in research and training activities at the heart of a physicochemical multiscale approach, which addresses the intermediate material scale between nanometer and millimeter scales. The tools such as experimental methods and laboratory characterisation, which include synchrotron methods and mathematical modelling, are widely used. They are applied to studies of a range of fundamental issues and their potential applications including energy storage and conversion, photovoltaic devices, water pollution control and environmental protection, sustainability of heritage, catalysis, aerospace, cosmetics, health, nanofluidic networks and nanomagnetic devices.





### UNITE DE RECHERCHE ZOOLOGIE FORESTIERE (URZF) - UR0633 - CENTRE INRA VAL DE LOIRE

Until the late 1990's, the laboratory was mainly focused on the understanding of population dynamics of forest insect pests, with regard to their impact on woody plants. Since then, the mission of the

laboratory has largely extended to the the topic of biological invasions: (1) analysis of the mechanisms responsible for the success of forest insect pest invasions; (2) study of the genetics, physiology and behavior of insect populations expanding with global warming or newly introduced in Europe; (3) estimation of the ecological and economical risks of invasive species and design management programs.

The URZF is recognized as a leading centre in ecology and genetics of forest insect pests. It has been involved in a number of major European and international research projects on biological invasions funded by the European Community.





From: V.N. Sukachev Institute of Forest, Russia

In residence at: URZF. Orléans

Nationality: Russian

Dates: August 2017 - August 2018

Dr Natalia KIRICHENKO is a forest entomologist from the V.N. Sukachev Institute of Forestry, Russian Academy of Sciences and the Siberian Federal University, Krasnoyarsk. Her interest area covers ecology, molecular genetics, systematics, and risk assessment of invasive forest and ornamental insect pests. In the last years, she has carried out research in Asian and European botanical gardens in order to detect potentially harmful herbivorous pests and to study colonization of native and exotic plants by folivore insects. She has taken part in several EU research projects and postdoctoral programs in Germany, Belgium, Switzerland and France. She is a deputy of working party «Population dynamics of forest insects» at the International Union of Forest Research Organisation (IUFRO). She combines her research work with teaching and student supervision. She has coauthored 42 peer-reviewed papers, one book and four book chapters, and presented about 100 communications at international conferences.

### AROUND THE PROJECT

### Scientific Publications

- 1 Kirichenko, N. I.; Triberti, P.; Ohshima, I.; Haran, J.; Byun, B-K.; Li, H.; Augustin, S.; Roques, A.; Lopez-Vaamonde, C. From east to west across the Palearctic: Phylogeography of the invasive lime leaf miner Phyllonorycter issikii (Lepidoptera: Gracillariidae) and discovery of a putative new cryptic species in East Asia, PLoS ONE, 2017, 12,
- 2 Kirichenko, N. I.; Petko, V. M.; Magnoux, E.; Lopez-Vaamonde, C. Diversity and distribution of leaf mining insects on Birches (Betula spp.) in Siberia, Entomological Review, 2017, 97, 183–198.

### INTERESTING LESSONS WE CAN LEARN **USING PAST HERBARIUM COLLECTIONS FOR** STUDYING FOREST INSECT PEST INVASIONS

The aim of the project is to study the expansion history and the past distribution of invasive forest insect pests using historical herbarium collections. We are particularly focused on an invasive gracillariid - the lime leafminer Phyllonorycter issikii (Kumata) (Lepidoptera: Gracillariidae). During the last three decades, this East Asian species has spread to most of Europe and became a pest of limes Tilia spp. (Malvales: Malvaceae), especially in urban plantations.

Past herbaria provides not only important source of data for botanical studies but can also be useful for invasive ecology research allowing to define past ranges of forest insect pests and track their following expansions. Larvae and pupae of endophagous insects, such as leafminers, found in mines in herbarized leaves could be efficiently used for genetic analysis, providing unique data from the past time.

We intend to examine one to two century old herbarium of Tilia stored in the largest European herbarium collections. Besides assessment of lime infestation in various regions in the Palaerctic, we plan to sample archival insect specimens found in mines on the attacked leaves for genetic characterization of the pest expansion.

So far, we have investigated the herbarium of Tilia deposited in the two biggest herbarium collections in the Palearctic: in the Botanical Institute of the Russian Academy of Sciences (Saint Petersburg, Russia) and in the National Museum of Natural History (Paris, France) for the presence of typical mines on lime leaves in East Asia (the putative region of the insect origin of P. issikii) and in Europe (the putative region of invasion of P. issikii). Our findings support the hypothesis about recent occurrence of Tilia-feeding Phyllonorycter on the west and its long-term occurrence on the east, and provide new curious data on the pest distribution in the primarily range.

In the following month, herbarium collections stored in other European museums (in Moscow, Berlin, Vienna, and Geneva) will be investigated to obtain a robust dataset that, together will our early data, will allow us to clarify the origin and genetics of invasion of this leafmining insect pest.

### **Dr Alain Roques**

### Laboratory Host Scientist



Dr Alain ROQUES is a former Research Director at the French National Institute for Agricultural Research (INRA); he leaded the Unité de Recherche Zoologie Forestière at Orléans in the period 2004-2017. He has an extensive experience in biology, ecology and behavior of forest insects. During the last 10 years, he has been largely focused on biological invasions and the impact of global warming on the populations of terrestrial invertebrates. He has participated in a number of EU-funded projects dealing with biological invasions. He coordinated the inventory of alien terrestrial invertebrates in Europe realized in the DAISIE project. He was the main editor of the book 'Alien terrestrial arthropods of Europe', published in 2010, which provided the first comprehensive review of the fauna of alien terrestrial arthropods having colonized the European continent. He published more than 170 peer-reviewed papers, about 30 books and book chapters, and presented several dozens of communications at international conferences.



### Pr AKKIHEBBAL RAVISHANKARA

LE STUDIUM Research Professor

From: Colorado State University, USA

In residence at: ICARE, Orléans

Nationality: American

Dates: June 2017 - July 2017

Ravishankara currently is a Professor in the Departments of Chemistry and Atmospheric Science at Colorado State University and a co-chair of the WMO/UNEP Science Assessment Panel on Stratospheric Ozone and a member of the Science Advisory Panel of the Climate Clean Air Coalition of UNEP. Before that he was the Director of the National Oceanic and Atmospheric Administration's Chemical Sciences Division of Earth System Research Laboratory where he served for nearly 30 years in Boulder, CO. He has served or continues to serve on many national and international committees.

Pr Ravishankara has worked over the past three and a half decades on the chemistry of the Earth's atmosphere as it relates to stratospheric ozone depletion, climate change, and regional air quality. His measurements in the laboratory and in the atmosphere have contributed to deciphering the

atmosphere have contributed to deciphering the ozone layer depletion, including the ozone hole; to quantifying the role of chemically active species on climate; and to advancing understanding of the formation, removal, and properties of pollutants. He is an author or coauthor of nearly 350 peer-reviewed publications.



# INTERLINKAGES IN THE CHEMISTRIES OF THE TROPOSPHERE AND STRATOSPHERE: IMPACTS OF NITROUS OXIDE ON EARTH SYSTEM

The mission of the project lays out the key needs to better understand the role of nitrous oxide in the Earth's environment and information needed to make any policy. Simply put, the major need is to quantify the emissions of nitrous oxides from various source, both natural and anthropogenic. To this end, as noted in the Mission section, accurate knowledge of the atmospheric lifetimes and rates of  $\rm N_2O$  loss in the various parts of the atmosphere are needed. The goal of this proposed work is to provide that information through a combination of laboratory studies, chemical calculations, field measurements, and atmospheric modeling.

The laboratory studies of the reaction of OH with  $N_2O$  has been completed. In addition, we have also looked at the potential removal of electronically excited OH (A2S) by  $N_2O$  to explore the reactivity of this molecule. Theoretical studies have been carried out in collaboration with a scientist from Lille in order to provide an explanation for the non-reactity of  $N_2O$  with the OH radical. It was realized that we should also explore the potential reaction of  $N_2O$  with the ubiquitous  $NO_2$  radical.

This work was carried out using a unique experimental system that was assembled in ICARE that utilized the cavity ring-down spectroscopy to detect  $\rm NO_3$  radicals at very low concentrations (part per trillion). Based on the results from these two studies, we have been able to rule out tropospheric chemical loss of  $\rm N_2O$ . This work greatly improves our understanding of the atmospheric lifetime of  $\rm N_2O$ . A paper describing this work is being prepared and it is expected to be submitted for publication in the next 4 months.

### Pr ABDELWAHID MELLOUKI

### Laboratory Host Scientist

Pr Abdelwahid Mellouki's undergraduate and graduate studies were conducted in the Universities of Tours, Orleans and Paris 7 (France). He spent two years as a Research Associate at the National Oceanic and Atmospheric Administration's Aeronomy Laboratory (Boulder-Colorado). His main research fields are Chemical Kinetics, Atmospheric Chemistry, Air Pollution and Climate change.

Pr Mellouki joined the CNRS in 1992, where he is currently a Research Director at the Institut de Combustion, Aerothermique, Reactivite, et Environnement (ICARE) in Orleans (France). He is leading the Atmospheric Reactivity Group. He has been nominated National Distinguished Professor at Shandong University (China) and Guest Professor at the Chinese Academy of Science (CAS/RCEES-Beijing) and Fudan University (Shanghai). His research over the years has focused on many aspects of atmospheric chemistry, including the studies of the atmospheric oxidation mechanisms of anthropogenic and biogenic carbon-containing species and halogen chemistry. He has conducted a large number of experimental studies on the atmospheric fate of chlorofluorocarbons (CFCs) substitutes, namely hydrofluorocarbons (HCFCs) and hydrofluocarbons (HFCs) as well as on CH, and N<sub>2</sub>O which are considered to be important greenhouse gases (GHGs). Within the last ten years, Pr Mellouki has been very active in field measurements studies in different regions of the world. He is author or co-author of over 200 scientific publications/chapters related to atmospheric chemistry.



# Dr MARIUS SEBASTIAN SECULA

LE STUDIUM Research Fellov

**From**: Gheorghe Asachi Technical University of Iasi, Romania

In residence at: ICMN. Orléans

Nationality: Romanian

Dates: October 2017 - October 2018

Research interests of Marius Sebastian Secula have been mainly focused in the field of advanced technologies for water and wastewater treatment, and in particular towards electrocoagulation, electrochemical oxidation, photocatalysis, Fenton processes and coupling processes such as UV/TiO<sub>2</sub>/Fe(II)/H<sub>2</sub>O<sub>2</sub> or Electrocoagulation/GAC.

He defended his doctoral thesis in October 2007 at Gheorghe Asachi Technical University of Iasi, where has been offered a full-time position as a scientific researcher.

He managed his own financed research projects (2010-2012 and 2015-2017) financed through national Romanian competitions.

Marius Sebastian Secula authored 43 papers published in ISI indexed journals; 32 papers presented at international conferences and 2 patents.

He has co-directed 3 Postdoctoral fellows and 6 PhD Students at Faculty of Chemical Engineering and Environmental Protection, Gheorghe Asachi Technical University of Iasi.



# DEVELOPING A NEW ADVANCED TREATMENT TECHNIQUE FOR MICROPOLLUTANTS REMOVAL FROM WATER AND WASTEWATER

The presence of emerging micropollutants in surface water, groundwater and sediments is currently of major concern, which will lead to the establishment of more stringent standards for the quality of surface water, municipal and industrial wastewater, especially in the member states of the European Union.

Emerging organic micropollutants are known to be poorly removed by the conventional biological treatment methods. With regard to the possibilities of removing trace organics from waste and drinking water, the performance of various technologies, mostly conventional (adsorption, membrane and oxidation processes), have already been investigated. Recently conducted studies showed that processes such as ozonation and adsorption on powdered activated carbon are promising treatment techniques for real wastewaters containing emerging micropollutants.

For several years, the laboratory Interfaces, Confinement, Matériaux et Nanostructures (ICMN-CNRS, Orléans) has been active in the development of advanced oxidative processes, in particular the Ozone/Granular Activated Carbon combined system for the elimination of phthalates and pharmaceutical compounds. It is necessary now to develop a new advanced oxidative process by coupling several processes for the mineralization of refractory emergent organic micropllutants.

One of the goals of the present research project consists in establishing the synergistic effects of the combination of several advanced oxidation processes. It is of interest to carry out the implementation of the process and to determine the optimal conditions where the global process cumulates more synergistic effects resulting in a powerful treatment system for micropollutants.

Another goal is to establish the kinetics degradation mechanisms by coupling experimental analyses (by HPLC coupled with an electrochemical cell) and theoretical approach by modeling using chemical simulation. The degradation mechanisms of several model micropollutants will be investigated to establish optimal synergistic effects in collaboration with two academic labs. It is expected that the suggested technique to be more efficient and cost-effective towards the removal of micropollutants than most of the available techniques. The economic optimisation of this system might prove it to be a feasibly technique for practical applications or a first step towards further approaches such as the development of more efficient catalysts (aerogels, xerogels), and enhancements by means of photoelectrochemical devices.

Up to date, the experimental set-ups and methods have been established, and the required analytical apparatuses have been purchased. The experimental designs and the general approach of the studies were also established.

### Dr BENOÎT CAGNON

### Laboratory Host Scientist



Benoît Cagnon obtained his PhD in 2002 at the University of Perpignan on the elaboration of activated carbons with controlled texture. He joined the IUT Orléans as Associated Professor in 2004, and ICMN laboratory (CNRS) in 2012. His research activities focus on the development of water treatment technologies, and in particular on the elaboration of activated carbon materials from biomass applied in adsorption processes. He is also working on the development of new advanced oxidation processes (i.e. ozone/activated carbon coupling). His research results have been valorized in 33 publications.



### Pr VLADIMIR SHISHOV

LE STUDIUM / Marie Skłodowska-Curie

From: Siberian Federal University, Russia

In residence at: BioForA, Orléans

Nationality: Russian

Dates: August 2017 - August 2018

Vladimir Shishov is currently employed as Professor at the Siberian Federal University, Krasnoyarsk, Russia, where he is Head of the Mathematical Methods and Information Technology Department. As a scientist with a mathematical background and 24 years experience in dendrochronology and dendroclimatology, he is focused on data mining and decoding information preserved in tree rings. and on applying the data to study small and large scale systems using modern mathematical approaches (e.g. nonparametrical statistics, classification methods, singular spectrum analysis, GIS technologies and mathematical modeling). He has a particular interest in process-based tree-ring modeling and the multi-dimensional parameterization of such models. V.

Shishov published more than 30 papers in peerreviewed ISI journals. He made 36 presentations to general public and experts in natural resources in the universities and research institutes of UK, USA, Australia, Spain, France, China, Finland and Russia



### **GLOBAL TREE-RING GROWTH EVOLUTION NEURAL NETWORK (VS-GENN)**

The research led in partnership with Dr Philippe Rozenberg focuses on retrospective assessment and a short-term forecast of annual treering productivity (seasonal cell production) of the major conifer plant species in terrestrial forest ecosystems around the world forced by climate and non-climatic factors.

The analysis is based on an Interactive Information platform "Global Tree-Ring Growth Evolution Neural Network" and available datasets developed for the European, Asian and South American dendrochronological test-polygons.

The Global Tree-Ring Growth Evolution Neural Network is a parameterisation procedure of the VS-model which combines three novel parallel process:

- Direct parameterisation based on optimisation evolutional IT-
- Proxy parameterisation based on a VS-metamodel (artificial neural network which operates as direct VS-model but can produce cell profiles much faster)
- Re-training of VS-metamodel to reduce a discrepancy between simulation tree-ring growth curves obtained by the direct and proxy

One of the principal project targets is to test a Global Tree-Ring Growth Evolution Neural Network (VS-GENN) as an information platform to simulate tree-ring growth of conifer species in automatic mode for the well-documented test-polygons in the Europe, Siberia and Latin America.

Instead of VS-GENN, the project uses other on-line tree-growth simulations and GIS applications developed by the authors of the project and other research teams from France and US.

Results should allow to estimate the long-term annual tree-ring productivity (cell production) of woody plants impacted by the principal climatic and non-climatic factors, and to predict tree-ring productivity in the short-term context for the research regions. VS-simulations based on direct long-term field observations for the well-documented tree-ring test-polygons in Europe, particularly in France, Asia and South America will be used as well as state-of-art techniques, including unique approaches developed by the authors.

The project has no analogues in Europe. All stated tasks are novel and are key for understanding undergoing global processes in the forest ecosystems and under observed climatic changes and disturbances. Results will impact palaeo-climate researchers, scientists studying and testing models and processes of sub-components of the climate system and a variety of climate change impacts researchers.

### AROUND THE PROJECT

Shishov, V. VS-modeling and neural networks in dendroecology, Interdisciplinary research seminar at INRA, Orléans (France), November 10, 2017.



**Dr PHILIPPE ROZENBERG** Laboratory Host Scientist See page 72.



### Pr KARL MATTHIAS WANTZEN

CONSORTIUM COORDINATOR

LE STUDIUM

SMART LOIRE VALLEY

After studies on the Rhine (German Federal Institute of Aquatic Sciences), Karl M. Wantzen worked as fellow of the Max-Planck-Society to perform his PhD on stream ecology, and to coordinate a BMBF-funded project on the Ecology of the largest wetland of the World. 2007 habilitation on biodiversity, functioning and structural dynamics of river-floodplain-corridors. > 100 publications. Since 2010 he is professor (1st class) at the University of Tours, where he lectures river ecology and management, sustainable development and tropical ecology at different faculties, and researches in the DATE team (Landscape and urban ecology, and management) of CITERES. 2014 he was awarded the UNESCO Chair on River Culture (Fleuve et Patrimoine), and in 2015, "Talent de la Région Centre" acknowledging his scientific and conceptual achievements. KMW shares the coordination of the project with Pr Stéphane Rodrigues, sediment geologist at CITERES.

### **ECOHYDRAULICS AND DAM REMOVAL**

The decline of the ecological integrity in rivers is a global problem, menacing water security for human beings and biodiversity at the same time. While there are great achievements concerning technologies for water quality improvement, the re-establishment of physical structures suitable for ecosystem functions remains a scientific problem. Which kind of river management and engineering can re-establish these conditions? Specifically, the issue of dam removal is currently in the focus of debate to improve the ecological continuity for sediment transport and migratory organisms. In France alone, about 60,000 obsolete weirs and dams have been identified. However, the scientific baseline for this activity is still weak. Under the auspices of the UNESCO Chair "River Culture - Fleuve et Patrimoine" directed by the PI, the consortium gathers scientists from Europe (France, Spain, Italy), Latin and North America (Argentina, USA) to review the state of the art and to develop new scientific approaches for evidence-based policies for the future (facing a current massive trend of dam construction worldwide). Researchers and engineers from the University of Tours have been studying the quantitative geophysical (sediment transport and morphology) and biological (abundances of benthic invertebrates and fish) effects of dam removal at the Maisons Rouges Dam (Vienne River) since 1998 on an annual basis. The Spanish-Italian team has monitored a large number (>20) dam removals in the past ten years and that of the USA is well-known for their work on geomorphology, endangered fish habitats and algae biomass in the Upper Colorado River. The Argentinian team has recently provided excellent studies on invertebrate-flow relationships. Gathering this expertise from different disciplines and the comparison of a one-site-long-term study with a many-sites-short term study will create an excellent setting to improve our knowledge about physical habitat management in rivers. The results of a series of workshops will be published and policy options will be debated in public.

### **PARTNERS**



Pr Mercedes Marchese Consejo de Investigaciones Científicas y Técnicas

CONICET - Argentina



Dr Martin Blettler Consejo de Investigaciones Científicas y Técnicas CONICET - Argentina



Pr John Pitlick University of Colorado, Boulder - USA



Dr Askoa Ibisate González de Matauco University of the Basque Country UPV/EHU -Spain



Dr Simone Bizzi Institute for Environment and Sustainability - Water Resource Unit - Italy





### Dr MAURO SIMONATO

LE STUDIUM / Marie Skłodowska-Curie

From: University of Padova, Italy

In residence at: URZF. Orléans

Nationality: Italian

### Dates: November 2016 - November 2017

Mauro Simonato obtained his PhD in Crop science - Plant protection at the University of Padova. He is currently working on the different applications of genetic markers for the identification of different species of insects and for the characterisation of the structure of their populations. In particular, He is interested in the present and past biotic and abiotic factors that have led to the distribution of some of the main forestry and agronomic pest. He is also interested in the molecular identification of bacterial symbionts associated with insects and in the reconstruction of the origin of this association.



### TRACKING THE COLONISATION PATTERNS OF AN EXPANDING FOREST PEST AND ITS NATURAL **ENEMIES USING MOLECULAR MARKERS**

The main aim of this project is to identify expansion patterns of one of the major pest of pine forests originated from Mediterranean countries, the pine processionary moth. During the last decades this species has naturally expanded both to higher latitudes and altitudes due to the recent climate change. In France, the northward expansion occurred in a few decades reaching up to date the north east part of the country. Both host tree distribution and accidental human transportation also seem to play a key role in the spread of the moth.

Samples from several populations of pine processionary moth (PPM) in the front expansion edge as well as from potential source populations in the native range will be genotyped using 22 microsatellite loci. The population genetic structure of these samples will be assessed in order to identify the main dispersal patterns of this species and the environmental factors such as host plant distribution determining the colonisation routes.

The PPM dispersal patterns will be then compared with those of its main egg parasitoid, using, for this species, a first set of microsatellite loci to determine whether it can follow its host during the expansion.

Finally, an assignment tool will be developed in order to genetically characterise both PPM and parasitoid individuals in new front populations and thus quickly identify the source of these new pioneer colonies through a comparison with the reference populations.





### SPECIES SPREAD IN A WARMER AND GLOBALIZED WORL D

The objectives of the conference were to discuss the different aspects of biological invasions driven by the ongoing climate change and the increase of international trade. In particular the main topics of the conference were focused on evaluating of the role of climate change in the range expansion of several invasive species, and the consequences of the ornamental plant trade in the establishment and spread of native and alien species.

The presentations and the discussions in the conference highlighted these aspects, underlining the factors that are enhancing the dispersal and the range expansion of several pests and the role of the landscape anthropisation in the establishment and adaptation to new environments of invasive species. Methods for assessing and tracking species invasion and expansion were also discussed, with a special focus on new statistical tecniques to disentangle different expansion patterns reconstructed using genetic data.

### INSECTES EXOTIQUES RAVAGEURS: COMMENT PROTÉGER NOS FORÊTS?

The volume of intercontinental trade has risen sharply in recent decades. Many goods are transported around the globe, often in very short times. Live plants, imported into Europe in large numbers from all over the world, are important vectors for woody plant pests and forests. The diversity of imported plants is immense, as is the potential associated pests.

Exotic pests have done, and are doing, significant damage in different countries, which can endanger biodiversity and sometimes the local economy. For example, the box-tree moth, recently arrived from East Asia with ornamental boxwood, threatens native boxwood and boxwood planted in gardens; or Xylella fastidiosa, a bacterium that arrived a few years ago, probably with coffee trees from Costa Rica, threatens olive trees in Italy, Spain and Corsica and can attack several other European species. It is therefore essential to aim to reduce the risks of importing other important pests in order to avoid further damage.

There is a great diversity of potential pest species that have not yet reached Europe. This is why phytosanitary services identify potential pests and the most risky routes of introduction and put in place measures to reduce the risk of pest introduction in Europe. Most of these organisms are not known and we do not know their potential damage. New methods of detecting and identifying pests before they arrive could help protect our forests.

### Dr JÉRÔME ROUSSELET



Dr Jérôme Rousselet (URZF), PhD, is a population biologist and geneticist interested in the responses of forest insects to global changes since the 2000s. He obtained his PhD in population biology at the University of Tours in 1999. He got a permanent position in the INRA Forest Zoology Research Unit (URZF) in 2000. He has been particularly studying the recent evolutionary history, the population genetic structure and the climate-driven expansions of the pine processionary moth at various spatial and temporal scales. Currently, his work focuses on the role of ornamental trade in generating both long distance dispersal events and landscape connectivity accelerating range expansion of native or exotic pest species. He participated to several projects funded by the European Union, the French Ministries, the French National Research Agency or the Regional Council Centre Val de Loire and is author of 25 scientific articles in peer- reviewed international journals and four book chapters.

### AROUND THE PROJECT

### Oral communication

Simonato, M.; Auger-Rozenberg, M.-A.; Pilati, M.; Sauné, L.; Magnoux, E.; Courtin, C.; Kerdelhué, C.; Rousselet, J. Patterns of expansion of pine processionary moth and its specialist egg parasitoid at the northern edge of its distributional range, IUFRO 125th Anniversary Congress, Freiburg (Germany), September 18-22, 2017.

### Poster

Simonato, M.; Sauné, L.; Courtin, C.; Kerdelhué, C.; Rousselet, J. Genetic patterns in the range expansion of pine processiobary moth in Northern France, Joint Meeting of IUFRO's, Forest Insects and Pathogens in a Changing Enivronment: Ecology, Monitoring & Genetics, Thessaloniki (Greece), September 11-15, 2017.







### **Dr WOLFRAM KLOPPMANN**

CONSORTIUM COORDINATOR

LE STUDIUM

SMART LOIRE VALLEY

Dr Wolfram Kloppmann (HDR), task officer at the Laboratory Division of BRGM, head of the Isotope Unit from 2011 to 2017, works in a broad field of environmental issues. His specialties include chemistry and isotope characteristics of deep natural fluids including energy-relevant gases, groundwater, non-conventional water resources, water-rock interactions in aquifers, isotope fingerprinting of water contaminants, but also the identification of the provenance of cultural materials and the degradation of building stones. Most of his research work involved the use of environmental isotopes. He coordinated the BRGM research programme on non-conventional water resources and alternative concepts of water management (2006-2011). He has a long record of project management and participated in numerous EU projects under the 6th and 7th Framework Programme and coordinated the FP5 project BOREMED. He is the French coordinator of the ongoing ANR-NSERC Franco-Canadian G-Baseline project on impact assessment in the field of unconventional hydrocarbons. He is author/co-author of over 180 publications including 68 peer-reviewed papers.

### MULTI-ISOTOPE AND CHEMICAL TRACING FOR UNDERSTANDING THE SOURCES AND FATE OF MACRONUTRIENTS AT THE BASIN SCALE (MUTUAL)

Nitrogen and phosphorous flows induce water quality degradations which are a major obstacle for reaching the "good qualitative status" of European surface and groundwater bodies aimed by the European Water Framework Directive (WFD). A diverse array of macronutrient sources and a complex network of transport pathways and reactive transformations are evident for both groundwater and surface water receptors. This diversity of sources and pathways is a key challenge for the management of natural resources. Understanding macronutrient sources and fate across large scales requires a multimethod and multi tracer approach. This consortium gathers experience on nutrient cycling in a variety of hydroclimatic, hydrogeological and land use settings and a large variety of complementary tools in the field of environmental geochemistry. This will allow merging advanced tracer techniques into a diagnostic toolbox for characterising macronutrient (N and P) sources and fate in aquatic ecosystems for improved process understanding and catchment management. This work will allow a better understanding of nitrogen and phosphorous contamination of water resources, of their speciation and transformations and of residence and transfer times in the different subsoil compartments.

The project aims on a critical analysis of the current approaches of source- and fate identification in contaminated watersheds. The project partners produce a shared data base on chemical and isotopic fingerprints of N and P sources in a diversity of catchments worldwide as basis of a common publication and common presentations at dedicated conference sessions. An international workshop organised in Orléans (Centre Region, France) will bring together international experts in the field of nutrient cycling and -tracing with a variety of regional and national stakeholders.

The first meeting from Jan. 16-20, 2017 was dedicated to a critial evaluation of the potential of multi-tracer approaches to identify and quantify nutrient (N, P) sources and transfer times in groundwater. Main focus was the discussion of the concept, assets and limitations of "tracers" or "co-tracers" of nutrient pollution.

The second meeting from Dec. 4-8, 2017 was dedicated to the work on a common conceptual paper on catchments affected by N and P excess: Structure breakdown, contents to be included, the light of the current literature and the ongoing studies of all project partners.

### **PARTNERS**



### Dr Daren Gooddy

British Geological Survey, United Kingdom, biogeochemical cycling, hydrogeology and isotope hydrology: fate and transport of macronutrients using anthropogenic tracers of groundwater age and nutrient isotope techniques.



### Pr Bernhard Mayer

Calgary University, Canada, isotope geochemistry of nitrate, sulphate, boron and phosphate-oxygen: combination of hydrological, chemical, isotopic and modelling approaches to follow the fate of selected nutrient sources.



Dr Dan Lapworth British Geological Survey, United Kingdom



Barcelona University, Spain, isotope hydrology with a special focus on natural and induced attenuation of groundwater pollution: isotopic geochemistry in particular on analytical techniques.

Pr Neus Otero



### Dr Ben Surridge

Lancaster University, United Kingdom, biogeochemistry of phosphorus, nitrogen and carbon cycling in soil and freshwater ecosystems: phosphorus, nitrogen and carbon cycling across the soilwater continuum within catchments, development and application of new isotopic tracers for phosphorus biogeochemical research.



2 Carrey, R.; Margalef-Marti, R.; Merchán, D.; Otero, N.; Soler, A.; Causapé, J. Use of stable isotopes (15N and 180) to evaluate nitrate

reduction processes in a surface flow artificial wetland, IsoCycles 2017, AsconaS (witzerland), October 15-20, 2017

3 Ooddy, D. Understanding Sources And Processing Of Nitrate In Contrasting UK Rivers Using Established And Novel Techniques, Second Research Coordination Meeting (RCM) of the CRP on "Isotopes to study nitrogen pollution and eutrophication of rivers and lakes, Vienna (Austria), November 27 - December 1, 2017.



#### **Dr PHILIPPE ROZENBERG**

**CONSORTIUM COORDINATOR** 

LE STUDIUM

**SMART LOIRE VALLEY** 

Philippe Rozenberg is a Research Director at INRA Val de Loire, Orléans. Originally a Forest Engineer from the former "Ecole Nationale des Ingénieurs des Travaux des Eaux et Forêts", he got a Master in ecology from the Paris VI University, a PhD degree on Forest Sciences from AgroParisTech (Paris) and an Habilitation degree from the University of Orléans. He is a research director at INRA Val de Loire, Orléans, the leader of the "genetic and Physiology of Adaptation" team of the research unit BIOFORA (formerly AGPF) and a member of the INRA national scientific council. He develops a research program on "adaptation of forest trees to climate" in natural as well as in artificial forest tree populations. In this context, he investigates the evolutionary adaptation and the phenotypic plasticity of forest trees using original approaches based on tree- ring analysis and wood formation studies. He coordinated more than ten national and international research projects, directed eight PhD thesis and published more than sixty research articles in international scientific journals.

#### DYNAMICS OF WOOD FORMATION AND ADAPTATION OF FOREST TREES TO **CLIMATE VARIATION**

The first objective of DYNAWOOD is to develop a pilot study to test, compare and validate the use of dendrometer data for the assessment of the phenotypic plasticity of cambial response to climate and to use this information to study adaptation of forest trees to climate. The second objective of the project is to use already available data of the same nature and of different origins to study and test the possibility to realise large-scale analysis of cambial response to climate. During the first meeting in January 2016, the concept of the low-cost dendrometers was presented to the partners and discussed. The partners selected two models of automatic point dendrometers and were taught how to install and run them. Seven copies (two species × three trees + one control) of each model of dendrometer were distributed to each partner. During the same meeting, the partners and the collaborators presented their previous experience with other dendrometer types and their achievements and interest in the general research line developed by the consortium. Data management and analysis process were also presented and discussed, as well as connections with other research groups and activities. Main outcomes: A common protocol for the installation of the dendrometers at each location. A plan for establishing a common database.

During the first experimentation period (2016), the dendrometers were installed at the six project locations (one in each country except two in Argentina) and the permanent data recording started. During the second meeting (October 2016), the partners reported and exchanged about their practical dendrometer experience. The problems observed during the first experimentation period were discussed and most of them were solved. The radial growth curves recorded with the dendrometers were inspected in detail and discussed. Complete radial growth curves were available for three countries, Canada, Switzerland and France. In the two other countries, the growth curves were incomplete, in one case for technical reasons and in the other case because the growing season was just starting at the time of the meeting. The results showed that in the three locations with complete growth curves there was a great similarity between the curves recorded by the two types of dendrometers. The experimental design for the second year of the project was reviewed and validated. Several decisions were implemented, in order to enlarge the study to other experiments and datasets: increment core collection in a larch altitudinal gradient in the Alps, methods for establishing norms of reaction for wood formation, data-sharing politics... Finally, the decision was taken to organise a joint international conference for the Dynawood project and for the Vladimir Shishov fellowship together at Orléans in 2018.

#### **PARTNERS**



**Dr Patrick Fonti** 

Swiss Federal Research Institute WSL. Switzerland



Pr Annie Deslauriers

Université du Québec à Chicoutimi. Canada



Dr Luc Pâques INRA, France



Dr Alejandro Martinez-Meier INTA, Argentina



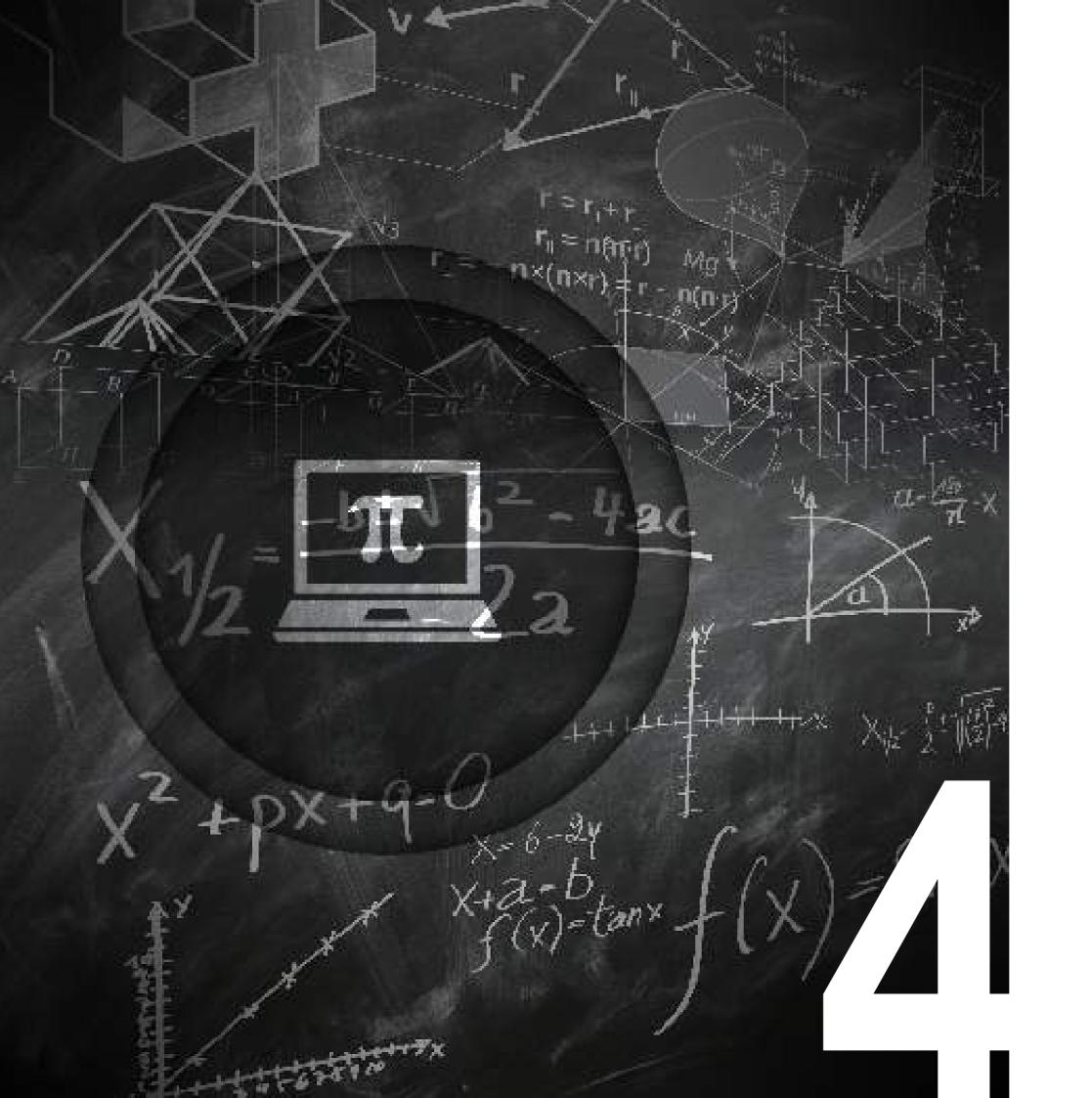
#### Pr Saúl Espinosa Zaragoza

Universidad Autónoma de Chiapas Mexico

Thanks to the diverse geographic origins of the consortium partners, the original approach proposed in the project relates to several forest tree species growing under an exceptionally large range of climates: from boreal to tropical and oceanic to semi-continental climates. Furthermore, three of the partners already had complementary practical experience of the use of permanent dendrometers and were able to teach the others the necessary technical skills. Finally, all the partners have diverse instructive views of the potential of wood formation for the study of the adaptation of forest trees to climate.

#### AROUND THE PROJECT

- 1 Rozenberg, P.; Chauvin, T. Certains l'aiment chaud ? Les arbres forestiers face au réchauffement climatique. Le cas d'une espècemodèle, le douglas, conférence grand-public, Conférence Centre Sciences, Tours (France), November 14, 2017
- 2 Rozenberg, P. Mejoramiento de la adaptación de los arboles al clima. Estrategia basada en el estudio de la madera, Seminario Posgrado Ciencias Forestales, Texcoco (México), December 13, 2017.
- 3 Pâques, L. Modern high-throughput Wood phenotyping tools, Seminario Posgrado Ciencias Forestales, Texcoco (México), December



COMPUTER
SCIENCE,
MATHEMATICS &
MATHEMATICAL
PHYSICS

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# **HOST LABORATORIES IN** COMPUTER SCIENCE, **MATHEMATICS** & MATHEMATICAL PHYSICS

# CENTRE DE BIOPHYSIQUE MOLÉCULAIRE (CBM) - UPR 4301 - CNRS



CBM is a key participant in the development of biophysics in France, and is one of the largest research laboratories in the region Centre-Val de Loire. It was founded in 1967 to set up interdisciplinary collaboration between chemists, biologists and physicists. Researchers at the CBM are investigating the structure, dynamics and interactions of biomacromolecules from the atomic level to the cell

and organism. This approach entails searching for the molecular causes of biological dysfunctions which trigger the development of diseases. The center is also recognized for its research in biomedical imaging. The laboratory has excellent facilities for small animal imaging. One key goal of CBM is to conceive new strategies in human therapy by combining innovative approaches in peptide/protein synthesis, biochemistry, bio-physics, molecular and computational biology. For this purpose, biomolecular interactions involving DNA, RNA, proteins and ligand are studied at the atomic and molecular level using a variety of experimental techniques. Moreover, some research projects are dedicated to the identification of new therapeutic targets and the development of innovative delivery systems for therapeutic and imaging agents in various pathologies such as cancer, cystic fibrosis and musculoskeletal defects. Biological targets are identified through the delineation of specific signaling pathways. Novel therapeutic strategies are developed using original nucleic acid delivery systems that combine chemical vectors and physical methods. One main area is the optimization of innovative vaccination based on messenger RNA coding for tumoral or viral antigens for cancer and viral infection, respectively.



# LABORATOIRE DE MATHÉMATIQUES ET PHYSIQUE THÉORIQUE (LMPT) - UMR 7350 - UNIVERSITÉ DE TOURS, CNRS



The LMPT is a joint research unit with about fifty permanent researchers that supervises about twenty PhD students. It is structured in two teams: a team of mathematics and a team of theoretical physics. The research is organized around seven axes: Algebra, Nonlinear analysis and EDP, Riemannian geometry, Probability and

Ergodic Theory, Gravitation, Field theory, Integrable systems, classical and quantum dynamics of complex systems. At the present moment in the field theory part of the laboratory led by Dr Maxim Chernodub there are 6 permanent academic staff. There are also 6 permanent academic staff who work on various aspects of gravity. Both these directions of research are related to the content of the given project. Besides, there are 14 permanent academic staff who work in the area of integrable systems and Riemannian geometry. This area also has a certain relation to the content of the project since the corresponding mathematical structures were used actively in the work on the project.





# LABORATOIRE D'INFORMATIQUE FONDAMENTALE D'ORLÉANS (LIFO) -

# EA 4022 – UNIVERSITÉ D'ORLÉANS. **INSA CENTRE VAL DE LOIRE**



The Laboratoire d'Informatique Fondamentale d'Orléans (LIFO) is a laboratory of the University of Orléans and the INSA Centre-Val de Loire, officially recognised and supported by the French Ministry of Research. The laboratory

is located in Orléans and in Bourges in order to develop its collaborations and to offer a window to the research in computer science in region Centre-Val de Loire. LIFO created a research federation, Fédération Informatique Centre-Val de Loire, together with the Laboratoire d'Informatique from the University François-Rabelais of Tours. LIFO is a computer sciences research laboratory. Research projects conducted at LIFO include algorithmics, scientific visualization, machine learning, massive parallelism, model checking and system security. To provide another approach to the laboratory and to foster inter-team cooperation, the following cross-laboratory thematics are put forward:

- Massive data sets and high performance computation,
- Modelisation and algorithms, and
- Security and safety.





# PLURIDISCIPLINAIRE DE RECHERCHE EN INGÉNIERIE DES SYSTÈMES, MÉCANIQUE ET ÉNERGÉTIQUE (PRISME) - UPRES 4229 - UNIVERSITÉ D'ORLÉANS, INSA CENTRE VAL DE LOIRE



The name of the host scientist's laboratory is PRISME (Pluridisciplinaire de recherche en ingénierie des systèmes, mécanique et énergétique). It is a laboratory of University of Orléans and INSA Centre Val de

Loire, labeled by the Ministry of Higher Education and Research (UPRES No. 4229). PRISME laboratory was created in January 2008 and brought together 106 researchers and 70 PhD students. The PRISME was merged by following laboratories:

- Laboratoire Vision et Robotique (EA 2078)
- Laboratoire D'électronique, Signaux, Images (EA 1715)
- Laboratoire de Mécanique et Énergétique (EA 1206)
- Laboratoire Énergétique, Explosions, Structures (EA 1205)

The main mission of the PRISME laboratory is multidisciplinary in the general field of sciences for the engineer on a wide spectrum of disciplinary fields including:

- Burning in engines, energy,
- Aerodynamics, the mechanics of materials,
- Signal and image processing,
- Automatic,
- The robotics.

The laboratory has chosen to structure itself with scientific clusters organised into thematic axes.









# **Pr Gary Gibbons**

From: University of Cambridge, United Kingdom

In residence at: LMPT, Tours

Nationality: British

Dates: March 2017 - May 2017

Gary Gibbons, Fellow of the Royal Society since 1999, is one of the rare universal theoreticians.

He started his studentship, in Cambridge, under the supervision of D. Sciama and S.

Hawking, two outstanding figures of relativity. It is under the direction of the latter that he defended his PhD in 1972, on Gravitational Radiation and Gravitation Collapse.

Fruitful collaboration with S. Hawking has resulted in several top-level publications, which have practically shaped the understanding of modern Cosmology and Quantum Gravity.

Subsequently, while maintaining his close contacts with S. Hawking, he managed to broaden his scientific horizon by making a profound contribution to String Theory.

He not only knows about relativity, but also about dynamical symmetries in general and of soliton scattering in particular, group theory, topology and differential geometry applied to physics.

#### **CLASSICAL AND QUANTUM SPACE-TIME AND ITS** SYMMETRIESAND FRACTIONAL ORDER SYSTEMS

In this project we study theoretically both the classical and quantum properties of space-time and its symmetries. In particular, we formulated certain inequalities for the geometric quantities characterising causal diamonds in curved and Minkowski spacetimes. These inequalities involve the redshift factor, which, we show explicitly in the spherically symmetric case, is monotonic in the radial direction, and it takes its maximal value at the centre. We suggest some possible applications of our results including comparison theorems for entanglement entropy, causal set theory, and fundamental limits on computation.

In addition, the last decade has witnessed an increased interest in non-Minkowskian spacetimes whose structures are invariant under boosts. These may be obtained by group contraction. The standard contraction of the Poincare group yields the Galilei group, for which pure Lorentz transformations become Galilei boosts. However what is less well-known is another rather unfamiliar limit, which yields instead a different but still boost-invariant theory. Levy-Leblond, who introduced this «degenerate cousin of the Poincare group», named it, the Carroll group, referring to the pseudonym of the author of Through the Looking-Glass. We define curved Newton-Cartan and curved Carroll spacetimes modelled on their flat versions



#### Pr SERGEY SOLODUKHIN

Laboratory Host Scientist

Sergey Solodukhin studied physics at the Moscow State University where his PhD adviser was D. D. Ivanenko, the Soviet physicist who theoretically predicted synchrotron radiation.

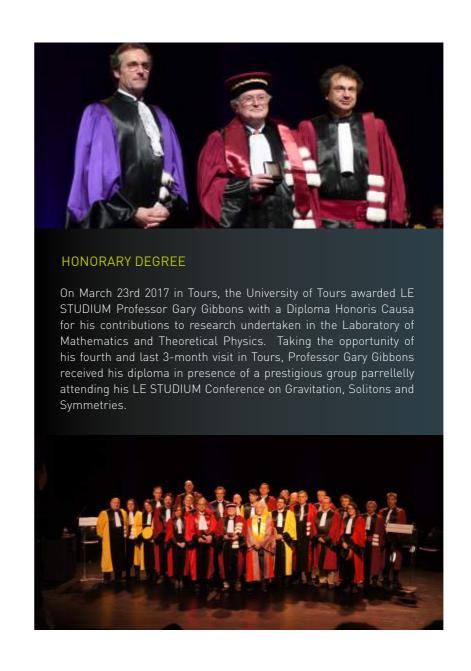
He held a postdoctoral position at the University of Waterloo as a NATO Postdoctoral Fellow and then moved to the University of Alberta in Canada. From Canada he moved to the University of Utrecht, in the Netherlands, where he worked in the group of Professor G. 't Hooft for two years during which time Professor G. 't Hooft received the Nobel prize in physics. He then moved to the Ludwig Maximilian University of Munich, Germany, where he worked in the group of Slava Mukhanov, and later to the University of Bremen, Germany. Since 2007 he has been at the University of Tours, France where he is a professor in LMPT. In recent years, his work has focused on the study of entanglement entropy and its applications to conformal field theories and the black hole physics.

#### **GARYFEST: GRAVITATION. SOLITONS AND SYMMETRIES**

This focused conference celebrates Gary Gibbons' remarkable contributions and continuing influence in diverse fields of contemporary physics including gravity, the theory of solitons and classical and quantum symmetries. The meeting will focus on current developments in these fields. The discussions are intended to be informal and to provide with the opportunity to exchange new ideas. The event is organised on the occasion of the award of the Honoris Causa Doctor of Science degree to Gary Gibbons by the University of Tours.

#### AU-DELÀ D'EINSTEIN. TROUS NOIRS ET ONDES **GRAVITATIONNELLES**

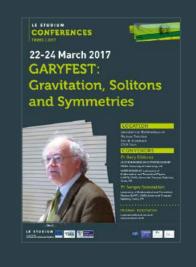
A new chapter of Physics is opening up, that of the Astronomy of Gravitational Waves. Predicted and then renounced by Einstein, we have known for forty years that they are at the origin of the slow coalescence of certain binary systems of stars. But it is only recently that gravitational waves, emitted during the fusion of two black holes, have been directly detected by dedicated terrestrial observatories. This conference retraced the main stages of this major turning point in the history of Astronomy.



#### AROUND THE PROJECT

#### **Scientific Publications**

- 1 Zero mass limit of Kerr spacetime is a Gibbons, G. W.; Volkov, M. S. Zero mass limit of Kerr spacetime is a wormhole, Phys. Rev. D96,
- 2 Gibbons, G. W.; Volkov, M. S. Weyl metrics and wormholes. Journal of Cosmology and Astroparticle Physics, 2017, 5, 039.
- 3 Chanda, S.; Gibbons, G. W.; Guha, P. Jacobi-Maupertuis-Eisenhart metric and geodesic flows, J. Math. Phys., 2017, 3, 032503.
- 4 Cvetic, M.; Gibbons, G. W.; Pope, C. N. STU Black Holes and SgrA, Journal of Cosmology and Astroparticle Physics, 2017, 8, 016.
- 5 Zhang, P.-M.; Duval, C.; Gibbons, G. W.; Horvathy, P. Soft gravitons and the memory effect for plane gravitational waves, Phys. Rev. D96, **2017**, 6, 064013.
- 6 Zhang, P.-M.; Duval, C.; Gibbons, G. W.; Horvathy, P. The Memory Effect for Plane Gravitational Waves, Phys. Lett. B772, 2017, 4,
- 7 Zhang, P.-M.; Duval, C.; Gibbons, G. W.; Horvathy, P. Carroll symmetry of plane gravitational waves, Class. Quant. Grav., 2017,
- 8 Duval, C.; Gibbons, G. W.; Horvathy, P. Conformal and projective symmetries in Newtonian cosmology, *J. Geom. Phys.*, **2017**,









#### Pr ERIC GOLES

From: Universidad Adolfo Ibáñez. Chile

In residence at: LIFO. Orléans

Nationality: Chilean

Dates: January 2017 - March 2017

Eric Goles is Doctor honoris causa from the University of Orléans, 2012. From 1981 to 2000, he was in the Engineering School of the University of Chile where he lead the first group in Chile working on discrete mathematics and computer science and formed a group dedicated to modelling and industrial applications. He was instrumental in the creation of the Centre for Mathematical Modelling, inaugurated in 2000, of which he was the first director. From 2000 to 2006, Professor Goles was president of the National Commission in Charge of Financing Scientific Research. During this period, he created the Institute for Complex Systems in Valparaiso of which he was the first director. This institute is dedicated to the study of complex systems. Since 2006 he is Full Professor and researcher at the Universidad Adolfo Ibáñez, in Chile

#### **DISCRETE MODELS OF COMPLEX SYSTEMS:** COMPUTATIONAL COMPLEXITY AND (UN) PREDICTABILITY, THEORY AND APPLICATIONS

Complex systems analyses investigate the emergence of complex global behavior through the local interactions of a large collection of well understood components. Interdisciplinary by nature, it encompasses problems encountered in the diverse disciplines of physics, economics, biology, mathematics, computer sciences, linguistics from which it borrows both models and tools.

Discrete models of complex systems provide formal models that can be used both as modeling tools convenient for computer simulation to study particular complex systems and as a simple framework to study, define and characterise fundamental properties of complex systems.

Theoretical Computer Science, through the theory of computation, provide valuable tools to design efficient algorithms or, when not possible, prove unpredictability or characterise the inherent difficulty of predictability in discrete models of complex systems like cellular automata, Boolean or regulatory genetic networks, social science models, sand piles and Ising

The purpose of this project is to contribute to the organisation and development of the emerging research community on complex systems in the Loire Valley, disseminate tools and models from theoretical computer science among that interdisciplinary community and to confront other models to widen the scope of application of these tools.

Professor Eric Goles worked with his host scientist, Professor N. Ollinger, about freezing automata with PhD students from LIFO and DISC in Chile, on a model related with the origins of synonyms.

#### Pr NICOLAS OLLINGER

Laboratory Host Scientist



Nicolas Ollinger is a theoretical computer scientist who joined LIFO in the University of Orléans in September 2011.

His field of research includes theoretical computer science to discrete mathematics, covering topics like combinatorics on words, models of computation and complexity and decision problems for cellular automata

He connects to the complex systems community through his research both on classification of cellular automata according to their dynamics (bulking) and on decision problems on abstract formal discrete dynamical models, providing formal proofs of unpredictability.

He was a PhD student in Lyon in research team MC2 when the IXXI Institute emerged, then a founding member of the team Escape (équipe systèmes complexes, automates cellulaires et pavages) in Marseille where he participated to the national ANR projects Sycamore and EMC devoted to the relation in between computational models and discrete complex systems.

From 2008 until 2015, he was the scientific secretary of International Federation for Information Processing (IFIP) working group on Cellular Automata and Discrete Complex Systems.



#### Pr YIMING CHEN

From: Yanshan University, China

In residence at: PRISME, Bourges

Nationality: Chinese

Dates: April 2017 - June 2017

Yiming Chen has been a Full Professor of the College of Science of Yanshan University since 1998. He is a member of the Chinese Society of Induction and Applicative Mathematics, Chinese Society of Computing Mechanics and Chinese Society of Mathematics and has earned First Award of Science and Technology Progress of China Ministry of Mechanical Industry and Third Award of Education of Hebei Province in 1999 and 2000, respectively. Pr Chen has published more than 140 international journal articles.

#### AROUND THE PROJECT

#### Oral communications

- 1 Chen, Y. Fractional and variable order fractional differential equation with their application, Seminar INSA CVL, Blois (France), May 12, 2017.
- 2 Chen, Y. Characterization of viscoelastic materials' mechanical properties and development of viscoelastic materials" mathematical model based on the theory of fractional calculus, Seminar INSA CVL, Blois (France), June 19, 2017.
- 3 Chen, Y. Numerical methods and their applications, Seminar INSA CVL. Blois (France). June 14-26, 2017.

- 1 Chen, Y.; Liu, D.; Wei, Y.; Boutat, D. Model-free fractional order differentiator based on fractional order Jacobi orthonormal functions, Digital Signal Processing, 2017, 71, 69-82.
- 1 Li,W.; Cheng, J.; Dos Santos, S.; Chen, Y. Generalized fractional-order Legendre function to solve variable order linear cable equation and error analysis, International Journal of Computational and Engineering, 2017, 2, 235-242.

#### OBSERVER DESIGN FOR DISTRIBUTED-PARAMETER SYSTEMS AND FRACTIONAL ORDER SYSTEMS

The proposed research project is on observer design for Distributed-Parameter Systems (DPSs) and Fractional Order Systems (FOSs).

This is an interdisciplinary research project where the conception of observer is applied to DPSs and FOSs, and the obtained results will be applied to nonlinear acoustics and viscoelastically damped structures.

New research activities are being developed, which are complementary to those of the teams involved in the project.

Estimation of the states of DPSs and FOSs is important for engineers and scientists.

However, research on observer design for these systems has not been as extensive as in the case of Lumped-Parameter Systems, especially in nonlinear case. Consequently, the achievements to date of this research project are outlined as follows with the involvements of the partners:

- 1. Development of the Nonlinear Observer Canonical Forms for nonlinear DPSs and FOSs in order to easily apply existing observer design methods (cooperation of Pr Chen, Pr Boutat and Dr Liu);
- 2. Design of new observers for nonlinear DPSs and FOSs (with unknown inputs or not), such as proportional and integral observers, adaptive observers, and interval observers (cooperation of Pr Chen, Pr Boutat and Dr Liul:
- 3. Development of efficient numerical algorithm for considered equations, and new robust differentiators using wavelets, etc. (cooperation of Pr Chen, Pr Boutat and Dr Liu);
- 4. Application of the concept of observer to solve nonlinear acoustics equations. The obtained results will also be applied to context of new ultrasonic "pulse-echo" imaging for Non Destructive Testing applications (cooperation of Pr Chen and Dr Dos Santos);
- 5. Study on various aspects of fractional models for damped structures, using observer design. In particular, the system parameters will be identified (cooperation of Pr Chen and Dr Serra).

#### **Pr DRISS BOUTAT**

#### Laboratory Host Scientist



Driss Boutat has been a Full Professor in ENSIB since 2008, which developed into the INSA Centre Val de Loire in 2014. Since 2011, he is the leader of Control Team in PRISME Laboratory. In 2014, he was the dean of MRI and ERE Departments in INSA CVL.

Until now, Pr Boutat has published more than 110 international journal and international conference articles. Moreover, he is supervisor of 10 PhD students (7 have defended). He is selected as Associate Editor of Journal of Discrete Dynamics in Nature and Society, Associate Editor of Journal of Nonlinear Dynamics, Member of Editorial Advisory Board of Mediterranean Journal of Measurement and Control.

Pr Boutat earned the National order of France: Order of Academic Palms Chevalier (Knight) since January 2010, the National Award for doctoral supervision and research from 2008 to 2012, and the French Excellent Scientist Award since 2012. In 2011, he was selected in Who's Who in the World. Recently, he received the Best Paper Award in the 7th International Conference on Bio-inspired Systems and Signal Processing. In 2017, Pr Boutat is appointed as a foreign expert of high level by the Chinese government.



#### Pr GERALD KNELLER

**CONSORTIUM COORDINATOR** 

CONSORTIUM

SMART LOIRE VALLEY

Gerald Kneller is a Professor of Physics at the University of Orléans and group leader at the CNRS Molecular Biophysics Centre. Currently he is also coordinator of the Maison Interdisciplinaire des Systèmes Complexes, which is an interdisciplinary research network financed by the Centre-Val de Loire region. Pr Kneller is a specialist in statistical physics, theoretical biophysics, and computer simulation he develops multi-scale models for the structure and dynamics of biomolecular systems. He studied physics at the RWTH Aachen in Germany and he obtained a PhD in physical chemistry at the same university (1988). After a postdoc at IBM US, Kingston NY, in the group of Enrico Clementi (1989), he held the position of a research engineer at IBM France, working in a project on biomolecular dynamics and function with the Commissariat à l'Energie Atomique (CEA) in Saclay. In 1993 he returned to Aachen in order to pursue an academic career, working on the methodology of molecular simulation, in particular on constrained dynamical systems. In 1997 he obtained the Habilitation in Physics at the RWTH Aachen and since 1998 he holds the position of a professor at the University of Orléans where he heads the Theoretical Biophysics Group of the Moleculare Biophysics Centre (CBM/CNRS).

#### ANOMALOUS DIFFUSION PROCESSES IN BIOLOGICAL AND PHYSICO-CHEMICAL SYSTEMS

Diffusion is one of the most fundamental transport processes taking place in biological and physico-chemical systems. The diffusing particles can be as small as water molecules or as big as pollen grains, whose erratic motions have been observed in the 19th century by the Scottish botanist Robert Brown. The theory of "normal" diffusion goes back to Fick and Einstein, and although most spatially unconfined diffusion processes are well described by Einstein's theory, there is an ever increasing number of observations of "anomalous" diffusion, in particular in biological systems, which are not in agreement with this theory. Corresponding generalizations are often of purely mathematical nature and lack physical interpretation. The aim of the project is to improve the understanding of the physical origins of anomalous diffusion by gathering together specialists whose expertise in diffusion phenomena is largely complementary to each other. The partners have considerable expertise in stochastic processes, statistical physics, large-scale computer simulations, and single particle tracking methods, and they have worked on anomalous diffusion considering very different length and time scales in fluids, soft matter, as well as in biological systems. Therefore, the added value expected to emerge from this network is profound. The first phase of the project serves to broaden and consolidate the knowledge of all partners and to establish a basis for fundamental physical concepts leading to anomalous diffusion (such as bulk memory effects, geometry, boundary conditions, etc.) and their relation to established models. In this context, the impact of coarse-graining in time and space will be particularly emphasized. The results of the project will be published in a booklet or in terms of a review article, and the last meeting of the Consortium will combine with a mini-colloquium on anomalous diffusion, including discussions of potential applications of the new knowledge generated in this project.

#### **PARTNERS**



**Pr Ralf Metzler**University of Potsdam,
Germany



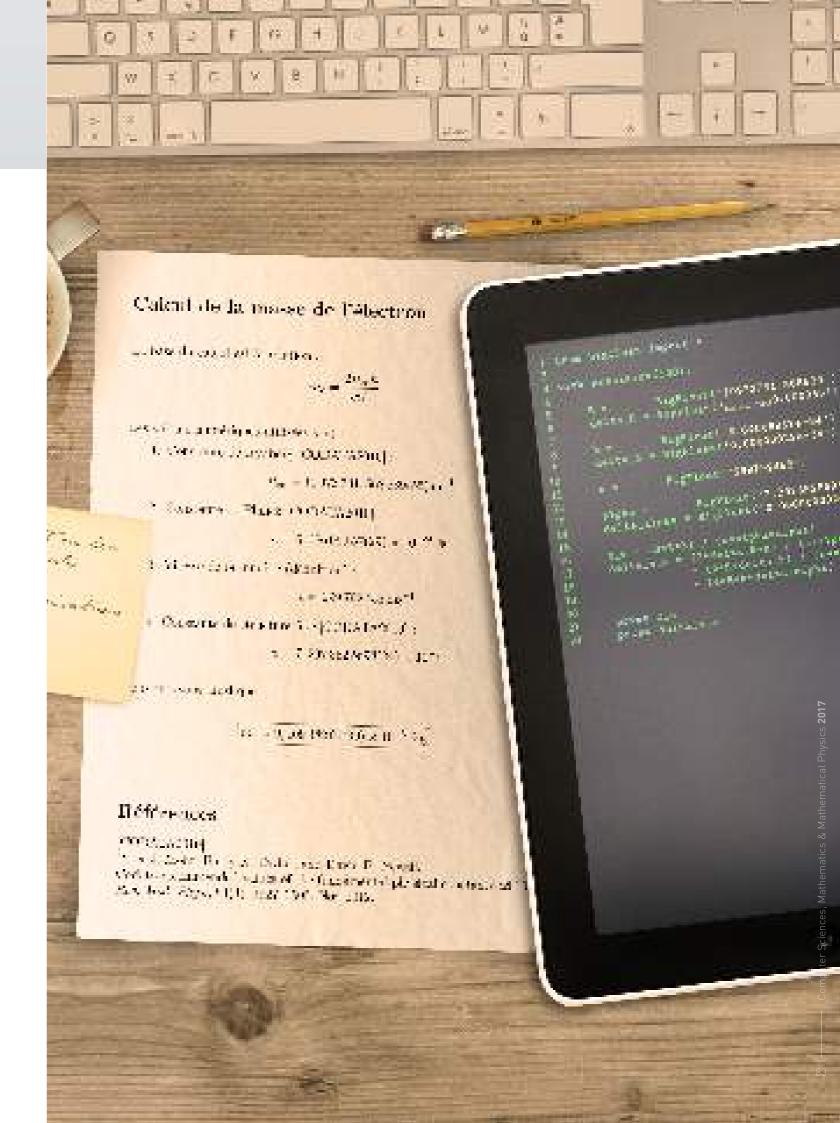
**Pr Matthias Weiss**University of Bayreuth,
Germany



**Pr Yael Roichman**Tel Aviv University,
Israel



**Pr Ilpo Vattulainen**University of Tampere,
Finland





# HUMAN AND SOCIAL SCIENCES

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# **HOST LABORATORIES IN HUMAN AND SOCIAL SCIENCES**

# CENTRE D'ÉTUDES SUPÉRIEURES DE LA RENAISSANCE (CESR) -**UMR 7323 - UNIVERSITÉ DE TOURS, CNRS**



The Center of Advanced Studies of the Renaissance (CESR) is the Education and Research Unit (UFR) of University of Tours and Mixed Research Unit affiliated with the CNRS. Set up through the initiative of Gaston Berger in 1956 and affiliated at that time with the University of Poitiers, the CESR became an integral part of the newly established University of Tours in 1970. Successive

agreements in 1983 and 1992 enhanced the institutional links between the CESR and the CNRS. In 1996 the CESR reaffirmed its commitment to interdisciplinary research into key themes of European patrimony (for instance, around musicology, art history and the history of the book), in an accord with the French Ministry of Culture, the CNRS and University of Tours. The CESR celebrated its half-centennial in 2006. The CESR is an education and research centre, which welcomes students and researchers wishing to acquire an initial or additional university education in all domains of the Renaissance. The CESR's research programmes are structured according to disciplinary teams (history, history of art, French, neo-Latin and European literature, philosophy, musicology, history of science and techniques), research fields and team projects.





# INTERACTIONS, TRANSFERTS, RUPTURES ARTISTIQUES ET **CULTURELLES (InTRu) - EA 6401 - UNIVERSITE DE TOURS**



The InTRu research unit was created in 2008 by the art historians Eric de Chassey, Jean-Baptiste Minnaert, France Nerlich and Pascal Rousseau (Université de Tours). The aim was to create a formal structure for the work they had started to carry out together

with several colleagues based in other universities, and different institutions, such as museums, art schools and the Services de l'Inventaire (Inventory of Architectural Heritage), around the methodological issues and historical investigation of modes of circulation, cultural transfer and legitimisation strategies in the creative industries (visual arts, architecture, literature, etc.) and cultural practices using images.

The team decided to structure their collaboration around the following research themes: modes of cultural transfer (reception, influence, intertextualities), transmediation between the arts (visual arts, music, dance, architecture, literature) and hierarchies (image/ text, mass-culture/ high culture, banal/ unique, etc.). The idea was to advance the study of cultural circulation, by looking beyond simple shifts from one medium to another, to consider the recycling, translation or transformation of images, and to look at practices and knowledge acquisition. With an emphasis on interdisciplinary approaches, the team decided the different themes should not be closed entities, but rather they should form the building blocks for thinking together about epistemological questions.



# INSTITUT DE RECHERCHE SUR LES ARCHEOMATERIAUX (IRAMAT) **CENTRE ERNEST-BABELON -UMR 5060 - CNRS, UNIVERSITÉ D'ORLÉANS**



IRAMAT-Centre Ernest Babelon (Research Institute on Archaeomaterials) was founded in 1980 and belongs both to the CNRS and the University of Orléans. During its first years, the IRAMAT-CEB was specialised in the development and application of non-destructive techniques using nuclear methods for

the characterisation of ancient coins. Then, the applications and analytical methods both diversified. Beside coins, other metallic objects, glass, obsidian, pigments and colorants were analysed by the means of laser ablation ICP-MS, X-Ray fluorescence, Scanning electron microscopy with an EDX... The originality of the laboratory is to gather historians, archaeologists and numismatists as well as chemists and physicians in the same team. Its mission is to develop new methodologies for the characterisation of ancient materials, and apply them to answer historical questions.





# LABORATOIRE D'ECONOMIE D'ORLEANS (LEO) -UMR 7322 - UNIVERSITÉ D'ORLÉANS, CNRS



LÉO is a research center supported by the CNRS and the University of Orléans (France). It was created on 1 January 1996 following the merger of the Orleanais Institute of Finance (created in 1974) and the Center for Research on Employment and Production (created in 1984). Initially located in Orléans, LÉO

is the only research center in Economics in the region Centre-Val de Loire. Since January 2013, it has been designed to welcome, in addition to Orleans colleagues, the researchers in Economics of the University of Tours.

LÉO has about 42 permanent researchers (full professors and associate professors) and 37 PhD students. LÉO is specialised in three research areas: (1) Macroeconomics and Finance, (2) International Economics and Sustainable Development and (3) Econometrics.





# **HOST LABORATORIES IN HUMAN AND SOCIAL SCIENCES**

# LABORATOIRE VAL DE LOIRE RECHERCHE EN MANAGEMENT (VALLOREM) - EA 6296 - UNIVERSITÉ D'ORLÉANS. UNIVERSITÉ DE TOURS



The public service mission of VALLOREM is to support and promote research in the field of Management VALLOREM Science at the University of Tours and the University of Orléans. To participate in the progress of scientific and technical knowledge in this field and develop Regional recognition of such research. VALLOREM is also the

education structure that provides the platform for junior postdoctoral training and the support to research academics and university professors with Masters and PhD students in Management Science. In addition, VALLOREM is a host structure that welcomes French and foreign researchers and doctoral students, through the creation or participation in worldwide networks of inter-university exchanges. VALLOREM puts at the heart of its scientific studies the issue of relations between management and society by studying ways to improve the overall performance of organisations. The systematic research of the overall performance of organisations provides a prism of management practices and including innovative management. This research mainly involves small to medium enterprises, their market and non-market services, as determined by laboratory research interests. With research grant funding and research agreements with various public and private partners the research activities continue to develop. The VALLOREM team has the mission to link university research and practices to public or private organisations. VALLOREM develops its partnership relations with the socioeconomic actors of its territory and also favors research intervention to achieve desired socioeconomic outcomes.





# POUVOIR, LETTRES, NORMES (POLEN) -**EA 4710 - UNIVERSITÉ D'ORLÉANS**



Emerging from the collaboration of literary historians belonging to the META research laboratory and the "Littératures et civilisations" and "Savoirs et pouvoirs de l'Antiquite à nos jours" research centres, the PoLeN (Pouvoirs, Lettres, Normes) research laboratory is a pluridisciplinary group of researchers from the fields of history, literature, linguistics, anthropology and law. It comprises three main research centres - on late

medieval culture, early modern culture, and modern and contemporary culture - each of which is dedicated to investigation of the ways in which texts from a range of historical periods engage with questions of power and authority, particularly as regards their role in the dissemination of the discourses that prescribe societal norms in any given period and in the potential resistance to these norms.





#### **Dr RENAUD ADAM**

LE STUDIUM / Marie Skłodowska-Curie

From: University of Liège - Belgium

In residence at: CESR, Tours

Nationality: Belgian

Dates: October 2017 - September 2018

Dr R. Adam is a book historian, specialised in early modern period. He is also teaching history of the book in the Renaissance at University of Liege.

He previously worked for Fund National of Research (Belgium) under the supervision of Pr A. Delfosse at University of Liège, in the Royal Library of Belgium and in the University Library Moretus Plantin in Namur (Belgium).

He has collaborated with collective and interdisciplinary research projects devoted to the study of the urban history of the historical Low Countries, the spread of Italian culture in Frenchspeaking Europa and the role of print revolution in the diffusion of medieval French texts.

He was invited to give lectures in different countries of Europe as well as in America, and he published seven books, written alone or in collaboration, and more than forty articles in scientific journals and

His publications deal with the early history of printed books, the profession of printer at that time and the history of libraries and book consumption from the Late Middle Ages to 20th century.

His last book, devoted to the spread of printing press in Low Countries, is forthcoming.

#### AROUND THE PROJECT

Renaud, A. La circulation du livre médical dans les anciens Pays-Bas au second tiers du XVIe siècle, Histoire des sciences médicales, **2017**, *51*, 47-59.

#### BIBLIOPOL@: THE BOOK MARKET IN THE RENAISSANCE BETWEEN FRANCE AND THE LOW **COUNTRIES**

This project aims to renew our knowledge of cultural exchanges between France and the Low Countries during this crucial period of transitions between Middle and Modern Ages. This phenomenon will be explored through the still widely under-exploited prism of early modern books circulation between these two countries.

This project starts from the fact that if we are now in position – thanks to valuable works - to evaluate with any degree of confidence the number of books published in France and in the Low Countries in the Renaissance, where and when, we are still not yet able to say which books – with the same degree of confidence – were really bought from a country to another and read there; leading de facto to an incomplete and partial assessment of the cultural substratum of these two countries. To narrow the field of research, which could otherwise result unmanageable, the best solution is to focus on the transnational book trade. This is surely one of the most efficient ways to understand how and which books were in movement, how they travelled across borders and, by extension, the nature of cultural exchanges between France and the Low Countries in early modern period.

The book trade is made of two principal components: men and books. This is why the attention is focused on the circulation of books and the men behind it. The project "Bibliopol@" will rely on a dual and complementary corpus: inventories of bookshops and archives materials involved in this business. It will cover the second half of the 16th century, a period of intense economic activities between the two countries interrupted by the difficult context of the War of Religions in

The specific scientific objectives of the project are: 1) study of the circulation of books between France and the Low Countries; 2) reconstruction of networks and legal framework for the distribution and sale of books between Low Countries and France; 3) renewal of our knowledge of cultural exchanges between France and the Low

The project «Bibliopol@» started on the 1st of October 2017. Until now, our work concentrates on the circulation of books between France and the Low Countries. We focus our attention on the unedited archives written by inquisitors in the wake of the visits carried out, at the request of the Governor of the Low Countries in 1569, within the bookshops of the city of Mons in the County of Hainaut.

#### Pr CHIARA LASTRAIOLI

#### Laboratory Host Scientist



Chiara Lastraioli is the director of the Maison des Sciences de l'Homme Val de Loire. Professor of Italian Studies at the CESR and at the Faculty of Languages and Literatures of the University of Tours, her teaching and research explore the relation of Italian and French Renaissance Literatures to theology, propaganda, book trade and the history of scholarship. She is in charge of the "Bibliothèques Virtuelles Humanistes" program (CESR) and she has published numerous essays on Renaissance authors and printers. Recently she has published a monographic volume on Pasquinate, grillate, pelate e altro Cinquecento librario minore. She's also the coordinator of the EDITEF project on Italian Books and Book Collections in Early Modern French Speaking Countries, financed by the "Agence Nationale pour la Recherche", and the project ECRISA (L'Ecriture, ses supports, ses archives) financed by Region Centre-Val de Loire.



# **Dr MASSIMILIANO** TRAVERSINO DI CRISTO

From: University of London - United Kingdom

In residence at: CESR, Tours

Nationality: Italian

Dates: October 2017 - September 2018

Dr Massimiliano Traversino Di Cristo obtained his Ph.D. In Law, Theology, and Humanities from the Universities of London (Birkbeck College). Geneva, and Trento, respectively. Founder and codirector, along with Dr Anton Schütz, of the Centre for Research in Political Theology at the Birkbeck College School of Law of University of London, Dr Traversino Di Cristo studied and worked in different countries during his past studies academic experience.

His main research interests lie in the fields of Legal History, Moral Philosophy, and Church History, with special attention to the relationship between the history of late-mediaeval and earlymodern legal institutions and the contemporary history of philosophical and theological thoughts. Recipient of a series of awards and grants from different European institutions and scientific coordinator of a series of international colloquia on 'potentia Dei' and of two cultural events named 'Festival Bruniano' and 'Festival della Teologia del Triveneto', Dr Traversino Di Cristo also edited or co-edited the four volumes of transactions from these colloquia and events and published a number of essays in the above fields of studies.

#### WILL. POWER. AND BEING: UNCOVERING THE ANCIENT AND MEDIAEVAL BLUE-PRINTS OF THE SIXTEENTH-CENTURY QUESTION OF POWER

Throughout the twentieth century an impressive amount of scholarship has been devoted to the origin of the concepts of the prince and sovereignty. By focusing here on the ancient and mediaeval sources of sixteenthcentury authors, the project presents an exhaustive narrative of their contribution to these ideas nor to exalt their career in the Western history of power but rather to determine the degree to which the modern fate of the notion of power depended on the bearing of early-modern writers on ancient and mediaeval scholarship. The employments and embodiments of ancient and mediaeval authors' ideas and their bearing on the modern investigation of power are carefully reviewed. Attention is being paid both to classical antiquity (Roman law and philosophical traditions such as Aristotelianism, Platonism, and Stoicism) and to Scholasticism (School of Chartres, Franciscan dogmatic, Thomism, etc.). Through such a distinction and by covering a period of time that spans from eleventh to sixteenthcentury authors, its an attempt to demonstrate the relevance of mediaeval theologians and their debate on classical sources to the subsequent evolution of Western discourse on power.

This analysis is an opportunity to trace some of the most central and innovative trends of modern debates on Native Americans and, more generally, on the question of power, back to the last decades of the sixteenth

Special attention was paid to two Italian exiles religionis causa, Giordano Bruno and Alberico Gentili, for the reason that these authors help take a closer look at the doctrinal trends on Native Americans that are contemporary with both Renaissance and Reformation.

When formulating their ideas, both Bruno and Gentili had recourse to the earlier work of other sixteenth-century authors like Francisco de Vitoria and Bartolomé de Las Casas and were moved to comment on the European political events and the expansionism that they witnessed in their own time.

Through Bruno's and Gentili's eyes, the project aims to show the interrelation between the debate on Native Americans and a variety of sources of modern history of ideas, which include early-modern philosophy, cosmology, theology, and public and international law.

#### **Dr PAUL-ALEXIS MELLET**

#### Laboratory Host Scientist



After concluding his studies in Philosophy (Paris IV/Paris-Sorbonne), he aroused his interests in History by obtaining an 'agrégation' certificate (Pari I/Panthéon-Sorbonne) and by writing a thesis (Université de Tours/ CESR) on Protestant Monarchomachs—jurists, diplomats, and theologians who theorized armed resistance against tyrants (issued by Droz in 2007). Dr Mellet has published a number of ancient texts, notably Le réveillematin des Français et de leurs voisins (1574), issued by Garnier in 2015, and Conseil à la France désolée (1562), issued by Droz in 2017. His present interests are central to the concern of religious warfare in Renaissance Europe and he devoted his recent HDR thesis (Paris IV/Paris-Sorbonne) to a research on the remonstrances that were printed during such epoch. His position consists in showing that during the conflicts of this time, all the parties involved (Catholics, Protestants, Royalists) undertook permanent efforts to restore peace and establish justice.



#### Pr GRAEME BOONE

LE STUDIUM / Marie Skłodowska-Curie

From: The Ohio State University - USA

In residence at: CESR, Tours

Nationality: American

Dates: July 2017 - July 2018

Graeme Boone received the Premier Prix in Histoire de la Musique from the Conservatoire National Supérieur de Musique in Paris in 1979, and a PhD in Music from Harvard University in 1987. He is Professor of Music at the Ohio State University, and also serves as director of the interdisciplinary Center for Medieval and Renaissance Studies there, producing or managing a course curriculum, lecture series, annual colloquia, conferences, and many other activities pertinent to some twenty departments and over 100 faculty. He has served on the Board of Directors of the American Musicological Society and has chaired several of its committees; he was recently nominated for the positions of both Vice-President and President. He is currently on the Executive Committee of CARA, the regional centers association of the Medieval Academy of America, and serves on the editorial boards of several musicological journals. Boone has received numerous research grants from Ohio State, and his monograph Patterns in Play (1999) was selected as the inaugural volume of the Studies series published by the American Musicological Society. In 2015, he was appointed Invited Scholar at the Center for the History of Emotion in Australia, where he gave lectures, seminars, and keynote addresses at several Australian universities and conferences.

#### AROUND THE PROJECT

- 1 Boone, G. Emotions and Music in Early Fifteenth-Century France, Le Studium Thursdays, Tours (France), November 2 2017
- 2 Boone, G. Exquisite Harmonies: Fifteenth-Century Counterpoint and Architectural Design, Sound and the Sacred Conference, Center for Medieval and Renaissance Studies, Los Angeles (USA), November 17,
- 3 Boone, G. The Rise of White Notation as a Scriptive Turn, Musikwissenschaftliches Seminar, Würzburg (Germany), November 24, 2017.

#### **EMOTION IN DUFAY**

The goals of the project are to construct, in scholarly terms, the fundamental ways in which the study of emotion can inform research on the music of Guillaume Dufay. Dufay has been called the first great Renaissance composer as well as the greatest composer of early and middle 15th century; and emotional expressivity has been essential to the reception of his music. But it has never been modeled in any thorough-going scholarly way. Such modeling will provide new and transformative approaches to Dufay's music, for specialists, musicians. and also the broader public. The project involves systematic analysis of Dufay's compositions in different genres, and the construction of a background of diverse affective social spheres surrounding Dufay, as evoked or described in fifteenth-century writings of different kinds, and in light of recent multi-disciplinary research on emotions. It sifts the evidence pertinent to constructing an emotional profile for Dufay as a once-living subject; it models the ways in which sensorial experience in general, and audition and the musical arts in particular, were understood to function psychologically and physiologically in Dufay's time, in their own right and in relation to emotion (including passion, affect, motus animi, and ethos). It analyzes the literary texts of Dufav's early compositions in their textual and social contexts; the musical horizons, techniques, and strategies reflected in Dufay's compositions; and draws conclusions regarding the emotional environment and content of his music, with implications for the future of such study.

The achievements of the project to date center on the wide-ranging study of source materials, together with their modern commentaries and theorisations, pertinent to the environment and career of Guillaume Dufay. These include literary theory, history, analysis, and poetic repertories of the earlier 15th century; sociological studies of 15th-century lifestyles, communities, artistic organisations, economic and bureaucratic structures; historical documents and interpretations, including those relative to the Black Death, the Hundred Years' War, the reign of Charles VI, the Council of Constance, and the duchy of Burgundy; philosophical writings current in the era and their modern evaluations, regarding the topics of soul, subjectivity, affectus, and mental faculties; studies on literacy, reading and writing, and their relationship to oral culture; and writings that set music into its philosophical, theological, social, and emotive perspective during this era. I have also had numerous conversations at the CESR with scholars in different fields working in related areas.

#### Pr PHILIPPE VENDRIX

#### Laboratory Host Scientist



Philippe Vendrix is the former Director of the Centre d'Etudes Supérieures de la Renaissance (2008-2015). He obtained his PhD in 1991 in musicology with the highest distinction from the examination jury at the University of Liège. He has been a member of Council of the American Musicological Society, 2001-2004. Elected in 2010 to the Alumni College of the Belgian Royal Academy. He has editorial management responsibilities of various collections including Ricercar. He is on the editorial board of leading publications in musicology and a member of the Scientific Council of Répertoire International de Littérature Musicale, New York and the European Science Foundation. He is currently the president of the University of Tours.

# Dr MARIA CLOTILDE **CAMBONI**

From: University of Fribourg - Switzerland

In residence at: CESR, Tours

Nationality: Italian

Dates: September 2016 - September 2017

Dr Camboni obtained her PhD in Italian studies from the University of Pisa. Her research focuses on the problem of the tradition of vernacular medieval literature and of medieval culture in general, with strong interdisciplinary aspects, and she has a special expertise about poetic form. Her academic career spans over three different countries: Italy, Switzerland and France. She was the recipient of the "Marco Praloran" Fellowship 2013-2015 (Ezio Franceschini Foundation, Florence, Italy - University of Lausanne, Switzerland). Her second monograph, the main result of her "Marco Praloran" Fellowship, reconstructing how the conception of poetic form evolved, in Italy, during the XIII and XIV century, has been published in 2017.

#### MIDDLE AGES IN RENAISSANCE

The project "Middle Ages in Renaissance" aims at investigating how Middle Ages Italian vernacular tradition was considered during the Renaissance. One of the main historical turning points between the two periods is the affirmation of the idea that art must consist in an imitation of the Classics, but with the rise of vernacular literature, since the second half of the XV century, and definitely since the beginning of the XVI, a new pool of models must be defined. They obviously could not be real "Classics" and had to be "medieval": however they were nevertheless chosen as models, and derogating from already established lexical uses, in few significant cases also referred to as "Ancients". Moreover, sometimes these texts were not circulating anymore: therefore they had to be recovered from "ancient" sources, just as the literature of ancient Greece and Rome had to be, finally being perceived in a parallel situation as the classics.

The project's aim is to set in context the process that lead to the final choice of vernacular authors, studying how medieval vernacular authors were considered, what was their appraisal, in some distinct Renaissance environments, focusing on vernacular poetry but taking into account nonlyric and also non-poetic works by which the medieval culture has been mediated to the Renaissance. The planned outcome of the research is a reconstruction of Renaissance attitudes towards a relevant part of Middle Ages literary tradition, and therefore towards their models, both possible and of choice.

The research work focused on the role played by the Raccolta Aragonese, a collection of early and contemporary Tuscan poems, assembled by Lorenzo de' Medici in 1476-7 to be sent to Federico of Aragon, the younger son of the King of Naples, regarding the access to the poems transmitted by it.



#### THE DYNAMICS OF THE RELATIONSHIP WITH THE MORE RECENT PAST IN EARLY-MODERN EUROPE: BETWEEN REJECTION AND ACKNOWLEDGEMENT

The "LE STUDIUM Conference" aimed at exploring the early-modern perceived reality of the continuities and the disruptions between the Middle Ages and the Renaissance, in connection with but nevertheless besides their objective actuality, from a highly interdisciplinary standpoint. The presence of researchers from different fields allowed for a lively exchange during the conference, which was one of its objectives. The fact that the speakers received feedback on their communications (e.g. of literary subject) from others who offered the viewpoint of their particular discipline (e.g. history of the book, paleography...) gave the opportunity to open new perspectives on the presented researches. Another desired and successfully achieved outcome of the conference was the establishment of new scientific relationships between the speakers and their institutions: a scientific cooperation has been put in place between Pr Degni and Dr Camboni concerning one of Dr Camboni's research strands; a scientific exchange is occurring between Dr Banella and Dr Camboni, as well as an ongoing discussion with Pr Gilson concerning the possibility of further developing Dr Camboni's research project at Oxford university (where Pr Gilson has since taken a position).

#### QUAND A-T-ON CESSÉ DE MANGER «COMME AU MOYEN ÂGE»?

In connection with the "LE STUDIUM Conference" a public "LE STUDIUM Lecture" took place: "Quand a-t-on cessé de manger «comme au Moyen Âge» ?". It was given by Bruno Laurioux, former Deputy Scientific Director for the ancient and medieval worlds and then Director of the CNRS Department of Humanities and Social Sciences, also former director of the InSHS, now professor of medieval history at the University of Tours and president of the IEHCA (Institut Européen d'Histoire et des Cultures de l'Alimentation: European Institute for the History and Cultures of Food). The subject of his conference concerned the evolution of alimentary habits and of the imagery and symbolism concerning food at the passage between Middle Ages and Renaissance. The unevenness of early modern value judgments in this regard mirrors the contradictory contemporary attitudes towards "foreign", "exotic", "ethnic", "fusion cuisine", and so on, providing an interesting counterpart for society at large to become aware of how our stances on such a fundamental element as food are shaped by cultural forces.







Pr CHIARA LASTRAIOLI Laboratory Host Scientist See page 89.

#### AROUND THE PROJECT

#### **Oral communications**

1 Camboni, M. C. La sensibilità formale di Guinizelli e Cavalcanti all'interno del panorama duecentesco, Journée d'études « Les deux Guidi (Guinizzelli et Cavalcanti) : quelques prolongements, Paris (France), February 6,

Variazioni ritmico-sintattiche e modalità di fruizione dei testi nel Medioevo, International conference « Misure del testo. Metodi, problemi e frontiere della metrica italiana », Lausanne (Switzerland), April 24, 2017. Camboni, M. C. Renaissance views of the Medieval vernacular tradition. The lyrical past in Lorenzo the Magnificent's Florence, Le Studium Thursday series, Tours (France), May

3 Camboni, M. C. The same trajectory of history for different stories: shifting views of the medieval vernacular poetic tradition during the Renaissance, International conference "The dynamics of the relationship with the more recent past in early modern Europe: between rejection and acknowledgement" - Le Studium Conference, Tours (France), June 21,

4 Camboni, M. C. Expérimentations graphiques dans la tradition de la lyrique vernaculaire italienne du Moyen Âge, International conference « « Belles lettres » : le figures de l'écrit au Moyen Âge », Fribourg (Switzerland), October 4, 2017.

1 Camboni, M. C. La formazione della Raccolta Aragonese, Interpres XXXV, 2017,

2 Camboni, M. C. La sensibilità formale di Guinizelli e Cavalcanti all'interno del panorama duecentesco, Chroniques italiennes web, 2017,

#### Books/book chapters

1 Camboni, M. C., Fine musica. Percezione e concezione delle forme della poesia, dai Siciliani a Petrarca, Firenze, Edizioni del Galluzzo per la Fondazione Ezio Franceschini,

2 Camboni, M. C. La novella di Lisabetta da Messina (Decameron IV 5), in Esercizi di lettura per Marco Santagata, a cura di A. Andreoni, C. Giunta, M. Tavoni, Bologna, Il Mulino, 2017, pp.





#### **Dr ANDREA GRIGNOLIO**

From: University of Rome La Sapienza - Italy

In residence at: CESR & VALLOREM, Tours

Nationality: Italian

Dates: November 2015 - February 2017

Andrea Grignolio, PhD in history of science, focuses his research on the history of biomedical disciplines in twentieth-century western society, with special regard to immunology and molecular biology. In 2004 he studied at the Centre Cavaillès of École Normale Supérieure in Paris, in 2006-2007 was a Post-doctoral Fellowship at the Center for Philosophy and History of Science, Boston University, and in 2009 was a visiting scholar at the Office for History of Science and Technology, UC Berkeley. He teaches History of Medicine at University of Rome «La Sapienza», is on the Editorial Board of the Series «Interfacing Science, Literature and Humanities» Vandenhoeck & Ruprecht (V&R) Unipress, Goettingen (Germany) and of the international journal "Medicina nei Secoli, Rivista di Storia della Medicina", University of Rome, "La Sapienza". He is the author of papers in international journals, of the 2016 book Chi ha paura dei vaccini? (Who is afraid of the vaccines?) and editor of the volume Immunology Today. Three Historical Perspectives under Three Theoretical Horizons (Bononia University Press, Bologna,

#### THE ACCEPTABILITY OF BIOMEDICAL INNOVATION: **HISTORICAL APPROACH**

This research looks at the historical origins of one of the first French producers of biopharmaceuticals (vaccines), Edmond Chaumier (1853-1931) who founded in 1887 the Institut Vaccinal of Tours. The laboratory locally produced from heifer calves a vaccine against smallpox through an original technique known as "vaccin de conserve" consisting of glycerined vaccine stored in refrigerators, which turned out to be safer and storable in contrast to the "vaccin frais" then available in France. Produced during 1910-1920's in collaboration with the "Istituto Vaccinogeno" (CNR) directed by Danete di Blasi at the University of Rome, Chaumier's vaccin de conserve spread throughout Europe, including France, United Kingdom, Italy, and in many African colonies.

A primary research goal is the analysis and acceptability of the original economic costs and social acceptability of biomedical innovations. This research offers a historical perspective of the social perception of risk applied to biomedical innovation. Scientific literature confirms that education and income correlate to longevity, suggesting a positive effect on health outcomes. In particular, more educated individuals have a better understanding of, and more rapidly absorb, information about medicine and health care. Less is known about the underlying mechanism through which these associations may occur. The controversy raised by vaccination against measles, mumps, and rubella (MPR) provides a useful case study for understanding individual behavioral responses to new information about risks or new medical technologies, suggesting that information processing, rather than simply access to education and income, is the key driver. Evidence shows that more educated and affluent parents are more selective/hesitant and more often choose not to vaccinate their child.

The second part of this research looks at why individuals making decisions under uncertainty and risk give undue weight to information indicating risk. Finally, a review of the biomedical literature to analyse the risk perception of biopharmaceuticals will be undertaken.

#### Pr VÉRONIQUE DES GARETS

#### Laboratory Host Scientist

Véronique Des Garets, a former student of the Ecole Normale Supérieure de Cachan, was awarded her PhD in Management Science in 1991. She was Associate Professor of Management Science in 1995. Professor Des Garets is at the Institute of Enterprise Administration, University of Tours. She is the deputy director of the Loire Valley Management Science laboratory - VALLOREM at the University of Tours and University of Orléans. Professor Des Garets teaches business studies through business management simulations and marketing.

#### **Dr CONCETTA PENNUTO**

#### Laboratory Host Scientist

Concetta Pennuto did her PhD studies at the University of Geneva and is a historian of science and medicine. She is Assistant Professor at the Centre d'Études Supérieures de la Renaissance, University of Tours and teaches at this Centre and the Faculty of Medicine. Dr Pennuto does research on the history of disease and the therapeutic relationship between doctors and patients in Early Modern and Modern-Contemporary Medicine. Her research focuses on women's health, childbirth and fertility, history of infectious and contagious diseases, such as syphilis, plague and fevers. She also studies medical gymnastics, music therapy and the links between astronomy and medicine.







#### **Dr SOPHIE HEYWOOD**

LE STUDIUM / Marie Skłodowska-Curie

From: University of Reading - United

Kingdom

In residence at: InTRu, Tours

Nationality: British

Dates: September 2016 - December 2017

Sophie Heywood is Associate Professor in French Studies at the University of Reading.

Her research specialism is in the history of childhood, particularly children's literature, culture and publishing in France from a transnational perspective, and she has over four years' experience working on international intersectorial collaboration and policy in the field of literary archives.

She has published widely, in both French and English, on the subject of children's history and literature.

Her monograph on the classic French children's author the comtesse de Ségur was published with Manchester University Press, and obtained a Faculty Prize for the best output of an early career scholar (2012).

Her research has been funded by the Carnegie Trust for the Universities of Scotland, the Institute of Historical Research, the Leverhulme Trust. and, most recently, the LE STUDIUM/ Marie Skłodowska-Curie Research Fellowship.



#### THE CHILDREN'S '68

The global upheaval caused by the protest movements around 1968 revolutionised social structures, overturned cultural conventions, challenged political ideologies, and catalysed civil rights activism by women, gay people and ethnic minorities. Childhood historians stress the importance of this period in altering the authority structures that shaped children's lives. However, many of the fields driving these changes - children's media, childhood studies, children's heritage and art education – remain pushed to the margins within historical master narratives of 1968. These disciplines have had little chance to reflect on their own development, to draw the connections stemming from their shared heritage in 1968, or to trace the historical legacies that have shaped the assumptions underpinning them.

The overarching aim of this project is to analyse 1968 as a watershed moment in children's culture and its related disciplines, following Marwick's (1998) now canonical definition of 1968 as the crystallisation of the cultural revolution of the 'long sixties' (c.1958-c.1974). We are pursuing this objective through a new research collaboration with specialists from cognate fields in childhood studies, children's history and media, and practitioners involved in children's culture, heritage and art education, and historians of 1968.

By thinking about children's culture as a site for artistic and intellectual experimentation, at the centre of ideological activity across disciplinary boundaries and national borders, this project aims to open up new ways of understanding the 1968 liberation movements and their legacies. With the fiftieth anniversary of 1968 approaching, it is important that the children's perspective is finally brought to the fore of scholarly debate and public commemorations.

The scientific communications and outputs therefore have a strong public engagement element. The first major scientific event was an exhibition on the theme of non-sexist and multi-racial children's books from the '70s and today - bringing together examples of militant feminist and multiracial publishers from the 70s from the United States and France, and contemporary items from the library's collection.

This was a collaboration between Kim Dhillon and Andrea Francke of 'Invisible Spaces of Parenthood', the Children's section of the municipal library in Tours and the research project 'The Children's '68/ Le '68 des enfants', and it was held at the municipal library in Tours, September-October 2017.

#### Dr CÉCILE BOULAIRE

#### Laboratory Host Scientist



Dr Cécile Boulaire is Associate Professor in children's literature at the University of Tours, and in 2015 she obtained her professorial thesis [Habilitation à diriger des recherches]. Her research focuses primarily on two areas: first, the history of publishing for the young; and second, on the aesthetics of children's picturebooks. In 2008 she was awarded a large collaborative grant from the French National Research Agency to investigate the history of the Mame publishing house, the largest publisher for children in France in the 19th century. Her most recent monograph (2016) studies the publisher's series 'Un Petit livre d'or', the French translations of the iconic American picturebooks series 'Little Golden Books', and reveals the close links between children's publishing, ideology and politics in the context of the Cold War. To date she has published 50 articles and 7 books or special issues of academic journals.

#### 1968 AND THE BOUNDARIES OF CHILDHOOD

Our conference focused on experimental ideas of children and culture for children, children's rights, participation and access to culture in the '68 years. The aim was to generate dialogue between specialists from cognate fields within childhood studies (including children's history and media, children's culture, heritage and art education), historians of '68, and contemporary practitioners involved in working with children and culture (publishers, artists, children's librarians etc). It was held at the Bibliothèque Municipale de Tours, and included the project's exhibition of non-sexist and multiracial children's books from the 1970s from France and the US (for details on this exhibition. refer to section 2)

As Isabelle Nières-Chevrel, a round table participant, and leading authority on French children's literature put it, investigating the impact of the '68 years on children's culture has long been 'an intellectual necessity', and the conference underscored that such a project also had to be international and comparative in scope. The international and cross-disciplinary approach proved stimulating, and modified our initial ideas in the following key ways:

- 1. Provided us with greater understanding of how radical avant-gardes in children's culture flourished in different ways, and only partially converged in terms of timing and ideas.
- 2. We identified that there were nevertheless important connections between these movements, and scope for comparing very different national traditions in ways that could advance understanding in these fields.
- 3. By juxtaposing different historical narratives of developments in children's culture, we could identify patterns, notably the important role of cultural exchange between East and West Europe, and the Trans-Atlantic axis.
- 4. It opened up our vision of the period considerably to include new texts, new ideas, new media, new countries and topics for consideration.

Finally, a selection of the papers is due to be published as part of the special issue of the scientific journal Strenae in May 2018.

#### LE '68 DES ENFANTS: LIVRES POUR ENFANTS ET CONTRE-CULTURE

Public lecture delivered by Cécile Boulaire and Sophie Heywood.

This talk introduced the audience to a range of books produced in the '68 years, with the aim of showing how ideas of what is appropriate for children can change dramatically over time and space.









#### Dr EWA ANNA ŁUKASZYK

LE STUDIUM / Marie Skłodowska-Curie Research Fellow

From: University of Warsaw - Poland

In residence at: CESR, Tours

Nationality: Polish

Dates: September 2017 - August 2018

Ewa Łukaszyk, PhD habil.; professor at the interdisciplinary Faculty "Artes Liberales", University of Warsaw. Specialised in comparative literary and cultural studies, with competences in Romance and Orientalist area. In her extensive track of publications (approx. 200 items, including 6 authored books), the major group has been dedicated to Portuguese and Lusophone topics. She has realized various research projects financed by Polish institutions (Foundation for Polish Science, National Science Center), as well as the Calouste Gulbenkian Foundation and Instituto Camoes in Portugal. Since 2012, she has been working on the innovative, comprehensive approach to the transcultural dimension of the human symbolic activity, realising several interconnected projects (the research on Adamic language being one of them) and building up a theoretical language especially destined to the analysis of transcultural problems

#### AROUND THE PROJECT

#### Oral communications

- 1 Łukaszyk, E. Congregatio mundi today. Neohumanist perspectives of Guillaume Postel (1510-1581), European Humanism and its Challenges, Ljubljana (Slovenia), September 8-9, 2017.
- 2 Łukaszyk, E. Defining the symbolic space. From a cluster of transcultural case studies to a topological conceptualization, LE STUDIUM Thursday series, Tours (France), November 2, 2017.

# THE SEARCH FOR THE ADAMIC LANGUAGE AND THE EMERGENCE OF TRANSCULTURAL ASPIRATION IN THE AFTERMATH OF THE EUROPEAN MARITIME DISCOVERIES

The main hypothesis of the project is connected to the notion of precultural origins of the humanity, situated in the paradisaical reality, not only before the fall, but also before the invention of the human language (Adam naming the animals created by God). The myth of the pre-lapsarian unity of the human kind became crucial to the development of the European relationship with other peoples in the aftermath of the maritime discoveries in the 16th century. The examination of this topic is an important element of the projected transcultural humanities, searching to establish a comprehensive outlook of the cultural inscription and limitations of the human thought.

In first place, it reviews the figure of the French heterodox thinker Guillaume Postel (specifically the stakes and implications of his Oriental project) in order to develop and prepare publications (thematic issue of the journal "Primerjalna Knizevnost" dedicated to the heritage of Renaissance humanism).

Secondly it studies the definition of transcultural condition that is the theoretical pivot of this research. This original approach doesn't entirely coincide with the meaning of "transculture" or "transculturalism" in such authors as Welsch, Epstein, Dagnino, etc. It is also connected with the innovative conceptualization of the symbolic space. A short monograph in Polish under the title Humanistyka, która nadchodzi. W poszukiwaniu kondycji transkulturowej ("The coming humanities. In search of the transcultural condition") explaining the idiosyncratic aspects of this theoretical approach was prepared. It connects to the heritage of postmodern humanities and the works of such authors as Giorgio Agamben. This book has just been peer reviewed and is currently prepared for publication in the editorial DiG in Warsaw.

The general lines and the target of this theoretical innovation was presented at LE STUDIUM Thursday seminar and situated the research on Adamic language in relation to the larger project: "Defining the symbolic space: From a cluster of transcultural case studies to a topological conceptualization". The host laboratory CESR also benefited from informal talk: "Pour une Renaissance transculturelle?», explaining what the transcultural studies are and what importance this inspiration might be for the research on the Renaissance.

#### Pr MARIE-LUCE DEMONET

Laboratory Host Scientist



Pr Marie-Luce Demonet, specialised in the relationships between literatures, languages and theories of the sign in the Renaissance (Les Voix du signe, 1992). Member of the Institut Universitaire de France (2005-2015) distinguished with Légion d'Honneur. She has published several studies on Montaigne and edited a digital edition of the Essais and the manuscripts of Montaigne (projet ANR « MONLOE », « Montaigne à l'œuvre »), as well as approx. 30 articles on Rabelais. She is also responsible for several other digital editions, including all the writings of Rabelais and their sources (projects Rablissime et ReNom). Responsible 2011-2015 of the consortium CAHIER (« Corpus d'Auteurs pour les Humanités. Informatisation, Edition, Recherche ») and other projects related to digital humanities.



# Dr JENS-CHRISTIAN MOESGAARD

LE STUDIUM / Marie Skłodowska-Curie Research Fellow

**From**: National Museum of Denmark - Denmark

In residence at: IRAMAT, Orléans

Nationality: Danish

Dates: September 2017 - September 2018

Jens Christian Moesgaard is a historian specialised in medieval numismatics. Graduated from the University of Copenhagen in 1992, he worked at museums in France (Evreux, Rouen) and England (Cambridge) until 1997 when he joined the National Museum of Denmark as Assistant Keeper of the Royal Collection of Coins and Medals. His research field is coin production and coin circulation in France and Scandinavia in the Middle Ages. He aims at using coins as evidence for political, institutional and economic history. He has in particular worked on Viking coinages and the archaeological context of coin finds. He was visiting professor at l'Ecole Pratique des Hautes Etudes in 2015 and has been awarded with the Holger Hede medal (Danish Numismatic Society), the jeton de vermeil of the French Numismatic Society and a free-of-charge membership of the Swedish Numismatic Society.

#### AROUND THE PROJECT

#### Poster

Moesgaard, J. C. Decision, management, control. Coinage as catalyst for societal change, 18th Viking Congress, Copenhagen-Ribe (Denmark), August 6-12, 2017



# COINS, DIES, SILVER: FOR A NEW APPROACH TO THE MAKING OF THE FEUDAL PERIOD

The project aims at using new evidence and methods to shed light on the transition from the centralised 9th-century Carolingian state of Charlemagne's heirs to the decentralised feudal principalities of the 10th-12th centuries.

At a first glance, 10th-century coinage indeed seems disorganised. Some coins carry the king's name, others do not. The discovery of a few hoards has provided numerous specimens of some coin types, whereas other coin types are only known by a few specimens. One easily gets the impression of an erratic variation in minting over time and from place to place, consistent with the idea of an unstable political situation. But what if the scarcity of some coin types was just a result of a low survival rate? Normandy has been chosen as case study. Indeed, the coinage struck in the name of the Duke shows a great variety of coin types that can be dated guite closely. A rapid look at the coin finds reveals that non-Norman coins as well as older local Norman coins were to a large extent excluded from circulation. This rather reflects a well-organised managed currency. The Duke probably had revenues in the form of fees from the compulsory exchange of foreign and old coins, as documented for later periods. It is thus important to know how large the mint output was. No mint accounts survive, but as the existing specimens carry minor variations in the motive and the inscriptions, they must have been struck by many different dies and consequently in large numbers. Therefore a die study is a main component of the project. The silver content of the coins is a key factor of the monetary policy of the coin issuer.

During the first four month of the Fellowship, a firm base has been established in the form of the basic catalogue of the relevant coins. Unsurprisingly, the number of recorded specimens has dwindled, as it turned out that many were duplicates (same coin quoted in different publications). Several hitherto unprovenanced specimens have regained their find spot, making them more valuable evidence. The first attempts of die studies confirm that the coinage was much larger than expected from the scarcity of surviving specimens. The first series of analyses of the metal composition of the coins shows a firm control of the silver content. Unexpectedly, it seems that there have been two distinct silver standards at the same time.

#### Dr MARC BOMPAIRE

Laboratory Host Scientist



Marc Bompaire studied at École des Chartes and is Doctor in History. He is specialised in medieval monetary history. He was Assitant Keeper at the Cabinet des Médailles of the Bibliothèque nationale in Paris before joining the CNRS in 1989, first as researcher and since 2003 as director of research at IRAMAT-CEB in Orléans. He directed the ANR-project « La filière de l'argent au haut Moyen Âge » that lead to the publication in 2017 with G. Sarah of Mine métal monnaie Melle. Les voies de la quantification monétaire au haut Moyen Âge. Since 2004, he holds a chair of Numismatics and monetary economy in the Medieval West at Ecole Pratique des Hautes Etudes. He is or has been director of 7 doctoral theses. He has been member of Comité national de la Recherche scientifique and president of Société française de numismatique. He is director of Revue numismatique and member of the board of 5 other French and foreign journals.

In residence at: LEO. Orléans

Nationality: Romanian

Dates: November 2016 - November 2017

Mihai Mutascu was professor of economics at West University of Timisoara (Romania), FEBA, and associate researcher at the Laboratory of Economics of Orléans (LÉO), University of Orleans. He has PhD diploma in Economic Sciences - Finance (West University of Timisoara), Habilitation in Finance (Bucharest University of Economic Studies) and Habilitation in Economic Sciences (University of Orléans). Pr Mutascu was visiting researcher at GREThA (University of Bordeaux) and invited researcher at Oxford Brooks University, University Complutense de Madrid. Poznan University of Economics, and University of Auvergne. He received several prizes for research activity, such as: Prize 'Dumitru Mares' (2016) and Awards for Research Results (2013, 2014, 2015, 2016). His main research topics include macroeconomics and applied economics



#### A WAVELET ANALYSIS OF GLOBALISATION AND **GROWTH IN EURO ZONE**

The main objective of the project is to start and develop a research in the field of economics, concerning the relationship between globalisation and economic growth, in the case of euro area. Actually, the aim is to investigate how the globalisation explains the economic growth and vice-versa, by using the wavelet tool, for each euro zone country. Further on, a parallel analysis of country wavelet spectra will be done in order to illustrate if there are or not some 'common' features with respect to the behaviour of 'globalization-growth' countries at euro zone level. In order to perform the preliminary wavelet estimations regarding the nexus 'globalisation-growth' in euro zone, the first research steps are focused on three main coordinates, chronologically ordered: the dataset construction, the preliminary estimations and the literature collection. As first step, a dataset with two time series has been performed, based on collected data: the trade, in term of imports and exports (as proxy for globalisation) and the Gross Domestic Product - GDP (as variable which captures the economic growth). The sample includes following euro zone countries: Austria, Belgium, Finland, France, Germany, Greece, Ireland, Italy, Netherlands, Portugal and Spain (not available data for Estonia, Cyprus, Latvia, Lithuania, Luxembourg, Malta, Slovakia and Slovenia). The dataset has quarterly frequency and covers the period 1960Q1-2016Q2. The source of data is the Organisation for Economic Co-operation and Development (OECD) online database - 2016. The brut series, expressed in billions of US dollars, have been adjusted for any seasonal component by using Census X12 methodology. The final work series will be in natural logarithm form.

We also dealt with stationarity property of the series, the Augmented Dickey-Fuller (ADF), Phillips-Perron (PP), Kwiatkowski-Phillips-Schmidt-Shin (KPSS) and Zivot-Andrew with structural breaks tests having performed. Second, preliminary estimations have been generated by using the wavelet tool. It was tested different combinations of variables to capture the globalisation: only exports, imports plus exports, and imports plus export as percentage of GDP. In those cases, the wavelet spectra and wavelet coherency reveal robust findings, excepting the case when the estimations are employed with different variable's order of integration. All these aspects can be a strong ground for the further research project steps. Finally, an extended collection of papers in the field was also employed by considering quasi all contributions which treats the impact of globalisation on economic growth. The collection includes both theoretical and empirical papers, with different targeted areas, different periods of time and various used tools.

#### Pr CAMELIA TURCU

#### Laboratory Host Scientist



Camelia Turcu is Professor in Economics at the University of Orléans (France) and a research affiliate at the Laboratoire d'Économie d'Orléans (LÉO). Her major research areas are international macroeconomics, growth and trade, with a specific focus on the European case. She has published numerous articles in national and international journals, several book chapters and a book. Currently Camelia is the President of INFER (International Network For Economic Research). She is also involved in the management (Conseil d'Administation) of the French Regional Science Association (ASRDLF). She received the TIMTED Young Researcher Prize and the European Commission Thesis' Excellence Certificate. She regularly acts as expert for the European Commission and for different universities and research networks around Europe.

#### **GLOBALISATION AND GROWTH IN EUROZONE: NEW** CHALLENGES.

The main objective of the conference was to integrate ideas and opinions of the economist and researchers all over the world in the field of globalization and economic growth with focus on Eurozone. The event provided a true environment of scientific debate.

Secondary objectives where related to the promotion of European financing funds, the integration of young researchers through a special poster session, and the multicultural exchanges, the participant coming from different continents and countries.

The outcomes are as follow:

- 8 quest speakers with specialized presentations;
- 10 regular papers presentations;
- 4 poster papers presentations;
- 1 public lecture;
- 1 EU financing promotion presentation (H2020 funding opportunities);
- more than 50 participants.

The speakers attending the meeting delivered homogenous presentation regarding the globalization and economic growth in Eurozone and not only, with different narrow topics. There were interventions from labour-market structures and policies, diverging monetary union, democracy and development to technology shocks and open borders.

#### L'EURO: UNE QUESTION POLITIQUE?

Pierre-Guillaume Méon is professor at Université libre de Bruxelles.

The speaker's topic was directly connected with the society at large as he addressed to a profane audience on actual very important aspects of socioeconomic life. The central idea of the lecture was the introduction of Euro. The currency played a crucial implication for the EU citizens and wrote a new page of European history. Several rhetoric questions were raised: how the Euro was received by people, who gained, how is managed a monetary union with 19 countries and more than 340 million inhabitants.



#### AROUND THE PROJECT

#### Oral communications

1 Mutascu, M. A time-frequency analysis of globalization and environmental degradation in France. International Conference

"Current Economic Trends in Emerging and Developing Countries" - Special Session Le Studium and LEO, Timisoara (Romania), May, 19-20, 2017.

- 2 Mutascu, M. Trade, oil price and exchange rates in China: a wavelet analysis, INFER annual conference, Bordeaux (France), June
- 3 Mutascu, M. French cosmetic industry in the globalization area: an analysis of exports and financial performances, INFER annual conference - Special Session Le Studium. Bordeaux (France), June 7-9, 2017.

Mutascu, M. New evidences regarding the tax-spending nexus in Romania through wavelet analysis, Post-Communist Economies, 2017, 29, 431-447,







#### Pr ROSALIND BROWN-GRANT

CONSORTIUM COORDINATOR

CONSORTIUM

SMART LOIRE VALLEY

Rosalind Brown-Grant is Professor of Late Medieval French Literature at the University of Leeds, UK. She is the author of Christine de Pizan and the Moral Defence of Women: Reading beyond Gender (Cambridge University Press, 1999) and French Romance of the Later Middle Ages: Gender, Morality, and Desire (Oxford University Press, 2008); and the translator of Christine de Pizan's Book of the City of Ladies (Penguin Classics, 1999). She is also co-editor, (with Anne D. Hedeman and Bernard Ribémont), of Textual and Visual Representations of Power and Justice in Medieval France: Manuscripts and Early Printed Books (Ashgate, 2015); and (with Rebecca Dixon), of Text/Image Relations in Late Medieval French and Burgundian Culture (Fourteenth- Sixteenth Centuries) (Brepols, 2015). Her research has been funded by awards from the Arts and Humanities Research Council, the Leverhulme Trust, the British Academy, and the Netherlands Institute for Advanced Studies; she was a LE STUDIUM Research Fellow in Orléans in 2011-12.

#### THE POWER AND THE PARATEXT IN THE MEDIEVAL MANUSCRIPT CULTURE

The chief aim of the Power and the Paratext in Medieval Manuscript Culture research consortium is to examine how paratext functions in multiple strands of the medieval sciences, taking the notion of a science in its broadest sense as a system of thought that organises, constitutes and disseminates a body of knowledge. Since the concept of the paratext was first formulated by Gérard Genette, who applied it to print Culture from the early modern period to the present day, this topic has regularly attracted attention from scholars working on printed texts from different historical periods and on specific paratextual elements. The approach of our consortium not only pushes the chronological and methodological boundaries of Genette's original study of paratext but also differs from more recent projects on the subject in two significant ways: first, it focuses exclusively on works from the Middle Ages; second, it examines how the paratextual apparatus of the medieval manuscript both inscribes and gives visual form to the power relations between the producers and consumers of knowledge in this important period of intellectual history.

The first June 2014 meeting focused on key critical readings in the field and determined a series of workshops which we each led in turn in order to establish how paratext relates to our particular research interests in fictional, historical, medical, legal, or liturgical texts, focusing on specific paratextual elements, such as prologues, glosses, rubrics, notes, and images.

The second June 2015 enabled to refine the methodology still further. Adopting both a synchronic and a diachronic perspective helped to define what paratextual features are common to manuscripts belonging to different branches of the medieval sciences and what are unique to any particular discipline, and to analyse how these visual expressions of power in organising and compiling thought on the written page are consciously applied, negotiated or resisted by the authors, scribes, artists, patrons and readers who produced, propagated and responded to these works. In June 2016 a major international and interdisciplinary conference was organised, entitled "Inscribing Knowledge on the Page: Sciences, Tradition, Transmission and Subversion in the Medieval Book", open to an even more diverse group of medieval scholars whose work is in intellectual disciplines such as law, Latin and vernacular texts both secular and religious, liturgy, music, medicine and philosophy.

The final meeting in June 2017 was dedicated to preparation of the conference proceedings, thus the consortium team completed the peer-review and initial copy-editing process of all the chapters, the bibliography and in the index, and began drafting an introduction to the volume to be submitted to the publisher in March 2018, with a view to publication later in 2018 or early 2019 at the latest.

#### PARTNERS



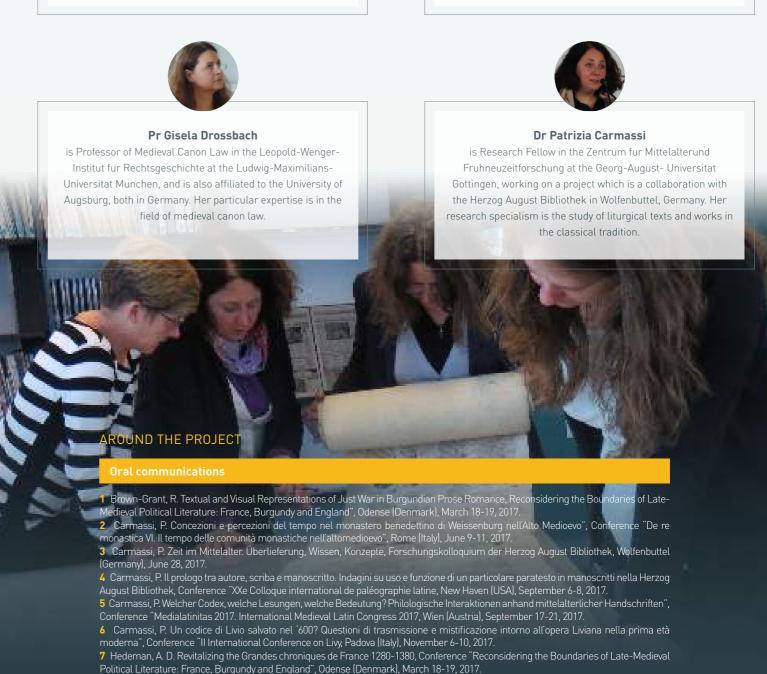
#### Pr Iolanda Ventura

Was and Associate Professor in History of Sciences and Technologies, as well as Chair of Excellence in the History of Scientific Knowledge in the Middle Ages at the Université d'Orléans/CNRS, France till November 2017 when she took up a new position at the University of Bologna (December 2017) Her particular expertise is in the study of medical and scientific manuscripts.



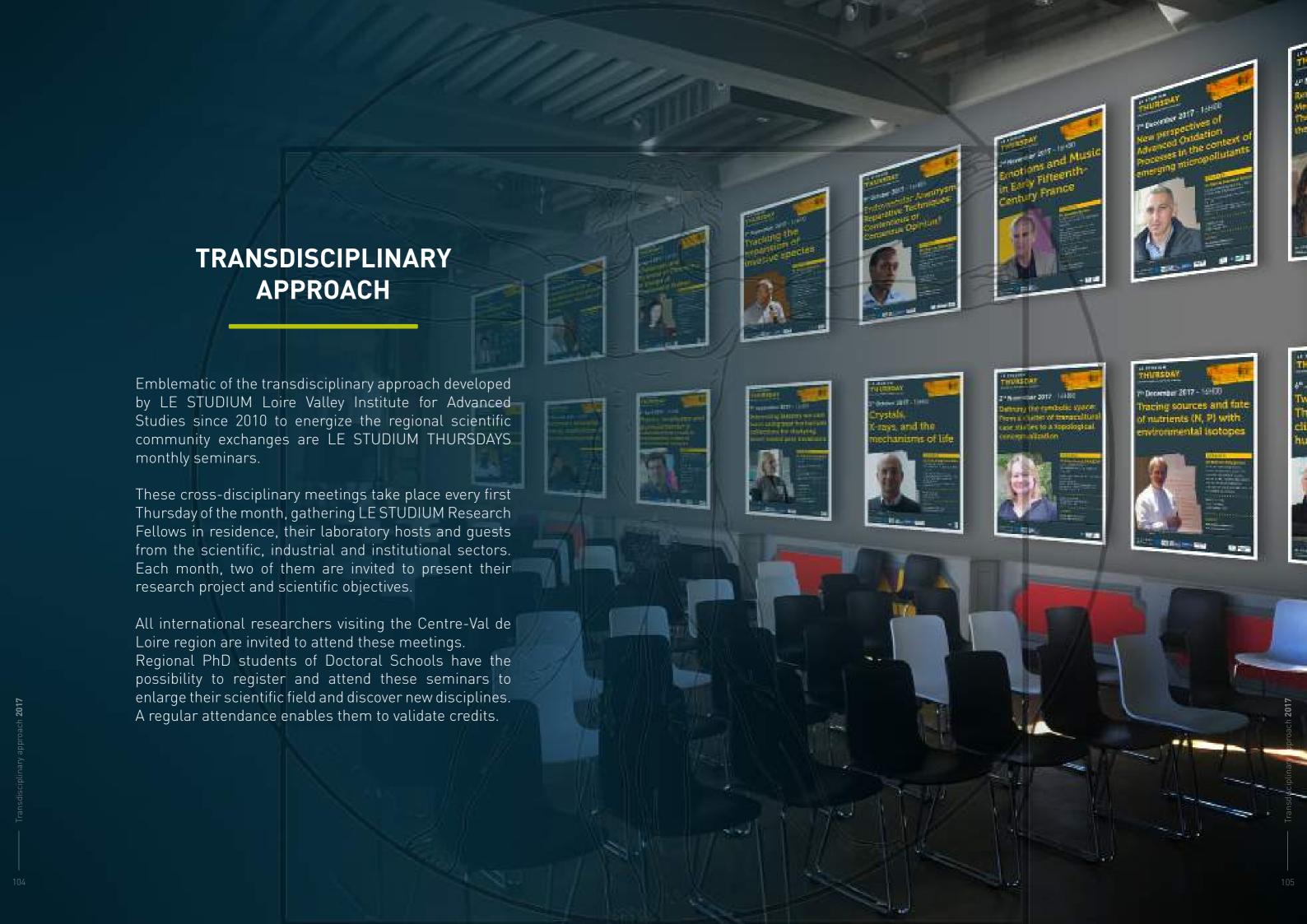
#### Pr Anne D. Hedeman

is Judith Harris Murphy Distinguished Professor of Art History in the Kress Foundation Department of Art History at the University of Kansas, USA. Her research specialism is the study of political and historical texts of the later Middle Ages.



#### Scientific Publications

- 1 Carmassi, P. Through the Hands of Librarians and Booksellers: Examples of Recent Changes in Medieval Manuscripts of German Collections, The Papers of the Bibliographical Society of America, 2017, 111, 167-184.
- 2 Carmassi, P. Übergänge Ornamente und Diagramme zwischen Text, Buchstabe und Bild in Handschriften des Frühmittelalters, *Das Mittelalter*, 2017, 22; 408-430.



# LIFE OF INTERNATIONAL RESEARCHERS IN THE REGION CENTRE-VAL DE LOIRE

In all regional cities (Blois, Bourges, Chartres, Orléans and Tours) LE STUDIUM Research Fellows benefit from exceptional living and working conditions. Well established research institutions and laboratories offer their office and equipment facilities and LE STUDIUM offers fully furnished residences and high-quality integration support and assistance. During their residency time in the region, each of them has the opportunity to attend many international events and to organize at least a major one.

In Orléans where LE STUDIUM headquarters are located, Research Fellows are regularly welcomed in the heart of the city in the prestigious Hôtel Dupanloup, the International University Centre for Research. This 16th century former bishop's residence has been brightly renovated using patrimony's architects and designers' talents and offers a prestigious modern and ancient decor to all scientific events. Walking distance from the Hôtel Dupanloup in Orléans, LE STUDIUM houses Research Fellows in a newly renovated castle of the 18th century, Le Chateau de la Motte Sanguin. This impressive building offers seven apartments with a view over the Loire river, a terrace and a garden in which to relax. In the dynamic city of Tours, LE STUDIUM maintains a few private residencies in the city centre. Tours is a university town with a highly developed touristic and cultural offer.

Every year social and networking events are organised giving international LE STUDIUM Fellows a chance to discover more of the regional scientific and cultural environment and deepen their interdisciplinary exchanges.



# **SCIENTIFIC COUNCIL**

LE STUDIUM Scientific Council establishes the final ranking of applications and recommends fellowship, professorship and consortium awards. It is composed of independent external senior scientists who gather once a year in June to analyse the scientific reviews provided by a pool of more than 600 experts and to finalize the selection of the Smart Loire Valley General Programme for Research Fellows who will next come in residence and other awards such as Professorship or Consortium. The Scientific Council members are also regularly consulted for their expertise to perform independent evaluations in the course of required recruitments occurring across the Ambition Research Development 2020 programmes.

For the campaign and call for applications 2017-2018, LE STUDIUM Scientific Council members were:

#### **PRESIDENT**

#### Dominique LANGEVIN

Research Director in physical chemistry, Centre National de Recherche Scientifique, Laboratory of Solid State Physics at the University of Paris-Sud - FR

#### **MEMBERS**

#### **Dominique ALLART**

Professor, Director of Service d'Histoire et Technologie des Arts plastiques (Temps modernes). Université de Liège - BF

#### Jean-Claude BERNIER

Professor, Chemistry and Interfaces in Physics and Biology, Strasbourg - FR

#### Gordon CAMPBELL

Professor in Renaissance and seventeenth century studies, University of Leicester - UK

#### Marie-Françoise COUREL

Geographer, Director of Research, Ecole Pratique des Hautes Etudes, Paris - FR

#### James A DIAS

Professor, Biomedical Sciences, University of the State of New York - USA

#### Jean ETOURNEAU

Professor, Solid State Chemistry/Materials Science. ICMCB-CNRS, University of Bordeaux - FR

#### Mark GOERBIG

Professor Theoretical Physiscs, CNRS Research Director, Laboratoire de Physique des Solides, Université Paris-Sud, Saclay - FR

#### Aylin Carla HANYALOGLU

Doctor in Molecular Biology, Imperial College London. Faculty of Medicine - UK

#### **Laurent FRANCIS**

Professor of Information and Communication Technology, Electronics and Applied Mathematics, University of Louvain - BF

#### Pierre KHURI-YAKUB

Professor, Electrical Engineering, Stanford University, CA - USA

#### Piotr LAIDLER

Professor, Head Chair of Medical Biochemistry, Jagiellonian University Medical College, Krakow - PL

#### Federica MIGLIARDO

Professor in Biophysicist, Universita'degli Studi di Messina, Italy / Institut de Biologie Intégrative de la Cellule, CNRS, Saclay - FR

#### Michael MORIARTY

Professor Early modern period of French literature, Cambridge - UK

#### John O'BRIEN

Professor, Director of Studies in the School of Modern Languages and Cultures, Durham University - UK

#### David OGDEN

Director of Research, Laboratory of Brain Physiology and Biophysics, University Paris-

#### Alain PAVE

Professor, Biometrics and Evolutionary Biology, Lyon. Member of the Academy of Technologies

#### Alain PRIOU

Professor, Physics, Université Paris Ouest Nanterre La Défense - FR

#### Yveline PONCET

Geographer, Sustainability and Territories - FR

#### Olivier RUSSO

Doctor in Pharmacology and in organic and medical Chemistry, Director Analytical Development, Servier - FR

#### Michel VAN DER REST

Professor, Biochemistry and Biophysics, Lyon - FR

#### Maria VOZMEDIANO

Professor Theoratical Physics, Department of Condensed Matter Theory, Instituto de Ciencia de Materiales de Madrid - SP

#### Ralph WATZEL

Professor, Geology and geophysics, President of the Federal Institute for Geosciences and Natural Resources (BGR), Hannover - DE

#### Friedrich-W WELLMER

Professor, Geology and geophysics, Former President of the Federal Institute for Geosciences and Natural Resources - DE

#### PERMANENT GUESTS: REPRESENTATIVES OF UNIVERSITIES, RESEARCH ORGANIZATIONS AND REGIONAL INSTITUTIONS

#### **Christian ANDRES**

Inserm Scientific Correspondent

#### Catherine BEAUMONT President Centre Inra Val-de-Loire

Jean-Marie CASTELAIN

#### Director INSA Centre-Val de Loire, represented by Gaël GAUTIFR

**Christian GINISTY** 

IRSTEA, Nogent sur Vernisson, represented by Nathalie KORBOULEWSKY

#### Hélène PAUWELS

Research Branch, BRGM, Orléans

#### Philippe SIMONNETTI

CEA Le Ripault, Tours

#### **Emmanuel LESIGNE**

Vice-President Research, University of Tours

#### Ioan TODINCA

Vice-President Research, University of Orléans

#### Anne BESNIER

Vice-President Higher Education and Research, Region Centre-Val de Loire (2016-2019)

#### Nicolas DUBOULOZ

Director of Higher Education, Research and Technology Transfer, Region Centre-Val de Loire

#### Yves-Michel GINOT

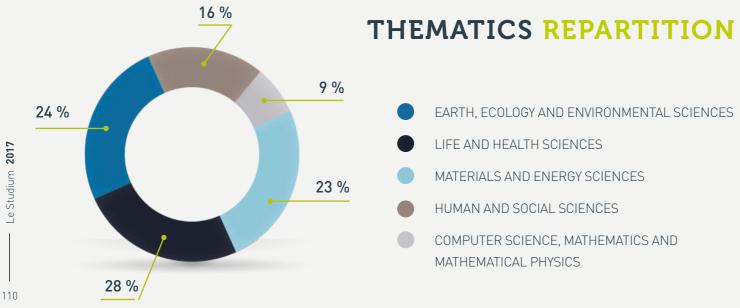
LE STUDIUM President

# **ORIGIN OF LE STUDIUM RESEARCH FELLOW**

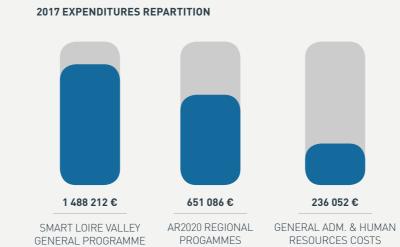
# **IN REGION CENTRE VAL DE LOIRE SINCE 1996**







# **2017 FINANCIAL DATA**



| 2017 FINANCIAL RESOURCES   | 2 797 762 € |
|----------------------------|-------------|
| REGION CENTRE VAL DE LOIRE | 63,43%      |
| EUROPEAN FUNDS             | 23,71%      |
| UNIVERSITY OF TOURS        | 3,10%       |
| ORLEANS METROPOLE          | 2,09%       |
| LOIRET COUNCIL             | 1,67%       |
| PRIVATE COUNTRIBUTIONS     | 2,49%       |
| VARIOUS                    | 0,71%       |

# **2017 EVENTS PANORAMA**

■ RENCONTRE LEONARDO
■ CONSORTIUM
■ AFFILIATED EVENTS

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Hôtel Dupanloup, Orléans

Turcu (LEO)

Hôtel Dupanloup, Orléans

Crystals, X-rays, and the mechanisms Dr Emmanuel Saridakis (CBM)

Hôtel Dupanloup, Orléans

# LIST OF RESEARCHERS IN RESIDENCE IN 2017

#### SMART LOIRE VALLEY GENERAL PROGRAMME

#### **Dr RENAUD ADAM**

Bibliopol@: The book market in the renaissance between France and the low countries

October 2017 - October 2018

In residence at : Centre d'Études Supérieures de la Renaissance (CESR) - UMR 7323 - Université de Tours. CNRS

Host scientist : Pr Chiara Lastraioli

#### Pr MADJID BIROUK

# Spray combustion: on the vaporization process of micro droplets

September 2017 – August 2018

In residence at : Institut de Combustion Aérothermique Réactivité et Environnement (ICARE) - UPR 3021 - CNRS

Host scientist : Dr Christian Chauveau

#### Pr GRAEME BOONE

#### **Emotion in Dufay**

July 2017 - July 2018

In residence at : Centre d'Études Supérieures de la Renaissance (CESR) - UMR 7323 - Université de Tours, CNRS

Host scientist : Pr Philippe Vendrix

#### Dr MARIA CLOTILDE CAMBONI

Middle Ages in Renaissance

September 2016 – August 2017

In residence at : Centre d'Études Supérieures de la Renaissance (CESR) - UMR 7323 - Université de Tours, CNRS

Host scientist : Pr Chiara Lastraioli

#### Pr YIMING CHEN

# Observer Design for Distributed-Parameter Systems and Fractional Order Systems

April 2017 - July 2017

In residence at : Pluridisciplinaire de recherche en ingénierie des systèmes, mécanique et énergétique (PRISME), Université d'Orléans, Insa Centre Val De Leire

Host scientist : Pr Driss Boutat

#### Dr KRISTINA DJANASHVILI

# Responsive Nanozeolites: Smart Porosity and Surface Tailoring for Multimodal Imaging and Therapy of Cancer

January 2017 - January 2018

In residence at : Centre de Biophysique Moléculaire

(CBM), UPR 4301, CNRS

Host scientist : Dr Eva Jakab-Toth

#### Dr EMRE ERDEM

Investigation of intrinsic and extrinsic defect centers of ZMO Nanowires for Nano-Generators

December 2017 - December 2018

In residence at : Groupe de Recherche en Matériaux, Microélectronique, Acoustique et Nanotechnologies (GREMAN) - UMR 7347 - Université de Tours, CNRS, INSA-CVL

Host scientist : Dr Guylaine Poulin-Vittrant

#### Pr GARY GIBBONS

Classical and Quantum Space-Time and Its Symmetrics

March 2017 - May 2017

In residence at : Laboratoire de Mathématiques et Physique Théorique (LMPT) - UMR 7350 - CNRS, Université de Tours

Host scientist : Pr Sergey Solodukhin

#### Pr ERIC GOLES

Discrete models of complex systems: computational complexity and (un)predictability, theory and applications

Januray 2017 - March 2017

In residence at : Laboratoire d'Informatique Fondamentale d'Orléans (LIFO) – EA 4022 – Université d'Orléans, INSA Centre Val De Loire Host scientist : Pr Nicolas Ollinger

#### Dr SOPHIE HEYWOOD

The children's '68

September 2016 – December 2017

In residence at : Interactions, Transferts, Ruptures artistiques et culturels (InTRu) - EA 6401 - Université de Tours

Host scientist : Dr Cécile Boulaire

#### Dr WILLIAM HORSNELL

Targeting acetylcholine receptors to enhance immunity to acute viral infection

July 2017 - July 2018

In residence at : Immunologie et Neurogénétique Expérimentales (INEM) - UMR 7355 - CNRS, Université d'Orléans

Host scientist : Dr Bernhard Ryffel

#### Dr NATALIA KIRICHENKO

Interesting lessons we can learn using past herbarium collections for studying forest insect pest invasions

August 2017 - August 2018

In residence at : Unité de Recherche Zoologie Forestière (URZF) - UR 0633 - Centre INRA Val de Loire

Host scientist : Dr Alain Roques

#### Dr NORINNE LACERDA QUEIROZ

Study of pulmonary damage in experimental severe Malariav: Malaria-Associated acute respiratory distress syndrome (MA-ARDS) and Malaria Sepsis Induced by secondary bacterial infection

October 2017 - October 2018

In residence at : Immunologie et Neurogénétique Expérimentales (INEM) - UMR 7355 - CNRS, Université d'Orléans

Host scientist : Dr Valérie Quesniaux

#### Pr MAREK ŁOS

Effects of electro-conductive, biomaterial-based tissue scaffolds on stem cells and transdifferentiation-derived somatic cells

October 2017 - October 2018

In residence at : Centre de Biophysique Moléculaire

(CBM) - UPR 4301 - CNRS

Host scientist : Dr Catherine Grillon

#### Dr EWA ANNA ŁUKASZYK

The search for the adamic language and the emergence of transcultural aspiration in the aftermath of the european maritime discoveries

September 2017 – August 2018

In residence at : Centre d'Études Supérieures de la Renaissance (CESR) - UMR 7323 - Université de Tours, CNRS

Host scientist : Pr Marie-Luce Demonet

#### Dr MAURO MANNO

The role of glycosylation in the functional activity and pathological consequences of serpin proteins

October 2016 - October 2017

In residence at : Institut de Chimie Organique et Analytique (ICOA) - UMR 7311 - CNRS, Université d'Orléans

Host scientist : Pr Richard Daniellou

#### **Dr JENS-CHRISTIAN MOESGAARD**

Coins, Dies, Silver: For a new approach to the making of the Feudal period

September 2017 – August 2018

Host scientist : Dr Marc Bompaire

In residence at : Institut de Recherche sur les Archéomatériaux (IRAMAT) Centre Ernest-Babelon -UMR 5060 - CNRS, Université d'Orléans

#### Pr MIHAI MUTASCU

A wavelet analysis of globalization and growth in euro zone

November 2016 – November 2017

In residence at: Laboratoire d'Economie d'Orléans (LEO) - UMR 7322 - Université d'Orléans, CNRS Host scientist: Pr Camelia Turcu

#### Pr MICHIEL POSTEMA

Sonic antibubbles in harmonic medical imaging and the rapy  $% \left( 1\right) =\left( 1\right) \left( 1\right) \left$ 

February 2017 - January 2018

In residence at : Imagerie et cerveau (IC) - U930 - INSERM, Université de Tours

Host scientist : Dr Ayache Bouakaz

#### Pr AKKIHEBBAL RAVISHANKARA

Interlinkages in the chemistries of the troposphere and stratosphere: impacts of nitrous oxide on Earth system

June 2017 - June 2018

In residence at : Institut de Combustion Aérothermique Réactivité et Environnement (ICARE) - UPR 3021 - CNRS

Host scientist : Dr Abdelwahid Mellouki

#### Dr EMMANUEL SARIDAKIS

New crystallization strategies for structure-guided pharmacological development – Large biological assemblies for RNA metabolism

January 2017 - January 2018

In residence at : Centre de Biophysique Moléculaire

(CBM), UPR 4301, CNRS

Host scientist : Dr Marc Boudvillain

#### Pr VLADIMIR SHISHOV

Global Tree-Ring Growth Evolution Neural Network (VS-GENN)

August 2017 - August 2018

In residence at : Amélioration Génétique et Physiologie Forestières (AGPF) - UMR 0588 - Centre INRA Val de Loire

Host scientist : Dr Philippe Rozenberg

#### Dr MAURO SIMONATO

Tracking the colonization patterns of an expanding forest pest and its natural enemies using molecular markers

November 2016 – October 2017

In residence at : Unité de Recherche Zoologie Forestière (URZF) - UR 0633 - Centre INRA Val de Loire

Host scientist : Dr Jérôme Rousselet

#### Dr VOLODYMYR SUKACH

Exploring the effects of trifluoromethyl group in the design of organocatalysts, enzyme inhibitors and in the conformational control of saturated nitrogencontaining heterocycles

November 2017 - November 2018

In residence at : Institut de Chimie Organique et Analytique (ICOA) - UMR 7311 - CNRS, Université d'Orléans

Host scientist : Pr Isabelle Gillaizeau

#### Dr MASSIMILIANO TRAVERSINO DI CRISTO

Will, Power and Being: uncovering the ancient and mediaeval blueprints of the sixteenth-century question of power

October 2017 - October 2018

In residence at : Centre d'Études Supérieures de la Renaissance (CESR) - UMR 7323 - Université de Tours, CNRS

Host scientist : Dr Paul-Alexis Mellet

#### Dr JÁN ŽABKA

Very high resolution mass spectrometry for space applications

July 2017 - July 2018

In residence at : Laboratoire de Physique et Chimie de l'Environnement et de l'Espace (LPC2E) - UMR 7328 - CNRS, Université d'Orléans

Host scientist : Dr Christelle Briois

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#### PROGRAMME ARD 2020 BIOPHARMACEUTICALS

#### Dr SOHAIL AKHTER

Synthesis and Biosynthesis of molecules -Development of mRNA cellular factories

June 2015 - June 2017

In residence at : Centre de Biophysique Moléculaire

(CBM), UPR 4301, CNRS

Host scientist: Pr Chantal Pichon

#### **Dr ANDREA GRIGNOLIO**

The acceptability of biomedical innovation: historical approach

November 2015 – February 2017

In residence at : Laboratoire Val de Loire Recherche en Management (VALLOREM) - EA 6296 - Université d'Orléans, Université de Tours & UMR 7323, CNRS, Centre d'études Supérieures de la Renaissance (CESR) - UMR 7323 - Université de Tours, CNRS Host scientist : Pr Véronique Des Garets

#### **Dr JORGE GUTIERREZ**

Lipids as modulators of the response to biodrugs

December 2014 - June 2017

In residence at : Nutrition, Croissance et Cancer (N2C) - UMR 1069 - Inserm, Université de

Tours

Host scientist: Pr Philippe G. Frank

## PROGRAMME ARD 2020 COSMETOSCIENCES

#### Pr SALVATORE MAGAZU

From sugars and polyols to innovative cosmetic formulations and technologies: Molecular mechanisms and nanoscopic characterization

July 2016 - July 2017

In residence at : Centre de Biophysique Moléculaire (CBM), UPR 4301, CNRS

Host scientist : Pr Francesco Piazza

#### Dr SIVAKUMAR PONNURENGAM MALLIAPPAN

Innovative nanocarrier delivery system for Active Cosmetic Ingredients (ACI) and In vitro model development of Stratum Corneum

October 2016 - October 2017

In residence at : Nanomédicaments et Nanosondes

(NMNS) - EA6295 - Université de Tours

Host scientist : Dr Emilie Munnier

# PROGRAMME ARD 2020 LAVOISIER

#### **Dr JOHNSON IRUDAYARAJ**

Engineering and Systems for Renewable Energy November 2016 – June 2017

In residence at : Groupe de Recherche en Matériaux, Microélectronique, Acoustique et Nanotechnologies (GREMAN) UMR 7347 - Université de tours, CNRS, INSA-CVL

Host scientist : Pr Marc Lethiecq

#### Dr SATYAJIT PHADKE

Energy storage systems – Storage 1

January 2016 - June 2019

In residence at : Physico-Chimie des Matériaux et des Electrolytes pour l'Energie (PCM2E) - EA 6299 -

Université de Tours

Host scientist : Pr Mérièm Anouti

# PROGRAMME ARD 2020 PIVOTS

#### **Dr Marius Secula**

Developing a new advanced treatment technique for MPs removal from water and wastewater

October 2017 - October 2018

In residence at : Interfaces, Confinement, Matériaux et Nanostructures (ICMN) 6 - UMR 7374 - CNRS,

Université d'Orléans

Host scientist : Dr Benoît Cagnon



# **SMART LOIRE VALLEY GENERAL** PROGRAMME AWARDS -**SELECTION OF CAMPAIGN 2017**

#### LE STUDIUM RESEARCH FELLOWSHIP

#### Dr Renaud ADAM

#### Bibliopol@: The Book Market in the Renaissance between France and the Low Countries

From: University of Liège, Belgium Host scientist: Pr Chiara LASTRAIOLI, CESR, CNRS, Université de Tours

#### **Pr Guoxian CHEN**

#### Numerical Simulation of Singular conservation laws and Related Applications

From: Wuhan University, China Host scientist: Pr Magali RIBOT, MAPMO, CNRS, Université d'Orléans

#### Pr Emre ERDEM

#### Investigation of intrinsic and extrinsic defect centers of ZnO nanowires for nano-generators

From: University of Freiburg, Germany Host scientist : Dr Guylaine POULIN-VITTRANT, GREMAN, CNRS, Université de Tours, INSA CVL

#### Dr Norinne LACERDA QUEIROZ

Study of pulmonary damage in experimental severe malaria: malaria-associated acute respiratory distress syndrome (MA-ARDS) and malaria sepsis induced by secondary bacterial

From: National Institute of Health, USA Host scientist: Dr Valérie QUESNIAUX. INEM. CNRS, Université d'Orléans

#### Pr Igor LIMA MALDONADO

#### Characterization of limbic system connectivity through fiber dissection and diffusion imaging techniques

From: Universidade Federal da Bahia. Brazil Host scientist: Pr Christophe DESTRIEUX, IC. Inserm, Université de Tours

#### Dr Marcelo Gustavo LORENZO

#### Genomics of learning and memory in disease vector insects

From: Fundação Oswaldo Cruz, Brazil Host scientist: Pr Claudio Ricardo LAZZARI IRBI, CNRS, Université de Tours

#### Pr Marek ŁOS

Effects of electro-conductive, biomaterialbased tissue scaffolds on stem cells and transdifferentiation-derived somatic cells From: Jagiellonian University, Poland Host scientist: Dr Catherine GRILLON, CBM, CNRS

#### Dr Ewa Anna ŁUKASZYK

The search for the Adamic language and the emergence of transcultural aspiration in the aftermath of the European maritime discoveries From: University of Warsaw, Poland

Host scientist: Pr Marie-Luce DEMONET, CESR, CNRS. Université de Tours

#### Dr Jens Christian MOESGAARD

#### Coins, dies, silver; for a new approach to the making of the feudal period

From: National Museum of Denmark Host scientist: Dr Marc BOMPAIRE, IRAMAT, CNRS, Université d'Orléans

#### Dr Volodymyr SUKACH

Exploring the effects of trifluoromethyl group in the design of organocatalysts, enzyme inhibitors and in the conformational control of saturated nitrogen-containing heterocycles

From: National Academy of Sciences of Ukraine Host scientist: Pr Isabelle GILLAIZEAU, ICOA. CNRS. Université d'Orléans

#### Dr Massimiliano TRAVERSINO DI CRISTO

Will, Power, and Being: Uncovering the Ancient and Mediaeval Blueprints of the Sixteenth-Century **Question of Power** 

From: University of London, United Kingdom Host scientist: Dr Paul-Alexis Mellet. CESR. CNRS. Université de Tours

#### Pr Temenuga TRIFONOVA

#### European Identity: Migration, Immigration and Homelessness in European Cinema

From: York University, Canada Host scientist: Pr Raphaele BERTHO, InTRu. Université de Tours

#### Dr Agnieszka SYNOWIEC

#### Biological effects of essential oils

From: University of Agriculture in Krakow, Poland Host scientist: Dr Christophe HANO, LBLGC, INRA, Université d'Orléans

#### LE STUDIUM RESEARCH PROFESSORSHIP

#### Pr Maxwell HINCKE

# Evolution of innate immunity at biomineralized

From: University of Ottawa, Canada Host scientist: Dr Sophie REHAULT-GODBERT, BOA, Centre Val de Loire, Université de Tours

#### Pr Dmitri KHARZEEV

Chiral matter: theory and applications

From: Stony Brook University, USA Host scientist: Dr Maxim CHERNODUB, IDP, CNRS, Université de Tours, Université d'Orléans

### LE STUDIUM RESEARCH CONSORTIUM

#### Dr Sébastien ROGER

Pharmacological and nutritional targeting of voltage-gated sodium channels in the treatment of epithelial cancers

Host Laboratory: NCC, Inserm, Université de Tours

#### CONTACTS

#### Sophie Gabillet

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#### Dr Aurélien Montagu

Scientific Relations Manager +33 2 38 21 14 86 aurelien.montagu@lestudium-ias.fr

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